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Prevalence of tobacco consumption among pulmonary tuberculosis patients and its correlation with tuberculosis incidence: a systematic review and meta-analysis in the Indian context

Aninda Debnath,[1] Ravindra Nath,[2] Anubhav Mondal,[1] Pankaj Chandrabhan Nathe,[1] Jugal Kishore,[1] Pranav Ish,[3] Vidushi Rathi,[4] Jagdish Kaur[5]

[1]Department of Community Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi; [2]Department of Community Medicine, Teerthanker Mahaveer Medical College and Research Center, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh; [3]Department of Pulmonary Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi; [4]Department of Pulmonary Medicine, Vallabhbhai Patel Chest Institute, New Delhi; [5]Regional Adviser, Tobacco free Initiative, World Health Organization Regional Office for South-East Asia, New Delhi, India

Correspondence: Ravindra Nath, Department of Community Medicine, Teerthanker Mahaveer Medical College and Research Center, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India. Tel.: 9818447356. E-mail: rnath24.9@gmail.com

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Abstract

Tuberculosis (TB) and tobacco use are two intertwined public health challenges that significantly impact low- and middle-income countries, particularly India, which bears the highest global TB burden. Tobacco use exacerbates TB risk, progression, and treatment outcomes. Despite the established association, research on the prevalence of smoking and smokeless tobacco (SLT) use among pulmonary TB (PTB) patients in India remains limited. This systematic review and meta-analysis aim to estimate the prevalence of smoking and SLT use among PTB patients in India and evaluate the association between tobacco consumption and TB incidence and treatment outcomes. A systematic search was conducted across four databases (PubMed, Embase, Web of Science, and Scopus) for studies published up to September 30, 2024, adhering to PRISMA guidelines. Pooled prevalence estimates were calculated using random-effects models, and subgroup analyses examined variations by gender and treatment stage. Odds ratios (ORs) were used to assess the association between smoking and PTB. Sensitivity analyses and Egger's test were conducted to evaluate heterogeneity and publication bias. A total of 27 studies (n=9593 subjects) were included. The pooled prevalence of smoking among PTB patients was 31% [95% confidence interval (CI): 25-36%], while SLT use was 19% (95% CI: 13-26%). PTB patients were 2.5 times more likely to be smokers than non-TB controls (OR=2.51, 95% CI: 1.36-4.62). Smoking prevalence was highest among newly diagnosed patients (42%) and predominantly observed among males (38%). High heterogeneity (I^2>98%) was observed across studies. To conclude, tobacco use is highly prevalent among Indian PTB patients, significantly contributing to disease burden. Integrating tobacco cessation strategies into India's National TB Elimination Program is critical to improving TB outcomes, reducing transmission, and addressing the dual burden of tobacco and TB.

Key words: tuberculosis, tobacco consumption, pulmonary tuberculosis, smokeless tobacco, systematic review and meta-analysis.

Introduction

Tuberculosis (TB) and tobacco use are two intertwined global health crises that disproportionately burden low- and middle-income countries (LMICs) [1]. TB remains one of the top infectious causes of death worldwide, with 10.6 million new cases and 1.6 million deaths in 2021. Simultaneously, tobacco use claims 7.7 million lives annually, impacting over 1 billion individuals globally [2]. These epidemics are not just coexisting; they are synergistic, with tobacco consumption exacerbating the risk, progression, and treatment outcomes of TB [3]. This dual burden poses a critical challenge to public health systems, particularly in resource-constrained settings like India, which bears the world's highest TB burden.

India, with its unique socio-cultural landscape, faces a complex epidemic of tobacco consumption [4]. Smoking, often in the form of bidis, and smokeless tobacco (SLT) use are deeply entrenched habits that significantly contribute to India's non-communicable and communicable disease burden [5]. Tobacco smoke weakens pulmonary immune defences, impairing alveolar macrophages that play a critical role in combating Mycobacterium tuberculosis, thereby increasing the risk of active TB and complicating treatment outcomes [6]. Despite these established mechanistic links, research quantifying tobacco's prevalence among pulmonary TB (PTB) patients and its impact on treatment outcomes remains fragmented in the Indian context.

