



OPEN Acceptance of preventive therapy for latent tuberculosis infection in Chinese children and adolescents: a systematic review and meta-analysis

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Tuberculosis preventive treatment (TPT) is essential for pediatric tuberculosis control in children and adolescents. Evidence indicates most attrition occurs prior to TPT initiation rather than from post-initiation nonadherence. This study systematically evaluated TPT acceptance for latent tuberculosis infection (LTBI) among Chinese children and adolescents and identified key influencing factors through comprehensive database searches (PubMed, Web of Science, Embase, Cochrane, CNKI, Wanfang database, CBM, VIP) up to February 21, 2025. The heterogeneity was assessed using I^2 statistics (95.770%, $P < 0.001$), with random-effects models employed for meta-analysis. Subgroup, meta-regression, and sensitivity analyses were performed to identify the sources of heterogeneity. Begg and Egger tests were used to detect any potential publication bias. Among 7,165 screened records, 31 eligible studies ($n = 4,929$) met inclusion criteria. The pooled TPT acceptance rate reached 64.0% (95%CI: 56.9%–70.9%), with significantly higher TPT acceptance rates observed among: central China residents (76.5%, 95% CI: 69.8%–82.5%), close household contacts (80.2%, 95% CI: 74.9% – 85.0%), IGRA positive (80.5%, 95% CI: 74.3% – 86.0%), recipients of isoniazid-rifapentine regimens (76.5%, 95% CI: 69.5%–82.9%), and twice-weekly dosing schedules (76.5%, 95% CI: 69.5%–82.9%). This study revealed the suboptimal uptake of TPT among children and adolescents with LTBI in China. These findings highlight the need to tailor interventions to regional epidemiological profiles, accurately identify the target population for TPT with reliable tools, and scale up optimized regimens under stringent monitoring, as these are critical strategies for enhancing TPT coverage and advancing the “End TB” initiative.

Keywords Latent tuberculosis infection, Preventive therapy, Acceptance, Children, Adolescents

Latent tuberculosis infection (LTBI) is a state of persistent bacterial viability, immune control, and lack of evidence of clinically manifested active tuberculosis (TB), constituting a public health problem that requires effective interventions^{1,2}. Approximately one-quarter of the global population is infected with *Mycobacterium tuberculosis*³. China is not only a high-TB burden nation but also ranks among the countries most severely affected by LTBI worldwide^{4,5}. Approximately 250 million individuals in China are diagnosed with LTBI. The prevalence rate of LTBI was 18.08% in populations aged ≥ 5 years and 20.34% among those aged ≥ 15 years^{6,7}. Latent tuberculosis infection constitutes a fundamental obstacle to TB epidemic containment and serves as a persistent disease reservoir that continuously generates new active cases⁸. Without intervention, approximately

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5%–10% of individuals with LTBI will eventually experience symptoms and develop TB⁹. Tuberculosis can affect anyone regardless of age or sex. Moreover, compared to adults, children with LTBI are at a higher risk of progression to TB^{1,10}. The 2-year cumulative incidence of LTBI in children aged < 5 years was up to 19%, and adolescents faced an increasing risk following childhood¹¹. In 2023, there were approximately 1.3 million new cases of TB in children and adolescents aged 0–14 years and approximately 200,000 deaths¹².

The implementation of tuberculosis preventive treatment (TPT) among children and adolescents plays a vital role in controlling pediatric TB¹³. Ayieko et al. demonstrated that isoniazid prophylaxis reduced the risk of TB development by 59% in children aged ≤ 15 years¹⁴. Moreover, Martinez et al. reported that, among children aged < 19 years who were in close contact of patients with TB and had tested positive for infection, the efficacy of preventive treatment reached 85%¹¹. However, despite the proven high efficacy of preventive therapy for LTBI in averting TB onset¹⁵, the progress in providing such treatments to children and adolescents has been slow¹³. In 2022, only 37% of 1.56 million eligible household contacts < 5 years accessed TPT and coverage was even lower for household contacts above 5 years, with only 11% out of 11.4 million initiated on TPT¹⁶. In 2023, the global coverage of preventive therapy for close family contacts of patients with TB was only 21%¹².

Reviews addressing the cascade of care for TB infection concluded that most attritions occurred before the initiation of TPT, rather than due to non-adherence to TPT after its initiation. However, at present, systematic reviews and meta-analyses regarding preventive therapy for LTBI in children and adolescents mainly focused on compliance, effectiveness, and safety of treatment regimens^{1,17,18}. Although Rustage et al.¹⁹ and Sagili et al.²⁰ evaluated the initiation and completion of LTBI treatment, their study populations were migrants and household contacts of patients with TB, respectively. No systematic review or meta-analysis has been conducted to assess the acceptance of preventive treatment in children and adolescents. We conducted this systematic review and meta-analysis to evaluate the acceptance of LTBI preventive therapy among Chinese children and adolescents and explore the factors influencing the acceptance of TPT, thereby providing evidence-based recommendations for strengthening TPT.

Methods

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards²¹ (see Supplementary File 1), and the protocol was registered in PROSPERO (CRD420250655042).

