

## A SYSTEMATIC STUDY AND META-ANALYSIS OF TUBERCULOSIS INFECTION PREVALENCE IN INDIA.

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### Abstract

#### Background and objectives

One of the most common infectious agent-related causes of death worldwide is tuberculosis (TB) which is brought on by *Mycobacterium tuberculosis*. Nevertheless, not much is currently understood regarding the prevalence of tuberculosis infection (TBI) in India's various risk groups. The purpose of this systematic review and meta-analysis was to calculate the prevalence of TBI in India by risk categories, sociodemographic profile, and geographic location.

#### Methods

Through a comprehensive analysis, this study investigated the prevalence of TBI in India between 2013 and 2022. Following the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis, 70 papers were examined using databases such as Scopus, CINAHL, EMBASE, and MEDLINE.

#### Results

70 research, including approximately 40 prevalence studies and approximately 30 long-term studies, were included in this paper after a review of 10,510 papers. Based on population-based sample studies, the total prevalence of TBI in India was determined to be 40.79 %. When highly sensitive populations were excluded from the general population, this percentage remained constant at 35.99%. There was a commensurate increase in TBI prevalence in areas with higher active TB burdens, particularly in Tamil Nadu and Delhi.

#### Conclusion

The current thorough investigation demonstrated the high prevalence of TB infections in India, which corresponded with proactive TB infections and suggested a possible transition from latent to active TB. Notably, people living in the southern regions of the country were more likely to experience this possibility. In order to properly manage TBI in India, it is imperative that these regional variations be addressed in order to prioritize and adapt customized methods.

#### Recommendation

This study suggests giving priority to Tuberculosis Preventive Treatment in areas with high prevalence of Tuberculosis Infection and promoting a "No test, treat only" approach for resource efficiency in order to attain India's TB elimination targets.

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**Keywords:** Systematic Review, Tuberculosis, Tuberculin Skin Test, Interferon Gamma Release Assay, TB infection

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#### Introduction

One of the most common infectious agent-related causes of death worldwide is tuberculosis (TB), which is brought on by *Mycobacterium tuberculosis* (MTB) [1]. The Global TB Report 2021 estimates that 10.6 million TB incident cases were registered in 2021[1]. 90% of new TB incident cases and 95% of TB deaths are to be

eliminated by 2035, according to the World Health Organization's (WHO) END TB strategy [2]. Strengthening TB diagnostic, prophylactic, and treatment services is necessary to meet the global TB targets for lowering the disease burden of TB [3, 4].

TB infection (TBI) is characterized by a sustained immunological response brought on by MTB antigen

stimulation in the absence of any clinically evident active TB. TBI, especially in immunocompromised individuals, can act as a prelude to the onset of a full-blown TB illness [5]. This makes up a sizable reservoir of people with TBI; I, managing TBI is essential to international efforts to reduce the TB burden, especially in nations with high TB burdens like India. From a geographic perspective, India bears 28% of the global TB burden among the six high-burden nations in Southeast Asia. Additionally, it has the largest global burden of TBI [6]. According to the 2021 National TB Prevalence Survey, the crude prevalence of TBI in people older than 15 years was 31.3% [95% CI: 30.8-31.9] [7]. According to reports, 5–10% of people who have TBI go on to have clinically active TB illness [8]. A persistent reservoir of people with tuberculosis can be created by a single active case of the disease infecting other people before they receive anti-tubercular treatment because of delayed diagnosis [9].

The main goal of the WHO End TB strategy is to prevent active TB disease by treating TB-infected patients and breaking the chain of transmission, as they represent a constant source of risk for development towards active disease. Although TB disease prevention by TBI treatment is generally underestimated, it is still a key element of the National Strategic Plan 2017–25 for Ending TB in India by 2025, which is five years ahead of the Sustainable Development Goals [10]. TB preventive treatment (TPT) must be incorporated into the overall strategy for the diagnosis and treatment plans to eradicate TB to be successful, according to the Lancet Commission on TB [11]. It is necessary to facilitate the efficient and quick scale-up of proven interventions, such as novel TPT regimens, and to enhance their implementation [12]. Finding high-risk groups and starting TPT are examples of this. With programmatic ramifications, it is imperative to evaluate the burden of TBI throughout India's states and populations.

This study aims to conduct a comprehensive analysis of the various research for looking into tuberculosis infections in the Indian subcontinent's population.