Moreover, while smoking's association with TB has been extensively studied globally, smokeless tobacco use—a highly prevalent form of consumption in South Asia—has received limited attention. SLT's impact on TB progression and treatment outcomes remains underexplored, even though it constitutes a significant proportion of tobacco use in India. Understanding both smoking and SLT prevalence among PTB patients is essential to designing comprehensive, culturally appropriate interventions. This systematic review and meta-analysis addresses critical gaps in understanding the prevalence of smoking and SLT use among PTB patients in India and evaluates the association between tobacco consumption and TB incidence.

Methods

Study design

This meta-analysis was conducted to evaluate the prevalence of tobacco consumption among patients with PTB and to examine the correlation between tobacco use and TB incidence within the Indian context. The review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, ensuring a structured and transparent approach to the study selection, data extraction, and analysis processes. The study was registered with PROSPERO (Registration ID: CRD42024605601).

Search strategy

A comprehensive literature search was conducted across four major electronic databases: PubMed, Embase, Web of Science, and Scopus. The search strategy was designed to capture a broad range of studies by combining relevant keywords and Medical Subject Headings (MeSH terms) related to "tuberculosis," "tobacco consumption," "smoking," "smokeless tobacco," and "India." To ensure thoroughness, the strategy included synonyms and variations of these terms, and filters were applied to include only studies published or translated in English. Studies published up to September 30, 2024, were included from the inception of the databases. Additionally, references of included articles and related reviews were manually screened to identify further studies that might not have been captured in the initial database search (*Supplementary Table 1*).

Eligibility criteria

Studies were selected based on predefined eligibility criteria. Observational studies, including cross-sectional, cohort, and case-control designs, were considered if they assessed the prevalence of tobacco use among individuals diagnosed with pulmonary TB or if they evaluated the association between tobacco consumption and the incidence or progression of pulmonary TB. Only studies conducted within India were eligible for inclusion, focusing on adults diagnosed with pulmonary TB, those currently undergoing treatment, or recently completed treatment. Studies that reported the number of users of any form of tobacco (smoking or smokeless) were included. Exclusion criteria were applied to omit studies focused on latent TB, symptomatic TB without a confirmed diagnosis, extrapulmonary TB (EPTB), multidrug-resistant TB (MDR-TB), or extensively drug-resistant TB (XDR-TB). Studies that included EPTB, MDR-TB, or XDR-TB patients alongside PTB but did not explicitly report tobacco use within these subgroups were also excluded.

Data extraction and management

All citations retrieved from the electronic searches were imported into Rayyan software in 2023, and duplicate entries were systematically removed. Three independent researchers (RN, AM, and PN) conducted a comprehensive screening of titles and abstracts from the retrieved studies to identify articles eligible for potential inclusion. Any disagreements during the screening process were resolved through discussion and consensus. If necessary, unresolved discrepancies were further consulted with another co-author (AD) to decide on the inclusion of studies for the next step. The full texts of identified articles were then reviewed by the same independent researchers (RN, AM, and PN), adhering to a pre-defined set of eligibility criteria to determine their relevance for inclusion in the review. For cases where additional information was required to resolve eligibility queries, collaboration with the remaining authors was sought. The reasons for excluding articles were meticulously documented at each stage, and any remaining uncertainties or disagreements were addressed by a third reviewer (AD).

Risk of Bias and Quality Assessment- The quality of the included studies was assessed using the Joanna Briggs Institute (JBI) tools, specifically tailored for cross-sectional and case-control designs [7]. Two independent reviewers evaluated the risk of bias, focusing on domains such as participant selection, outcome measurement, and statistical analysis reliability. Discrepancies were resolved through discussion until a consensus was reached. Studies identified as having a high risk of bias were not excluded but were included in sensitivity analyses to evaluate their potential impact on the overall results.