Research strategy

We searched PubMed, Web of Science, Embase, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Biomedical Database, and VIP database for eligible studies published in English or Chinese as of February 21, 2025. This study aimed to collect articles on the prophylactic treatment of LTBI in Chinese children and adolescents. The search strategy combined MeSH and keywords for key concepts (e.g., China, students, tuberculosis, latent infection, preventive therapy). For instance, the Web of Science query was: (ALL= (China OR Chinese) AND TS= (schoo* OR kindergar* OR studen* OR infant OR infants OR newborn OR child OR children OR kid OR kids OR pediatri* OR adolescen* OR teenage* OR juvenil* OR freshman OR freshmen) AND TS= (tuberculo* OR TB OR MTB OR PTB) AND TS= (latent infectio* OR latent tuberculo* OR latent pulmonary tuberculo* OR latent TB OR LTBI OR tuberculosis infectio* OR TB infectio* OR latent Mycobacterium tuberculo* OR latent M. tuberculo* OR inactive tuberculo* OR inactive TB OR inactive mycobacterium tuberculo* OR Mycobacterium tuberculosis infectio* OR dorman* tuberculo* OR dorman* TB OR TBI) AND TS= (therap* OR treatmen* OR treat* OR prophyla* OR preven* OR precautio* OR pharmacotherap* OR immunotherapy OR chemotherapy)) OR (ALL= (China OR Chinese) AND TS= (schoo* OR kindergar* OR studen* OR infant OR infants OR newborn OR child OR children OR kid OR kids OR pediatri* OR adolescen* OR teenage* OR juvenil* OR freshman OR freshmen) AND TS= (tuberculo* OR TB OR MTB OR PTB) AND TS= (prevent* therap* OR prevent* treatmen* OR prophylactic therap* OR prophylactic treatmen* OR prevent* medication OR TPT OR chemoprevent* OR chemo-prevent* OR chemoprophyla* OR chemo-prophyla* OR chemical prophylaxis OR immunoprophylaxis OR immun* prevention)). Full strategies are in Supplementary File 2. The reference lists of the relevant articles or reviews were manually checked for other potentially relevant studies.

Inclusion and exclusion criteria

Studies relevant to children and adolescents aged < 18 years in China who had LTBI, irrespective of the definition of LTBI adopted by the authors, were included in this meta-analysis. The inclusion of studies was not restricted by study type; randomized controlled trials, case-control studies, cohort studies, and cross-sectional studies were all eligible. Studies that reported on preventive treatment regimens, the number of individuals eligible for TPT, and the number of individuals who initiated TPT were included. Studies that reported regimens including isoniazid monotherapy (INH, H), rifampicin monotherapy (RIF, R), combination therapy of isoniazid and rifampicin (INH-RIF, HR), combination therapy of isoniazid and rifapentine (INH-RFT, HP), and immunoprophylactic treatments were included. In case of multiple publications by the same researchers, only the earliest or the most complete dataset or the largest population study was adopted.

The exclusion criteria were as follows: (1) studies that focused on the contacts of patients with drug-resistant TB; (2) studies that implemented multiple preventive therapies but did not report the outcomes for each intervention separately or studies that failed to provide extractable data even after contacting the authors for clarification; (3) case reports, conference literature, reviews, editorials, letters, animal studies, and in vitro studies; and, (4) studies not published in English or Chinese and studies without full text.

Data extraction and quality assessment

Two reviewers (L.A.P and Y.Q.Z.) independently screened the studies retrieved from the literature search based on the inclusion and exclusion criteria and independently completed data extraction using a predefined data extraction form to ensure accuracy. Attempts were made to retrieve missing data by contacting the corresponding author. The following data were extracted from each included study: first author's name, year of publication, title, study design, research setting, timing of data collection, study location, target population criteria for TPT, prophylactic treatment regimen, duration of treatment, number of individuals eligible for TPT, number of individuals who initiated TPT, and reasons for refusal of TPT.

Referring to previous meta-analyses^{22–24}, two reviewers (L.A.P and Y.Q.Z.) independently used the Newcastle–Ottawa Scale (NOS) to assess the quality of cohort studies and a modified NOS to assess the quality of cross-sectional studies. The NOS²² has been widely employed to evaluate the methodological quality of observational studies. Official versions exist for cohort and case–control studies²², whereas modified versions exist for cross-sectional studies^{25,26}. The maximum NOS score for cohort studies was nine points, and the maximum score for the modified NOS was 10 points.

Any discrepancies during data extraction and quality assessment were resolved by consulting a third reviewer (B.C.).

Data analysis

The extracted data were imported into Stata version 18.0 for the meta-analysis. The statistical heterogeneity among the included studies was assessed using Cochran Q test and the I^2 statistic. A random-effects model was employed for the meta-analysis when there was significant heterogeneity among studies ($P < 0.10$ or $I^2 > 50\%$). Conversely, a fixed-effects model was used when no heterogeneity was detected²⁷. The potential sources of heterogeneity were explored using subgroup, meta-regression, and sensitivity analyses. Subgroup analyses were conducted according to the region, research setting, regimen, duration of preventive therapy, dosage frequency, and study start time. Begg test and Egger linear regression test were used to assess publication bias^{28,29}. Unless otherwise specified, P -values were two-tailed, and statistical significance was defined at $P < 0.05$.

In particular, China was categorized into four major regions (eastern, central, western, and northeastern) according to the latest economic zone classification standard issued by the National Bureau of Statistics³⁰. This classification employs comprehensive socioeconomic criteria—covering geographical location, level of economic development, and technological advancement—to reflect regional disparities. Specifically, the eastern region includes 10 provinces/municipalities: Beijing, Tianjin, Hebei, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan. The central region comprises six provinces: Shanxi, Anhui, Jiangxi, Henan, Hubei, and Hunan. The western region consists of 12 provinces/autonomous regions/municipalities: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Shaanxi, Gansu, Qinghai, Ningxia, Xinjiang, and Tibet. The northeastern region includes three provinces: Liaoning, Jilin, Heilongjiang.