## Materials and Methods

### Study Design

Following the guidelines of the Preferred Reporting Items for the Systematic Reviews and Meta-Analysis (PRISMA), a comprehensive analysis of the various research looking into tuberculosis infections in the Indian subcontinent's population was conducted. The authors looked through databases, including Embase, Web of Science, the Cochrane Library, Medline, Google Scholar, and Scopus, to find pertinent studies. Using Boolean operators (or, and) and without regard to linguistic limitations, the authors combined keywords like “pulmonary tuberculosis”, “tuberculosis,” or “TB”, “latent tuberculosis infection”, and “inactive tuberculosis” with “prevalence study”, “cross-sectional study”, “survey” and “India”. To gain further understanding, the authors also looked at the list of references for review papers and original research.

### Study Setting

From 2013 to 2022, this analysis assessed the studies using their titles and abstracts. The full texts of the selected documents were then obtained. Details like the year of publication, names of authors, duration of the study, participants, study setting, size of sample, research methods, and estimates of prevalence were among the information that was extracted from the included studies. Sputum smear-positive pulmonary tuberculosis cases were defined in this investigation as those in which, by microscopy, at least one sputum sample contained acid-fast bacilli. Regardless of the smear result, the authors referred to pulmonary tuberculosis with a positive test as having one culture showing the growth of the bacterium.

### Inclusion Criteria

This analysis included all primary studies that included Indian people, regardless of the technique employed to measure TBI. To differentiate TBI, several tests were taken into consideration, including the C-tuberculosis test, interferon-gamma release assay, T-cell test, tuberculin skin test (TST), and TB.

### Exclusion Criteria

Include abstracts from conferences, case reports, study protocols, posters, editorials, reviews, reports, opinion articles, any unpublished material, and theses. TBI was defined for this study as an immune response to the TB antigen that does not exhibit any clinical symptoms of TB.

### Bias

Efforts were made to minimize bias by ensuring a random selection of articles from the databases and by maintaining objectives for tuberculosis infections.

### Data Sources/Measurement

A consistent data extraction form was used to extract the study characteristics and findings from the included studies. Data was retrieved about the authors, the test utilized, the percentage of TBI, the nation, the study design, the study area, the sample size, the year of publication, the year of study, the sociodemographic characteristics, and the authors. Furthermore, data was gathered to evaluate the risk of bias. Critical appraisal tools from the Joanna Briggs Institute were used to source data and systematically assess the methodological quality and bias risk in a selection of studies that covered a range of designs, including cross-sectional, cohort, and randomized controlled trials [13]. Depending on their ratings, the evaluation classified research into “high”, “moderate,” or “low” risk of bias. This methodical procedure guaranteed a strong basis for combining results in the systematic review.

### Statistical Analysis

The number of patients per 100,000 people, or the ratio of reported cases to the total study group, was used to calculate the prevalence of tuberculosis. Additionally, to

maintain uniformity throughout the meta-analysis, the approximate incidence rates were calculated using tabular data derived from these investigations. Using STATA 12.0 and a mixed-effects model, the combined incidence and 95% confidence intervals were computed. Two-sided p-values and the Q-statistic and I-squared tests were used to assess between-study heterogeneity. Subgroup analyses took into account the distribution of inhabitants in rural and urban areas as well as gender.

## Results

We started by finding 10,510 studies in total. Initial screening was performed on 9,990 studies after 520 duplicates were removed. After 9,840 publications were rejected based on a subsequent analysis of abstracts and titles, 150 studies were chosen for a thorough full-text review. Unfortunately, it was not possible to obtain the full text of 50 studies. 12 other reports were also included via cross-referencing. In summary, 112 research papers met the requirements to be included in a thorough analysis. Following the removal of 42 reports owing to improper study design or invalid results, 70 studies were selected for additional evaluation.

## Tuberculosis Infection Incidence in Population-Based Cohort Studies

The 70 papers included 40 cross-sectional studies and 30 long-term studies. The study's distribution throughout the zonal divisions of the Indian subcontinent showed that the southern region had the highest concentration (40.79%), followed by the northern region (32.29%), the western region (8.79%), the central region (5.89%), and the eastern region (0.39%). For the diagnosis of TBI, 41.43% (29/70) used the Tuberculin Skin Test (TST), 7.14% (5/70) used the Interferon-Gamma Release Assay (IGRA), and 51.43% (36/70) used both. Eleven studies regarded TST positive as occurring when the induration was greater than 5 mm, while 54 studies regarded it as occurring when the induration was greater than 10 mm. 30,932 people in all were examined in the included publications. An overview of the key features of the included studies is given in the table.