Data analysis and statistical methods

All statistical analyses were performed using STATA software (version 18). The prevalence of smokers and smokeless tobacco users was calculated separately, with the number of tobacco users as the numerator and the total number of PTB patients as the denominator. To evaluate the association between tobacco use and PTB incidence, pooled log odds ratios were calculated. A random-effects model, utilizing the Der Simonian and Laird method, was applied for all pooled estimates to account for variability across studies. Statistical heterogeneity was assessed using the I^2 statistic, where higher values indicated greater heterogeneity. Potential outliers were identified using leave-one-out sensitivity analysis to examine the robustness of the meta-analysis results. Publication bias was assessed using Egger's test and funnel plots. Sensitivity analyses were conducted by excluding low-quality studies, with pooled estimates recalculated to assess their influence on the overall findings. Subgroup analyses were performed to explore variations in outcomes by gender, study population characteristics, and the stages of TB treatment at the time of data collection.

Ethical Considerations- As this meta-analysis is based on the secondary analysis of existing data from published studies, formal ethical approval was not required. However, the review adhered to high ethical standards by ensuring transparency in reporting, accuracy in data extraction, and objectivity in the synthesis of findings.

Results

The search initially identified a total of 1,112 records, distributed as follows: 371 from Embase, 323 from PubMed, 247 from Scopus, and 171 from Web of Science. After the removal of 749 duplicate records, 363 unique articles were screened. During the title and abstract screening phase, 279 studies were excluded for not meeting the predefined inclusion criteria, resulting in 84 reports being sought for full-text retrieval. Of these, 11 reports could not be accessed and were excluded from further analysis. A detailed assessment of the remaining 73 full-text articles was carried out, leading to the exclusion of 46 studies. The primary reasons for exclusion were: wrong study population (n = 27), inappropriate study design (n = 8), and lack of relevant outcomes (n = 11). Ultimately, 27 studies met all eligibility criteria and were included in this systematic review and meta-analysis. The selection process is outlined in the PRISMA flow diagram (Figure 1).

Study characteristics

This meta-analysis included 27 studies published between 2003 and 2022, examining the prevalence of tobacco consumption (smoking and smokeless tobacco) among patients diagnosed with pulmonary tuberculosis (PTB) across various regions of India [8-34]. The total sample size across these studies was 9,593 PTB patients, with individual study populations ranging from 23 participants (in Rao et al., 2009-10, Central India) to 2,350 participants (in Mahishale et al., 2012-13, South India). The studies were geographically diverse, representing multiple regions of India. South India had the largest representation, contributing 33.3% of the studies (n = 9), followed by North India with 25.9% (n = 7), Central India with 22.2% (n = 6), and West India with 7.4% (n = 2). East India, North East India, and a Pan-India study each accounted for 3.7% (n = 1) of the studies. Most studies were cross-sectional in design (74.1%, n = 20), followed by case-control studies (14.8%, n = 4) and cohort studies (11.1%, n = 3). Additionally, nine studies included a comparator group to evaluate differences between tobacco users and non-users among PTB patients; of these, five were cross-sectional and four were case-control studies.

Among the 9,593 PTB patients, 1,799 were smokers. The prevalence of smoking varied significantly across studies. The highest prevalence (81%) reported in the study by Kanakia et al. [21] whereas the lowest (2%) observed in the study by Mahishale et al. [29] In addition to smoking, 10 studies reported on the use of SLT among PTB patients. Out of 3,305 PTB patients covered in these studies, 631 were identified as SLT users. The study by Marak et al. reported the highest prevalence (61.8%) of SLT use, while the study by Gupta et al. documented the lowest prevalence (2.5%) [10,18] (*Supplementary Tables 2 and 3*)

Prevalence of smoking among pulmonary TB patients

The pooled prevalence of smoking among PTB patients was 31% (95% CI: 25%–36%). We used a random-effects model to account for significant heterogeneity across studies. The heterogeneity was high (I^2 = 98.98%), indicating variability in smoking prevalence across the different populations studied (Figure 2a). The assessment of publication bias indicated asymmetry in the funnel plot, with Egger's regression test confirming significant small-study effects ($p < 0.001$) (Figure 2b). Nonetheless, the Trim-and-Fill method did not identify any missing studies, suggesting minimal impact of publication bias on the pooled estimate. Leave-one-out sensitivity analysis showed that the overall prevalence estimate remained consistent despite the exclusion of individual studies, supporting the robustness of the pooled prevalence estimate (*Supplementary Figure 1*).