Results

Study selection and study characteristics

From our multi-database search, 7,165 potential articles were identified. After title, abstract, and full-text reviews, 31 articles with 4929 participants were included in this systematic review and meta-analysis, spanning 2004 to 2024^{31–61}. Among these, 19 were cross-sectional studies and 12 were cohort studies. Seventeen studies^{31,32,35,38,39,41,42,45,50–54,56,58,60,61} were conducted in the eastern region of China; seven^{36,37,43,47,55,57,59}, central; five^{33,34,40,46,48}, western; one⁴⁴, northeastern; and, one⁴⁹, both central and western regions. Eighteen studies focused on school outbreak screening; two, household contact screening; and, 11, routine screening. Based on the criteria for defining the target population for TPT, the literature distribution was as follows: three studies used tuberculin skin test (TST) ≥ 10 mm or a strong reaction, 22 studies used TST ≥ 15 mm or a strong reaction, three studies used TST ≥ 20 mm or a strong reaction, one study used interferon-gamma release assay (IGRA) positivity, and two studies used TST ≥ 15 mm or a strong reaction or IGRA positivity. Prophylactic treatment regimens included isoniazid monotherapy (H), combination therapy with isoniazid and rifampicin (HR), and combination therapy with isoniazid and rifapentine (HP). The H and HR regimens were administered once daily, whereas the HP regimen was administered twice weekly. The studies were initiated between 2004 and 2023, with sample sizes ranging from 11 to 846. Figure 1 presents a flowchart detailing the study selection process. Table 1 provides detailed information about the selected studies.

Quality of the included studies

The quality scores of the 19 cross-sectional studies ranged from 5 to 9, whereas those of the 12 cohort studies ranged from 6 to 8 (see Supplementary File 3).

Acceptance rate of TPT among Chinese children and adolescents

We conducted a meta-analysis of the included cross-sectional and cohort studies. Considering that the data extraction for cohort studies was restricted to the baseline survey time point and given the homogeneity of their data structure with that of cross-sectional studies, we merged and analyzed these cohort studies with cross-sectional studies during the meta-analysis process. The pooled results showed that the acceptance rate of preventive therapy among Chinese children and adolescents with LTBI was 0.640 (95% CI: 0.569–0.709, $P < 0.001$), with high heterogeneity ($I^2_{\text{random effects model}} = 95.770\%$, $P < 0.001$) (Fig. 2).

The results of the subgroup analyses are presented in Table 2. The subgroup analysis revealed significant heterogeneity among the subgroups stratified by region ($Q_{\text{between}} = 8.985$, $P = 0.029$), research setting ($Q_{\text{between}} = 19.766$, $P < 0.001$), preventive therapy criteria ($Q_{\text{between}} = 33.378$, $P < 0.001$), regimen ($Q_{\text{between}} = 9.755$, $P = 0.008$), and dosage frequency ($Q_{\text{between}} = 9.679$, $P = 0.002$). In particular, among 17 studies conducted