The pooled prevalence of TBI, as shown below, was calculated using the available IGRA data because it is a more specific diagnostic test for TBI than TST. TST results were taken into consideration for estimation when IGRA data was not available. Furthermore, because hospital-based and cross-sectional studies, in general, have inherent selection biases, the estimated poverty prevalence of TBI in India was based solely on community-based cohort studies. An overview of the key features of the included studies is given in Table 1. The pooled prevalence of TBI, as shown below, was calculated using the available Interferon Gamma Release Assay data because it is a more specific diagnostic test for TBI than the Tuberculin Skin Test. The results of the Tuberculin Skin Test were taken into consideration for

estimation when Interferon Gamma Release Assay data was not available. Furthermore, because hospital-based and cross-sectional studies, in general, have inherent selection biases, the estimated pooled prevalence of TBI in India was based solely on community-based cohort studies.

According to the random effects model, 40.79 percent (95% CI: 29.49–52.59%,  $Q=1648.89$ ,  $P<0.0001$ ,  $I^2=99\%$ ) was the pooled community-based cohort study-based prevalence of TBI. In community-based studies, the pooled prevalence of this infection among the general public, after risk categories were excluded, was 35.99% (95% CI: 27.9–44.9%,  $Q$ -statistic = 17.37,  $p$ -value < 0.0001,  $I^2 = 83\%$ ). With a focus on adults (those over 15), the prevalence of TBI in the general population was determined to be 34.99% (95% CI: 23.99–45.99%,  $Q$ -statistic = 13.92,  $p$ -value < 0.0001,  $I^2 = 86\%$ ). In light of high heterogeneity ( $p$ -value < 0.00001,  $I^2 = 99\%$ ), a sensitivity analysis was done. Following the elimination of studies contributing to this heterogeneity, the total prevalence of TBI was adjusted to 37.99% (95% Confidence Interval: 28.99–45.99%,  $Q$ -statistic = 10.73,  $p$ -value = 0.02,  $I^2 = 72\%$ ).

## Based on community-based cohort research, the prevalence of tuberculosis infection by year, age, gender, and geography

The incidence of Tuberculosis Infection (TBI) was remarkably high in different regions from population-based cohort studies. It was 67.99% (95 percent CI: 45.99–86.99%) in Delhi, 41.9% (95 percent CI: 23.9–60.9%) in Tamil Nadu, and 25.99% (95 percent CI: 15.99–35.99%) in Maharashtra. A comparison of rural, urban, and tribal areas revealed that the pooled prevalence was 36.99% (95% CI: 15.9 to 59.9%) in urban areas, 26.99% (95% CI: 11 to 48%) in rural areas, and 32.9% (95% CI: 20.01 to 47.01%) in tribal areas. In the children's demographic, the combined incidence of tuberculosis infection was 32.9% (95% confidence interval: 23.9 to 41.9%) for children < 5 years old and 39.9% (95% confidence interval: 30.01 to 51.01%) for those in the age group 6 to 14 years. In the adult cohort, specifically between the ages 15 to 45 years, the incidence of TBI was 52.01% (95% confidence interval: 39.01 to 69.01%), while in the geriatric population (> 45 years), it was identified to be 61.9% (95% confidence interval: 49.9 to 73.9%). Breaking down by gender, the total prevalence of TBI was 41.01% (95% confidence interval: 19.01 to 65.01%) in men and 30.9% (95% confidence interval: 9.01 to 59.01%) in women.

## Bias Risk and Quality

The JBI critical assessment score of more than 70% indicated that the majority of the research (69) had a low risk of bias. Just one study scoring between 50–69% was deemed to have a bias risk in the moderate range.