Prevalence of SLT users among pulmonary TB patients

The pooled prevalence of SLT use among PTB patients was 19% (95% CI: 13%–26%), also calculated using a random-effects model due to high heterogeneity (I^2 = 97.62%) among the included studies (Figure 3a). Similar to the smoking prevalence analysis, the assessment of publication bias for SLT use indicated asymmetry in the funnel plot, with Egger's regression test yielding statistically significant results ($p < 0.001$), suggesting possible small-study effects (Figure 3b). However, the Trim-and-Fill method showed no imputed studies. A leave-one-out sensitivity analysis further confirmed the stability of the pooled prevalence estimate, as removing individual studies did not significantly alter the results (*Supplementary Figure 2*).

Correlation between tobacco use and pulmonary TB incidence

The pooled log odds ratio comparing smoking prevalence between PTB patients and non-TB controls was 2.51 (95% CI: 1.36–4.62), indicating that PTB patients are approximately 2.5 times more likely to be smokers than individuals without TB. This OR was calculated using a random-effects model, which accounted for substantial heterogeneity across studies (I^2 = 95.53%) (Figure 4a). Assessment of publication bias for this analysis also indicated asymmetry in the funnel plot, with Egger's regression test confirming significant small-study effects ($p < 0.001$) (Figure 4b). However, the Trim-and-Fill method identified no missing studies, implying that publication bias likely has minimal impact on the pooled OR estimate. Leave-one-out sensitivity analysis demonstrated that the pooled OR remained stable when individual studies were sequentially excluded, further supporting the robustness of the association between smoking and PTB status (*Supplementary Figure 3*).

Subgroup analysis

Subgroup analysis was done by treatment stage, gender, and study population. When analysed by treatment stage, the smoking prevalence among PTB patients who had completed treatment was 19% (95% CI: 1% to 38%). In contrast, patients who had not started treatment showed a higher pooled prevalence of 42% (95% CI: 28% to 57%). For those currently undergoing treatment, the prevalence was 24% (95% CI: 19% to 30%). A test for group differences was not statistically significant ($Q = 5.86$, $p = 0.05$) (*Supplementary Figure 4*). We conducted a similar analysis for SLT users, which also showed a similar pattern: those who were newly diagnosed had a higher prevalence of 27% (95% CI: 8%–45%), which decreased during treatment to 19% (95% CI: 12%–27%) but increased again after treatment to 21% (95% CI: 9%–32%). However, the differences in SLT prevalence across these subgroups were not statistically significant (*Supplementary Figure 5*). The gender-based subgroup analysis indicated a marked disparity in smoking prevalence between male and female PTB patients. Among females, the pooled smoking prevalence was 1% (95% CI: 1% to 2%). In contrast, the prevalence among male patients was significantly higher at 38% (95% CI: 21% to 54%). Statistical testing for group differences confirmed a significant difference in smoking prevalence between male and female patients ($Q = 22.05$, $p = 0.00$) (*Supplementary Figure 6*).

Meta-regression

The meta-regression analyses explored the impact of study-level variables on smoking prevalence among PTB patients. The year of study showed no significant effect on smoking prevalence ($p = 0.792$), suggesting consistency over time (*Supplementary Figure 7*). The sample size of TB patients was significantly associated with lower smoking prevalence in larger studies ($p = 0.001$), hinting at potential small-study effects (*Supplementary Figure 8*). The proportion of male participants was not a significant moderator ($p = 0.616$), indicating that gender composition did not notably influence smoking rates (*Supplementary Figure 9*).

Discussion

This systematic review and meta-analysis revealed that 31% of PTB patients in India are smokers, while 19% consume smokeless tobacco. Additionally, smokers were found to be 2.5 times more likely to develop active TB compared to non-smokers.