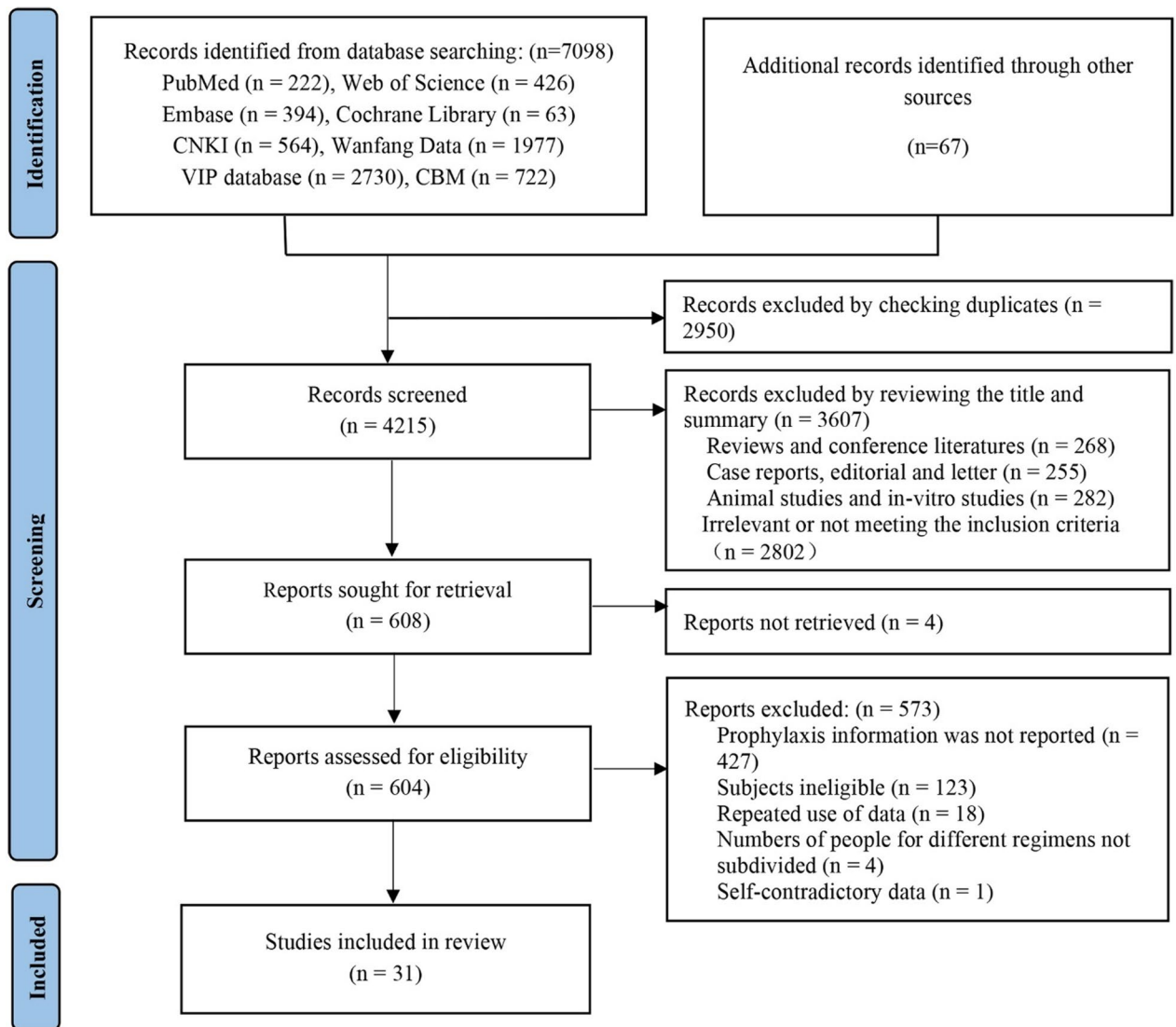


Fig. 1. PRISMA flow diagram for study selection.

in the eastern region of China, the TPT acceptance rate among children and adolescents was 0.615 (95% CI: 0.509–0.717). The TPT acceptance rate in the western region was slightly lower than that in the eastern region, at 0.531 (95% CI: 0.284–0.771). The central region had a significantly higher TPT acceptance rate than those in the other areas, reaching 0.765 (95% CI: 0.698–0.825). The acceptance rate of TPT among Chinese children and adolescents with LTBI was highest in LTBI cases identified through household contact screening (0.802), followed by those detected through school outbreak screening (0.663), and lowest in cases identified via routine screening (0.522). Among different preventive therapy criteria, the TPT acceptance rate was highest at 0.805 when using IGRA positivity as the criterion, followed by 0.657 for the TST ≥ 20 mm or strong reaction group, 0.615 for the TST ≥ 15 mm or strong reaction group, and 0.559 for the TST ≥ 10 mm or strong reaction group. Regarding the different preventive treatment regimens, the acceptance rate of TPT for INH and RFT regimens was the highest at 0.765. In terms of medication frequency, the TPT acceptance rate for a twice-weekly regimen was 76.5%, compared to 58.9% for a daily regimen. We also performed a meta-regression analysis that included covariates for the following six subgroups: region ($P=0.238$), research setting ($P=0.033$), preventive therapy criteria ($P=0.224$), regimen ($P=0.264$), duration of preventive therapy ($P=0.840$), dosage frequency ($P=0.086$), and study start time ($P=0.218$). Furthermore, the sensitivity analysis of the pooled acceptance rate of preventive therapy among Chinese children and adolescents with LTBI indicated that the results were stable (see Supplementary File 4).

Potential publication bias

We employed Begg test and Egger linear regression test to evaluate the potential publication bias for the pooled acceptance rate of preventive therapy among Chinese children and adolescents with LTBI (Fig. 3). The results of both Begg test ($P_B = 0.083$) and Egger test ($P_E = 0.093$) were consistent, suggesting no significant publication bias.