**Table 1: An overview of the study's characteristics in the included articles**

Citations	Study design	Study setting	Size of sample	Risk group	Test	Size of Tuberculin Skin Test (in millimetres)	Individuals Infected with TBI
[14]	Cohort	Hospital	43	Healthcare workers	Tuberculin Skin Test	≥10	24
[15]	Cohort	Hospital	100	Detachment of retina	Tuberculin Skin Test	≥10	16
[16]	Cross sectional	Community	476	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	266
[17]	Cross sectional	Community	77	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥5	32
[18]	Cohort	Community	869	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥5	478
[19]	Cross sectional	Community	170	Diabetes	Interferon Gamma Release Assay	-	50
[20]	Cohort	Community	74	General public	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	38
[21]	Cross sectional	Community	77	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥5	31
[22]	Cohort	Community	80	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	23
[23]	Cross sectional	Hospital	185	Dialysis	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	66
[24]	Cross sectional	Hospital	250	Inflammatory Bowel Disease	Tuberculin Skin Test	≥10	51
[25]	Cohort	Hospital	755	Healthcare workers	Tuberculin Skin Test	≥10	339
[26]	Cross sectional	Hospital	200	Diabetes	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	96
[27]	Cohort	Community	1020	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥5	257
[28]	Cross sectional	Community	789	General public	Tuberculin Skin Test	≥10	198
[29]	Cross sectional	Community	205	Contacts	Interferon Gamma Release Assay& Tubercul	≥5	173

					in Skin Test		
[30]	Cross sectional	Hospital	215	General public	Tuberculin Skin Test	≥5	27
[31]	Cohort	Hospital	206	Healthcare workers	Tuberculin Skin Test	≥10	76
[32]	Cross sectional	Hospital	271	Contacts	Tuberculin Skin Test	≥10	55
[33]	Cross sectional	Hospital	561	Healthcare workers	Tuberculin Skin Test	≥10	380
[34]	Cross sectional	Community	6177	General public	Tuberculin Skin Test	≥10	1220
[35]	Cohort	Community	200	Healthcare workers	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	45
[36]	Cohort	Hospital	60	COVID	Tuberculin Skin Test	≥10	23
[37]	Cross sectional	Hospital	100	HIV	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	33
[38]	Cross sectional	Hospital	702	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	69
[39]	Cross sectional	Community	200	Contacts	Tuberculin Skin Test	≥10	78
[40]	Cross sectional	Hospital	362	General public	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	297
[41]	Cohort	Community	162	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	44
[42]	Cohort	Hospital	200	Healthcare workers	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	45
[43]	Cohort	Hospital	125	Healthcare workers	Tuberculin Skin Test	≥10	14
[44]	Cohort	Hospital	171	Healthcare workers	Tuberculin Skin Test	≥10	48
[45]	Cohort	Hospital	327	Sarcoidosis	Tuberculin Skin Test	≥10	33
[46]	Cohort	Community	572	General public	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	174
[47]	Cohort	Community	398	General public	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	96
[48]	Cohort	Community	80	Contacts	Interferon Gamma Release Assay	-	43
[49]	Cross sectional	Community	1523	Contacts	Tuberculin Skin Test	≥5	801
[50]	Cohort	Hospital	60	COVID	Tuberculin Skin Test	≥10	15

					Test		
[51]	Cross sectional	Hospital	730	Rheumatoid Arthritis	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	36
[52]	Cohort	Hospital	598	Healthcare workers	Tuberculin Skin Test	≥10	120
[53]	Cross sectional	Hospital	44	Rheumatoid Arthritis	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	6
[54]	Cross sectional	Hospital	401	Pregnancy	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	150
[55]	Cross sectional	Community	780	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥5	460
[56]	Cross sectional	Community	2351	General public	Interferon Gamma Release Assay	-	1226
[57]	Cross sectional	Community	663	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	292
[58]	Cross sectional	Hospital	75	Psoriasis	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	16
[59]	Cohort	Hospital	257	Inflammatory Bowel Disease	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	48
[60]	Cross sectional	Hospital	252	Pregnancy	Interferon Gamma Release Assay& Tubercul in Skin Test	≥5	71
[61]	Cross sectional	Community	200	Contacts	Tuberculin Skin Test	≥10	96
[62]	Cohort	Hospital	105	Psoriasis	Tuberculin Skin Test	≥10	33
[63]	Cross sectional	Community	5351	General public	Tuberculin Skin Test	≥10	794
[64]	Cohort	Hospital	15	Sarcoidosis	Tuberculin Skin Test	≥10	4
[65]	Cross sectional	Community	150	General public	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	105
[66]	Cohort	Community	144	General public	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	57
[67]	Cross sectional	Hospital	100	HIV	Tuberculin Skin Test	≥10	44
[68]	Cross sectional	Community	70	General public	Tuberculin Skin Test	≥10	7
[69]	Cohort	Community	1189	Contacts	Tuberculin Skin Test	≥10	661