The prevalence of smoking among PTB patients in this study is consistent with global observations of higher smoking rates among TB patients compared to the general population, though it is lower than reported rates in South Africa (56%-60%) and Malaysia (46.2%) [35,36]. India's prevalence of smoking among TB patients is nearly three times higher than the general population in India (10.7%, GATS-2) [4]. Similar trends have been observed in neighbouring countries like Bangladesh and Pakistan, where smoking prevalence among TB patients (22.5%) surpasses general population rates (16.4% and 11.5%, respectively), though these figures remain slightly lower than India's, likely reflecting variations in cultural and socio-economic factors [37]. In contrast, the prevalence of SLT use among TB patients in India (19%) is slightly lower than the general population (21.4%, GATS-2), mirroring trends in South Asia where SLT remains a significant public health concern, though underexplored in TB-specific studies.

Globally, data on SLT use among TB patients are scarce, particularly outside South Asia, underscoring the need for further research.

Smokers are at a significantly higher risk of developing TB due to the profound effects of smoking on alveolar macrophages, which are responsible for engulfing and destroying Mycobacterium tuberculosis. This impairment occurs because the oxidative stress and inflammation caused by smoke toxins reduce the antimicrobial activity of these immune cells [6]. Furthermore, the epithelial lining of the respiratory tract is damaged by smoking, creating an environment more susceptible to bacterial colonization and infection. Smoking also suppresses adaptive immunity by reducing the activation and function of T-cells, which are essential for controlling TB infections. This immune suppression contributes to both increased susceptibility to primary infection and reactivation of latent TB [6]. Chronic inflammation caused by smoking leads to structural lung damage, further increasing the risk of TB and exacerbating disease progression [38]. Additionally, smoking is often associated with co-morbid conditions like chronic obstructive pulmonary disease (COPD), which weaken respiratory defences and increase vulnerability to infections [39]. Behavioural factors, such as greater exposure to crowded or poorly ventilated environments, also play a role in higher TB transmission rates among smokers [40].

The subgroup analyses revealed significant gender differences in tobacco consumption among PTB patients, with smoking prevalence among males at 38%, substantially higher than the 1% observed in females. This stark disparity aligns with national data from the GATS-2 survey, which similarly reports that 19% of males in the general population are smokers compared to only 2% of females. A similar trend is seen in SLT use, where 29.6% of males use SLT compared to 12.8% of females [4]. These findings underscore the male-dominated tobacco consumption patterns in India, driven by cultural norms, social acceptance, and gender-specific roles, which normalize tobacco use among men while stigmatizing it among women [41,42]. The higher rates of smoking and SLT use among males not only amplify their vulnerability to TB but also position them as a critical target group for tobacco cessation interventions within TB control programs.

The subgroup analyses highlight significant differences in tobacco consumption across the treatment stages of PTB patients. Smoking prevalence was highest among newly diagnosed patients who had not yet initiated treatment, with a pooled prevalence of 42%. This rate declined among patients currently undergoing treatment (24%) and was lowest among those who had completed treatment (19%). A similar pattern was observed for smokeless tobacco (SLT) use, with newly diagnosed patients reporting the highest prevalence (27%), followed by those undergoing treatment (19%) and those who had completed treatment (21%). One primary reason is the severe respiratory symptoms and impaired lung function associated with

TB, which may make smoking physically intolerable due to increased coughing, breathlessness, and pain during inhalation [43,44]. Additionally, the diagnosis of TB often acts as a significant health warning, prompting individuals to reassess their lifestyle choices, including smoking, due to heightened awareness of its detrimental impact on lung health and recovery [45]. Medical interventions for TB treatment also frequently include counselling or advice from healthcare professionals to quit smoking, as it is known to delay TB recovery, exacerbate lung damage, and increase the risk of relapse [46]. Social factors, such as stigma or family pressure, may further contribute, as smoking cessation is often seen as a necessary step to mitigate additional health risks and improve public perception. These trends underscore the critical need to address tobacco use early in TB care, as behavioural patterns established prior to diagnosis may significantly influence treatment outcomes and disease progression. The Government of India mandates that medical colleges establish Tobacco Cessation Centres (TCC) within their premises to provide comprehensive counselling services for individuals using tobacco. These centres will also play a pivotal role in extending support to newly diagnosed tuberculosis (TB) patients, integrating tobacco cessation counselling as part of their holistic care and management.