Study	Study design	Region	Study year	Research setting	Preventive therapy criteria	Regimen	Sample size	Initiated TPT
Dong et al. ³¹	Cross-sectional study	Jiangsu Province	2005	Routine screening	TST ≥ 20 mm or strong reaction (blisters, necrosis, lymphangitis)	6H ₂ P ₂	307	260
Guo et al. ³²	Cross-sectional study	Jiangsu Province	2018–2021	Routine screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis) or IGRA positive	3HR	397	215
Zhou et al. ³⁵	Cross-sectional study	Guangdong Province	2011	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	6 H	187	150
Wu ³³	Cross-sectional study	Chongqing Municipality	2017–2018	Household contact screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3H ₂ P ₂	25	20
Wu ³³	Cross-sectional study	Chongqing Municipality	2017–2018	Household contact screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	6 H	26	19
Shi ³⁴	Cross-sectional study	Sichuan Province	2016	Routine screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	31	3
Yu et al. ³⁶	Cross-sectional study	Henan Province	2010	Routine screening	TST ≥ 10 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	846	627
Hu et al. ³⁷	Cross-sectional study	Henan Province	2017	Routine screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	397	248
Guan et al. ³⁸	Cross-sectional study	Shandong Province	Not reported	Routine screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3H ₂ P ₂	24	16
Jiang et al. ³⁹	Cross-sectional study	Shandong Province	Not reported	Routine screening	TST ≥ 20 mm or strong reaction (blisters, necrosis, lymphangitis)	3H ₂ P ₂	26	16
Pan et al. ⁴⁰	Cross-sectional study	Guangxi Province	2019–2020	Routine screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	90	10
Jia et al. ⁴¹	Cross-sectional study	Beijing Municipality	2018–2019	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3H ₂ P ₂	62	39
Weng et al. ⁴²	Cross-sectional study	Zhejiang Province	2013–2014	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	23	21
Li et al. ⁴³	Cross-sectional study	Henan Province	2018	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3H ₂ P ₂	143	111
Zheng ⁴⁴	Cross-sectional study	Liaoning Province	2015	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	6 H	64	42
Gong et al. ⁴⁵	Cross-sectional study	Zhejiang Province	2016	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	11	10
Hou et al. ⁴⁶	Cross-sectional study	Guangxi Province	2023	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	100	31
Wang et al. ⁴⁷	Cross-sectional study	Shanxi Province	Not reported	Routine screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	6 H	63	38
Fan et al. ⁴⁸	Cross-sectional study	Chongqing Municipality	2020–2021	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis) or IGRA positive	3HR	44	36
Chen et al. ⁴⁹	Cross-sectional study	Henan and Hunan Province	2018–2020	Household contact screening	IGRA positive	6 H	228	185
Chen et al. ⁴⁹	Cross-sectional study	Henan and Hunan Province	2018–2020	Household contact screening	IGRA positive	3H ₂ P ₂	273	234
Chen et al. ⁴⁹	Cross-sectional study	Chongqing Municipality	2018–2020	Household contact screening	IGRA positive	6 H	149	120
Chen et al. ⁴⁹	Cross-sectional study	Chongqing Municipality	2018–2020	Household contact screening	IGRA positive	3H ₂ P ₂	39	25
Li et al. ⁵⁰	Cohort study	Jiangsu Province	2004–2007	Routine screening	TST ≥ 20 mm or strong reaction (blisters, necrosis, lymphangitis)	6 H	195	92
Li et al. ⁵¹	Cohort study	Beijing Municipality	2016–2019	School outbreak screening	TST ≥ 10 mm or strong reaction (blisters, necrosis, lymphangitis)	3H ₂ P ₂	91	72
Fang et al. ⁵²	Cohort study	Zhejiang Province	2016–2019	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	6 H	30	4
Fang et al. ⁵³	Cohort study	Zhejiang Province	2019–2020	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	6 H	122	69
Huang ⁵⁴	Cohort study	Guangdong Province	2013–2017	Routine screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	348	151
Zou et al. ⁵⁵	Cohort study	Hunan Province	2020–2021	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	144	130
Hu et al. ⁵⁶	Cohort study	Shanghai Municipality	2018–2020	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3H ₂ P ₂	12	5
Zhou et al. ⁵⁷	Cohort study	Henan Province	2019–2021	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	136	110
Weng et al. ⁵⁸	Cohort study	Zhejiang Province	2008–2012	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	179	86
Tang et al. ⁵⁹	Cohort study	Anhui Province	2018–2019	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	52	34

Continued

Study	Study design	Region	Study year	Research setting	Preventive therapy criteria	Regimen	Sample size	Initiated TPT
Zhang et al. ⁶⁰	Cohort study	Jiangsu Province	2014–2016	School outbreak screening	TST ≥ 10 mm or strong reaction (blisters, necrosis, lymphangitis)	3HR	34	4
Xu et al. ⁶¹	Cohort study	Zhejiang Province	2018–2020	School outbreak screening	TST ≥ 15 mm or strong reaction (blisters, necrosis, lymphangitis)	3H ₂ P ₂	31	30

Table 1. Characteristics of the studies related to TPT acceptance in Chinese children and adolescents. 6 H: Take isoniazid once a day and continue for six months. 3HR: Take isoniazid and rifampicin once a day for three months. 3H₂P₂: Take isoniazid and rifampentine twice a week for three consecutive months.