					Test		
[70]	Cross sectional	Hospital	371	General public	Tuberculin Skin Test	≥10	227
[71]	Cohort	Community	1511	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	917
[72]	Cohort	Community	997	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥5	484
[73]	Cross sectional	Community	53	HIV	Interferon Gamma Release Assay	-	25
[74]	Cross sectional	Community	133	COVID	Interferon Gamma Release Assay	-	61
[75]	Cross sectional	Community	196	Diabetes	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	47
[76]	Cross sectional	Hospital	33	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	14
[77]	Cross sectional	Hospital	200	Healthcare workers	Tuberculin Skin Test	≥10	29
[78]	Cross sectional	Community	639	Diabetes	Interferon Gamma Release Assay& Tubercul in Skin Test	≥5	354
[79]	Cross sectional	Community	152	Contacts	Tuberculin Skin Test	≥10	62
[80]	Cohort	Community	1389	Contacts	Tuberculin Skin Test	≥10	1172
[81]	Cohort	Community	299	Contacts	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	35
[82]	Cohort	Hospital	168	General public	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	27
[83]	Cross sectional	Hospital	62	Sarcoidosis	Interferon Gamma Release Assay& Tubercul in Skin Test	≥10	16

## Discussion

The current research evaluated the existing data on the prevalence of Tuberculosis infection in Indian citizens based on the findings of the Tuberculin Skin Test and Interferon Gamma Release Assay tests, which are used to identify and diagnose TB preventive treatment (TPT) - eligible persons. Information was obtained from more than 30,932 Tuberculin Skin Test and Interferon Gamma Release Assay results spanning India's various regions. More than one-third of Indians had TBI, according to

community-based cohort studies, and the prevalence rose with age.

Using the Bayesian approach, other researchers have already observed a comparable frequency of TBI in India. Hoben and Dodd [84], using mathematical modeling, provided a 31.9% estimate of TBI in the Southeast Asian region, whereas Woodruff et al. [85] and Collins et al [86] estimated 31.9% and 33.9% prevalence among Indians, respectively. A crude TBI prevalence of 31% was also reported by the national TB prevalence study conducted in 2019–2021. When taken as a whole, these data show that India has a sizable reservoir of TBI patients, many

of whom may develop TB. The prevalence of TBI increases with age, particularly in adults and older persons, according to this review. National efforts to eradicate tuberculosis are hampered by the high incidence among these groups. In their mathematical model, Chong et al. [87] proposed that screening and giving TPT to 20% % 40 % of the elderly might lead to a 50% overall decrease in TB incidence in nations with intermediate TB prevalence. This study found that TBI has been steadily increasing over the past ten years, which suggests that TB incidence is still present. India's high-risk groups have worse than ideal TBI treatment rates (12%). To accomplish the goals, the World Health Organization (WHO) suggests prevention and treatment as crucial measures. India's National Strategic Plan (2017–25) for TB elimination rests on the three main pillars of prevention, detection, and treatment. Treating active TB lowers the incidence and prevalence of infectious TB, which in turn reduces transmission and incidence.

In contrast, treating TBI stops latent infection from developing into disease and lowers incidence immediately. There is evidence that treating active TB and TBI works in concert to lower the development of TB [88, 89]. Therefore, increasing TBI treatment could have a comparable benefit when active TB treatment levels are high (95%). Therefore, increasing the TPT will speed up the reduction of TB incidence and help India reach its End TB goals. Significant regional variations in TBI prevalence were noted in the current analysis. In regions like Delhi, Tamil Nadu, and others where active TB is common, a high burden was discovered, suggesting that TBI most likely has a high conversion rate to active TB disease. Implementing TBI case discovery is expensive [90]. But without TBI case-finding, the number of contagious people will rise, necessitating more aggressive case-finding and case-holding initiatives [90]. To extend the implementation period, India's National TB Elimination Programme (NTEP) currently advises aggressive case-finding and case-holding initiatives for regions with high TB prevalence [91]. TBI case-finding has a shorter implementation period when taking into account that both active and TBI case-finding have comparable cost sensitivity. The utilization of TBI diagnosis and therapy is essential for TBI case-finding. There is no perfect method for identifying and testing TBI [92, 93, 94] according to the evidence. The immune response to MTB antigens is measured by the two primary tests in use, TST and IGRA. Despite its low cost, TST presents logistical challenges, yields inconsistent results based on the type of purified protein derivative (PPD) employed, and is hindered globally by a lack of quality-assured tuberculin [95,96]. Conversely, IGRA requires a single facility visit and has a high specificity; nonetheless, the cost and reproducibility of the results are problems.