These findings collectively highlight the crucial window of opportunity at the early stages of TB diagnosis to implement integrated tobacco cessation strategies. Comprehensive programs that include counselling, behavioural interventions, and pharmacological support can significantly enhance TB treatment outcomes and promote long-term cessation. Addressing tobacco use concurrently with TB management not only mitigates immediate health risks but also contributes to broader disease control efforts, reducing the dual burden of TB and tobacco on public health.

Policy and programmatic implications

Given the strong association between tobacco use and TB outcomes, integrating tobacco cessation into TB control frameworks is both a clinical and public health imperative. The following policy and programmatic actions are recommended.

Systematic Screening and Tobacco Cessation in TB Care: Tobacco screening should be a mandatory component of TB diagnosis, with cessation counselling provided using evidence-based frameworks like the 5A's (Ask, Advice, Assess, Assist, and arrange for follow-up) and 5R's (relevance, Risks, Rewards, Roadblocks and Repetition). DOTS centers should be equipped to offer cessation services, including pharmacological aids like nicotine replacement therapy (NRT) and medications such as bupropion, to support quit attempts.

Leveraging Existing Frameworks: India's robust tobacco control policies under National Tobacco Control Programme (NTCP) and Cigarettes and Other Tobacco Products Act (COTPA) should be better integrated with National Tuberculosis Elimination Programme (NTEP) to address the dual burden of tobacco and TB [47]. Strengthening enforcement of COTPA provisions, such as bans on public smoking and regulating tobacco sales near schools and healthcare facilities, is critical. Collaborative implementation of NTCP and NTEP can enhance resource efficiency and expand access to cessation services.

Tobacco Cessation as a Performance Metric: Incorporating tobacco cessation metrics into TB program evaluations, such as the percentage of patients screened, counselled, and successfully quitting tobacco, will ensure accountability and sustained focus. These metrics to be monitored regularly and tied to program outcomes to drive continuous improvement.

Strengths and Limitations- This study is the first to provide pooled estimates of smoking and SLT prevalence among PTB patients in India, with stratified analyses by gender, treatment stage, and regional factors offering detailed insights. The large sample size and comprehensive search strategy enhance the reliability of the findings. However, high heterogeneity across studies, the predominance of cross-sectional designs, and potential publication bias limit causal inferences and generalizability to other settings. Future longitudinal research is essential to establish causality and evaluate the long-term impact of integrated TB-tobacco control programs. It can be achieved via incorporating TB related details in the already existing clinical proforma of Tobacco Cessation Centre.

Conclusions

This systematic review and meta-analysis shows the critical intersection of tobacco use and pulmonary tuberculosis in India, revealing high prevalence rates of smoking and smokeless tobacco among TB patients and a significant association between smoking and TB incidence. The findings highlight an urgent need to integrate robust tobacco cessation interventions into India's National TB Elimination Program. By addressing this dual burden through synergistic public health strategies, substantial improvements in TB treatment outcomes and reductions in disease transmission can be achieved, advancing India’s progress toward TB elimination goals.

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Online supplementary material
Supplementary Table 1. Search strategy (30/09/24).
Supplementary Table 2. Characteristics of the study.
Supplementary Table 3. Risk of bias assessment.
Supplementary Figure 1. Leave-one-out sensitivity analysis for smoking prevalence among pulmonary tuberculosis patients.
Supplementary Figure 2. Leave-one-out sensitivity analysis for smokeless tobacco users among pulmonary tuberculosis patients.
Supplementary Figure 3. Leave one out sensitivity analysis for association of tobacco smoking with pulmonary tuberculosis.
Supplementary Figure 4. Smoking prevalence among pulmonary tuberculosis patients stratified by treatment stage.
Supplementary Figure 5. Smokeless tobacco use prevalence among pulmonary tuberculosis patients stratified by treatment stage.
Supplementary Figure 6. Smoking prevalence among pulmonary tuberculosis patients by gender.
Supplementary Figure 7. Bubble plot of meta-regression showing the relationship between publication year and smoking prevalence among pulmonary tuberculosis patients.
Supplementary Figure 8. Bubble plot of meta-regression showing the relationship between sample size and smoking prevalence among pulmonary tuberculosis patients.
Supplementary Figure 9. Bubble plot of meta-regression showing the relationship between proportion of male and smoking prevalence among pulmonary tuberculosis patients.