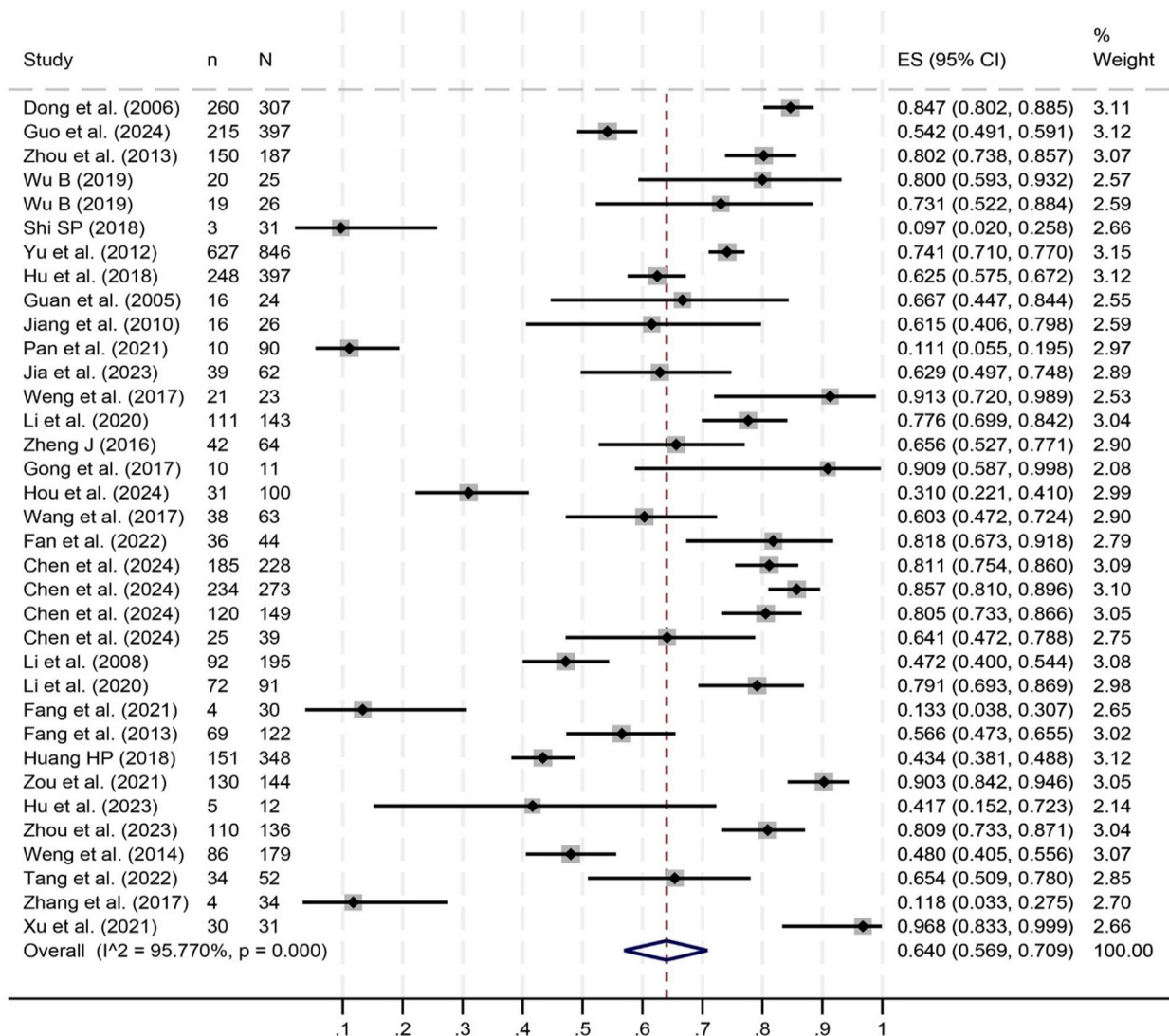


Fig. 2. Acceptance rate of TPT among Chinese children and adolescents analyzed by the Forest plot.

Discussion

Tuberculosis preventive treatment plays a pivotal role in controlling and eliminating TB. Achieving optimal TPT coverage is critical for protecting children and adolescents exposed to TB from developing TB^{17,62}. In September 2023, at the second United Nations High-Level Meeting on the fight against TB, renewed commitments to address TB in children and adolescents have been defined⁶³. By 2027, 90% of individuals at a high risk of developing TB will be provided with preventive treatment, which translates to providing TPT to 30 million household contacts of people with TB, including children. The political declaration also committed to urgently scaling up comprehensive efforts to close long-standing gaps in the prevention, diagnosis, treatment, and care of children with or at risk of TB^{62,63}.

Subgroup analysis type	No. of studies	Effect size		M	Heterogeneity	
		ES [95%CI]	P_{ES}		I^2 (%)	P_H
All studies	31	0.640 [0.569, 0.709]	<0.001	REM	95.770	<0.001
Subgroup analysis by region						
Eastern region	17	0.615 [0.509, 0.717]	<0.001	REM	95.181	<0.001
Central region	8	0.765 [0.698, 0.825]	<0.001	REM	91.045	<0.001
Western region	6	0.531 [0.284, 0.771]	<0.001	REM	96.688	<0.001
Northeastern region	1	0.656 [0.527, 0.771]	<0.001	NA	NA	NA
Subgroup analysis by research setting						
Routine screening	11	0.522 [0.398, 0.645]	<0.001	REM	97.313	<0.001
School outbreak screening	18	0.663 [0.551, 0.767]	<0.001	REM	94.433	<0.001
Household contact screening	2	0.802 [0.749, 0.850]	<0.001	REM	55.786	0.046
Subgroup analysis by preventive therapy criteria						
TST \geq 10 mm or strong reaction	3	0.559 [0.266, 0.832]	<0.001	NA	NA	NA
TST \geq 15 mm or strong reaction	22	0.615 [0.514, 0.711]	<0.001	REM	95.374	<0.001
TST \geq 20 mm or strong reaction	3	0.657 [0.347, 0.909]	<0.001	NA	NA	NA
IGRA positive	1	0.805 [0.743, 0.860]	<0.001	REM	69.512	0.020
TST \geq 15 mm or strong reaction or IGRA positive	2	0.572 [0.525, 0.618]	<0.001	NA	NA	NA
Subgroup analysis by regimen						
INH	8	0.632 [0.505, 0.750]	<0.001	REM	93.948	<0.001
INH and RIF	15	0.563 [0.445, 0.678]	<0.001	REM	97.077	<0.001
INH and RFT	10	0.765 [0.695, 0.829]	<0.001	REM	79.353	<0.001
Subgroup analysis by duration						
3 months	24	0.634 [0.544, 0.719]	<0.001	REM	96.067	<0.001
6 months	9	0.658 [0.539, 0.767]	<0.001	REM	94.669	<0.001
Subgroup analysis by dosage frequency						
Once a day	23	0.589 [0.501, 0.674]	<0.001	REM	96.341	<0.001
Twice a week	10	0.765 [0.695, 0.829]	<0.001	REM	79.353	<0.001
Subgroup analysis by study start year						
Before 2017	17	0.582 [0.476, 0.684]	<0.001	REM	95.851	<0.001
Since 2017	14	0.693 [0.592, 0.786]	<0.001	REM	95.839	<0.001

Table 2. Subgroup analysis of the acceptance rate of TPT in Chinese children and adolescents. *ES* effect size, *CI* confidence interval, *M* Model, *REM* random effects model, *NA* not available.