Evidence has recently raised doubts about the validity of these tests, indicating that only 10% of patients with viable MTB organisms that might cause illness exhibit immunoreactivity to these tests [97]. Additionally,

testing hesitation difficulties make it difficult to adopt comprehensive screening [98,99]. Newer regimens like three-month weekly rifapentine and isoniazid (3HP) regimens and one-month daily rifapentine and isoniazid (1HP) regimens are suggested by growing experience from clinical studies and field implementation. These regimens seem to be as effective as the daily isoniazid dosing-based preventive therapy, but they also have better safety profiles, higher acceptance rates, and higher completion rates.

The current review, which details the prevalence of TBI in India, was conducted by a multidisciplinary team using a thorough systematic literature search and manual reference searching. It was only possible to assess the pooled prevalence for community-based cohort studies. As well as providing a more thorough understanding of the burden of TBI across various categories and the general population, this improved the validity. The evidence did, however, represent every region of India except the east, which limited the ability to illustrate the findings throughout the country. Additionally, there were certain restrictions. Studies on TST were not divided into groups according to the PPD's intensity or the standardization of PPD employed. Additionally, there was inconsistent TBI diagnosis, particularly when employing the Tuberculin Skin Test approach, as some studies indicated TBI positive of greater than 5 mm regardless of the participation of immunocompromised patients. Furthermore, there is a chance that actual heterogeneity may not be well detected, particularly when a small number of papers are examined using the Higgins and Thompson I2 test and Cochran's Q.

## Conclusion

TPT beginning should be prioritized for areas with a high TBI prevalence. This is significant since the low predictive value of diagnostic tests and their high operating costs increase the likelihood of missing positive patients. In contrast to the existing strategy of active TB case-finding and case-holding for such locations, a more comprehensive approach is required that takes into account the "No test, treat only" approach after ruling out active TB for certain high disease burden geographies. The prevalence of TBI among people with multimorbidity—the co-occurrence of two or more chronic illnesses in one person—such as diabetics with rheumatoid arthritis or cardiovascular disease—needs greater investigation.

More data regarding TBI in inmates, migrants, and mental health facility patients must be produced. States with high rates of TBI and TB disease burden should be given priority for community-based screening to rule out active TB and carry out TPT policy at the population level. The data in this evaluation will help India implement more robust programmatic management of TBI since treating TBI is a prerequisite to reaching TB elimination goals. Overall, the current study's research showed that the prevalence of TBI was high and matched that of active TB, indicating that TBI could become an active TB illness.



There is a need for TBI country-specific initiatives aimed at population-level interventions because of the significant burden among residents in the northern and southern regions.

### Limitations

The absence of pure protein derivative (PPD) strength-based separation in TST trials and inconsistent TBI diagnosis were among the limitations of this study. This study's inability to detect actual heterogeneity stems from the fact that it only considered a small number of studies that were examined using the Q-statistic and I-squared tests. This study was not able to include articles written in languages other than English.

### Recommendations

For the sake of resource efficiency, this study suggests that in areas with high rates of tuberculosis infection (TBI), TB prevention treatment (TPT) be prioritized using a "No test, treat only" strategy. In order to effectively manage programs for India's TB elimination goals, targeted study on TBI in particular communities is essential.

### Data Availability

Data is available upon request.

### Author contributions

All authors contributed to the design of the research. PBM and RPJ collected and analyzed the data. BB wrote the manuscript. RPJ and PBM edited the paper. All authors read and approved the paper.

### List of abbreviations

TB- Tuberculosis  
TBI- Tuberculosis Infection  
PRISMA- Preferred Reporting Items for Systematic Reviews and Meta-Analysis  
TPT- Tuberculosis Preventive Treatment  
MTB- Mycobacterium tuberculosis  
WHO- World Health Organization  
TST- Tuberculin skin test  
IGRA- Interferon-Gamma Release Assay  
NTEP- National TB Elimination Programme  
PPD- Purified protein derivative

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### Conflict of interest

The authors have no conflicting interests to declare.

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