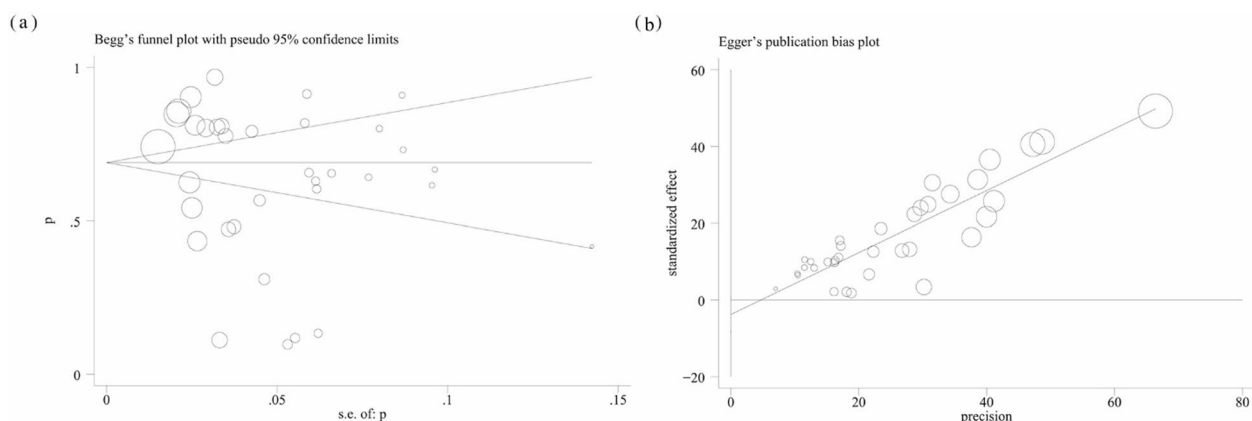


Fig. 3. Combined assessment of publication bias using Begg test and Egger regression.

This first meta-analysis evaluating the acceptance rate of TPT among Chinese children and adolescents synthesized individual-level data from 31 regionally diverse studies. The pooled analysis revealed that only 64.0% of the eligible individuals received preventive therapy. This proportion was lower than that observed among immigrants (69.0%)¹⁹, highlighting a considerable shortfall compared to the global targets⁶³. The acceptance

rates for various preventive treatment regimens exhibited a wide range, from 9.7% to 96.8%, implying that enhancing the preventive treatment rate is indeed feasible.

The TB epidemic in China exhibited significant spatial heterogeneity, which stemmed from the interaction of multidimensional factors such as regional economic development gradients, population structure heterogeneity, spatial density of medical infrastructure, and local fiscal input capabilities^{64–66}. Our study found significant heterogeneity in the acceptance rate of TPT across different regions of China. Unlike the situation in which regions with higher economic levels had lower TB epidemics, the Central region had the highest TPT acceptance rate, reaching 76.5%, whereas the acceptance rate in the Eastern region was only 61.5%. This phenomenon may be caused by multiple factors. First, owing to the high prevalence of TB, in addition to implementing the national TB strategy, central provinces implemented a series of non-fragmented local intervention combinations and achieved remarkable results^{67,68}. For instance, in 2024, Hunan province achieved the largest decline in the TB incidence rate nationwide, with the reported incidence rate among students dropping to < 10/100,000 for the first time. The acceptance rate of preventive treatment among students increased by 65.7%⁶⁹. Second, despite the relatively low prevalence of TB in the eastern region, awareness of the risk of TB may be inadequate. A survey of the public's awareness of core TB knowledge in 2020 revealed that the overall awareness rate of five key TB prevention and control messages among the general public in Hunan Province was 88.3%⁷⁰, compared with 81.5% in Beijing⁷¹. The acceptance of LTBI preventive treatment increases as the level of tuberculosis-related knowledge rises^{72,73}. Moreover, residents in economically developed regions (eastern region) generally have a higher level of education, and the level of education is negatively correlated with the TPT acceptance rate^{74,75}.

There were significant differences in the acceptance rates of targeted TPT for children and adolescents with LTBI across different research settings. In particular, the highest TPT acceptance rate was observed among household close contacts (80.2%), followed by those identified through school outbreak screening (66.3%). The lowest acceptance rate was observed among LTBI cases detected through general screening (52.2%). The disparities in the acceptance rate of TPT were primarily attributed to differences in awareness levels, intensity of medical management, social support, and policy safeguards^{76,77}. In contrast to routine screening, the propensity to accept TPT is elevated among individuals with LTBI who are close contact with patients with TB^{73,78,79}. Household close contacts generally had a higher level of awareness regarding the hazards of the disease and the necessity of TPT. Owing to their high exposure to and elevated risk of developing the disease, household close contacts were identified as the core target population for LTBI screening and intervention by the WHO and multiple countries^{12,80–83}. In high-burden TB countries, the initiation rate of TPT for LTBI among household contacts of patients with TB exceeds 90%²⁰. This rate was significantly higher than that reported in other populations. The Chinese government has attached great importance to TB control in schools. The “Guidelines for Tuberculosis Prevention and Control in Schools” explicitly required that once a case of active TB was confirmed within a school, a close contact investigation should be carried out, and individuals with a strongly positive result on the tuberculin skin test and normal findings on chest radiographs were advised to undergo preventive treatment⁸⁴. Household and school contacts were typically incorporated into mandatory or semi-mandatory screening systems where they receive more intensive education and follow-up. These actions have improved the management of LTBI in close contacts of individuals with active TB⁴.

Subgroup analysis revealed a gradient in TPT acceptance rates across populations defined by different diagnostic criteria. The rate was highest in the IGRA-positive group (80.5%), attributable to IGRA's superior specificity for LTBI. Unlike TST, IGRA was not affected by Bacille Calmette–Guérin (BCG) vaccination, most non-tuberculous mycobacterial infections, or subjective judgment of the operator, thus providing a more reliable diagnosis of true infection^{4,85}. This diagnostic accuracy, coupled with meta-evidence showing a higher progression risk to active TB among IGRA-positive individuals⁸⁶, enhanced both clinician recommendation confidence and participant acceptance. A dose-response relationship was observed with TST thresholds, where higher cut-offs (e.g., 10 mm, 15 mm, 20 mm) were associated with progressively increasing acceptance rates, consistent with clinical risk stratification. This trend aligned with evidence that larger TST induration reflects a greater risk of disease progression⁸⁷, reinforcing risk perception among clinicians and participants and promoting willingness to initiate treatment. The lower TPT acceptance rate (57.2%) observed in the composite criteria group (TST \geq 15 mm/strong reaction or IGRA positive) might be attributable to the limited number of included studies (only 2) and small sample size ($n = 441$), which could limit the precision and generalizability of the estimate.

The subgroup analysis also revealed that, compared with different preventive treatment regimens, the acceptance rate of INH and RFT administered twice weekly was higher than that of daily INH or daily INH and RIF. Combination drug therapy was more effective than single drug therapy for TPT⁸⁸. The combination of two bactericidal drugs with different mechanisms of action can enhance the therapeutic effects¹⁸. Although the INH regimen was the earliest, most widely used, and most mature scheme with a relatively high protection rate, its acceptance was relatively low owing to issues such as side effects and the long duration of medication^{89–91}. In contrast, the intermittent combination regimen of INH and RFT was more readily accepted and had higher compliance owing to its better tolerability, shorter duration, and long-acting intermittent dosing characteristics of RFT^{77,91}. The combination regimen of INH and RIF is characterized by a short treatment duration and comparable protective efficacy. However, its acceptance rate was relatively low, which may be partly attributed to the higher dosing frequency compared to the INH and RFT regimen, as well as the more pronounced hepatotoxicity⁹². Santos et al. conducted a systematic review and network meta-analysis to retrospectively compare the effectiveness and safety of different treatment regimens for LTBI in patients aged < 15 years. They found that the combination of INH and RFT was likely the most effective option compared to other active drugs and placebos for preventing TB in the overall pediatric population¹⁸. Considering the individual genetic background and the fact that the frequency of the rapid acetylator genotype of N-acetyltransferase 2 is higher among Asians (approximately 50%) than among Caucasians (approximately 5%), China has widely adopted a

3-month regimen of INH and RFT (3H₂P₂) administered twice weekly for the treatment of LTBI, rather than the WHO-recommended 3HP regimen (a 3-month regimen of weekly INH and RFT). This regimen has also been shown to have a high protection rate and low incidence of liver dysfunction⁴.

Additionally, our study found that the primary barriers to preventive treatment were concerns about drug side effects and inadequate awareness of the disease. The concerns of some individuals with LTBI and their families regarding the costs, resources, and time required for TB infection treatment also influence decision-making. These factors have been identified in previous studies^{74,77,79,93,94}. The existing evidence demonstrates that both the TPT regimen using INH alone and the combination of INH with RFT/RIF have good safety profiles. However, there was a deviation between the public's perception of risk and the actual risk. Future efforts should focus on bridging this gap by enhancing health education, optimizing services, and reinforcing policy safeguards. Moreover, continuous endeavors are needed to increase the population's acceptance of TPT.

This study has a few limitations. First, the included studies failed to provide detailed reports on TB awareness levels and economic status of individuals with LTBI (or their guardians), which are potentially important factors that could affect the true attribution analysis of the acceptance rate. Second, the eligible studies were mainly concentrated in the eastern provinces of China; however, the number of articles was still inadequate in some less developed or relatively sparsely populated regions. Third, compared to the vast population of individuals with LTBI, the sample size included in this study was relatively limited. Despite these limitations, this study systematically analyzed all available research data and, for the first time, revealed the acceptance rate of preventive treatment for LTBI among children and adolescents in China, providing important insights for advancing TPT in this population.

Conclusions

This study revealed the suboptimal uptake of TPT among children and adolescents with LTBI in China. Tailoring interventions to regional epidemiological profiles, accurately identifying the target population for TPT with reliable tools, and scaling up optimized regimens under stringent monitoring are critical strategies for enhancing TPT coverage and advancing the “End TB” initiative. Given the limitations of these studies, future research is recommended to collect sociodemographic variables related to individuals with LTBI and explore their impact on acceptance rates. Alternatively, mixed-methods approaches combining quantitative data with qualitative interviews can be employed to uncover the drivers of decision making.

Data availability

All original data generated or analyzed during this research are included in the article and its supplementary information. Additional requests may be directed to the corresponding authors.

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Author contributions

B.C. had the idea for the study and L.A.P., Y.Q.Z., M.W. and Z.P.Z. were responsible for the study inception and protocol design. L.A.P., Y.Q.Z. and B.C. searched literature, selected the studies, and completed the extraction of data. L.A.P. and Y.Q.Z. were involved in analysis of the data. Interpretation of the results and drafting of the manuscript was done by L.A.P., M.W., Z.P.Z., Q.W., X.Y.C., Y.Z., and B.X. contributed to revising it critically for intellectual content. B.C., Y.X.W., and L.A.P. were involved in the final approval of the version to be published. All authors reviewed and approved the final manuscript, confirmed that they met the established authorship criteria, and agreed to be accountable for all aspects of the work.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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