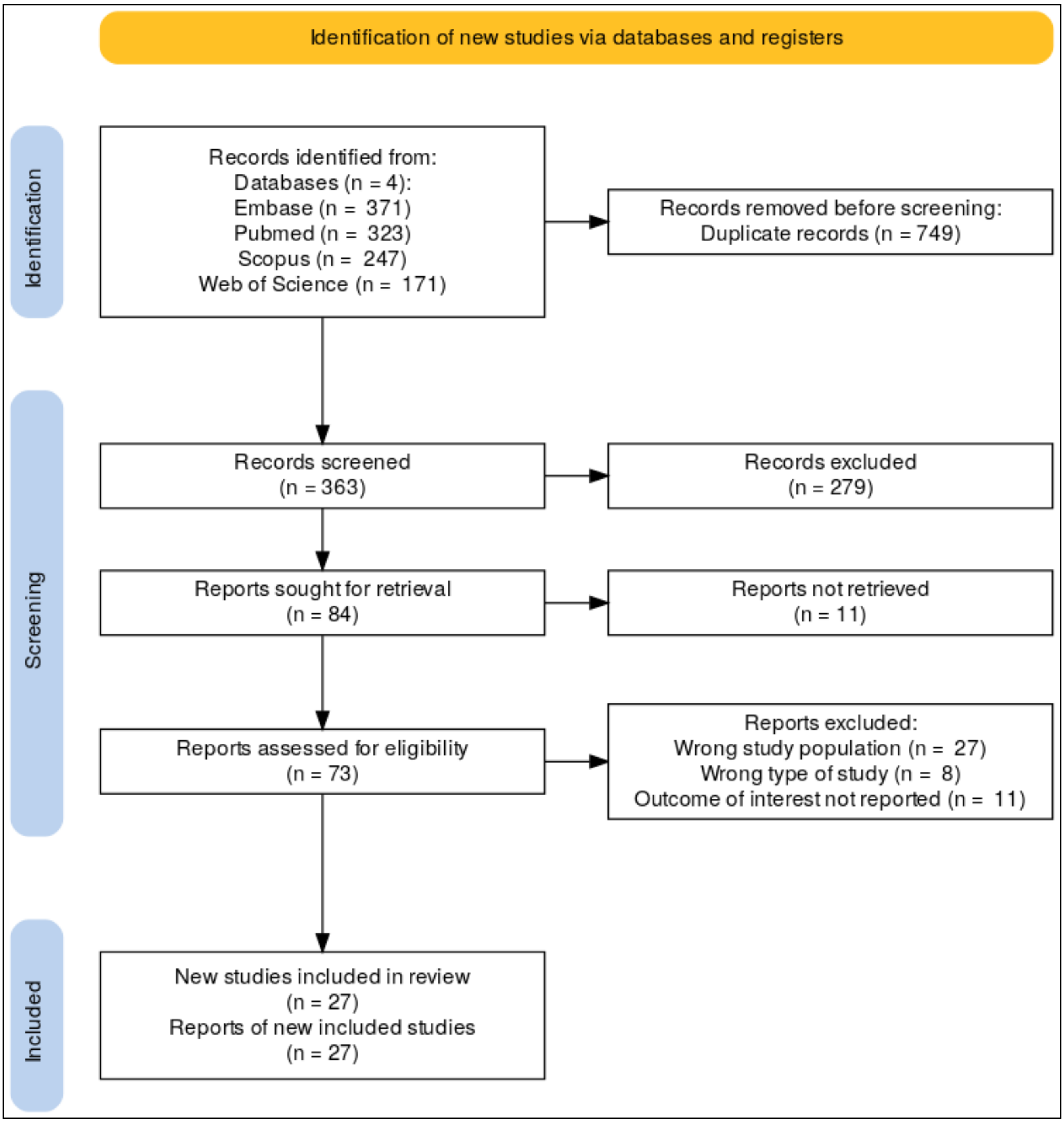

Figure 1. PRISMA flow diagram for study selection.

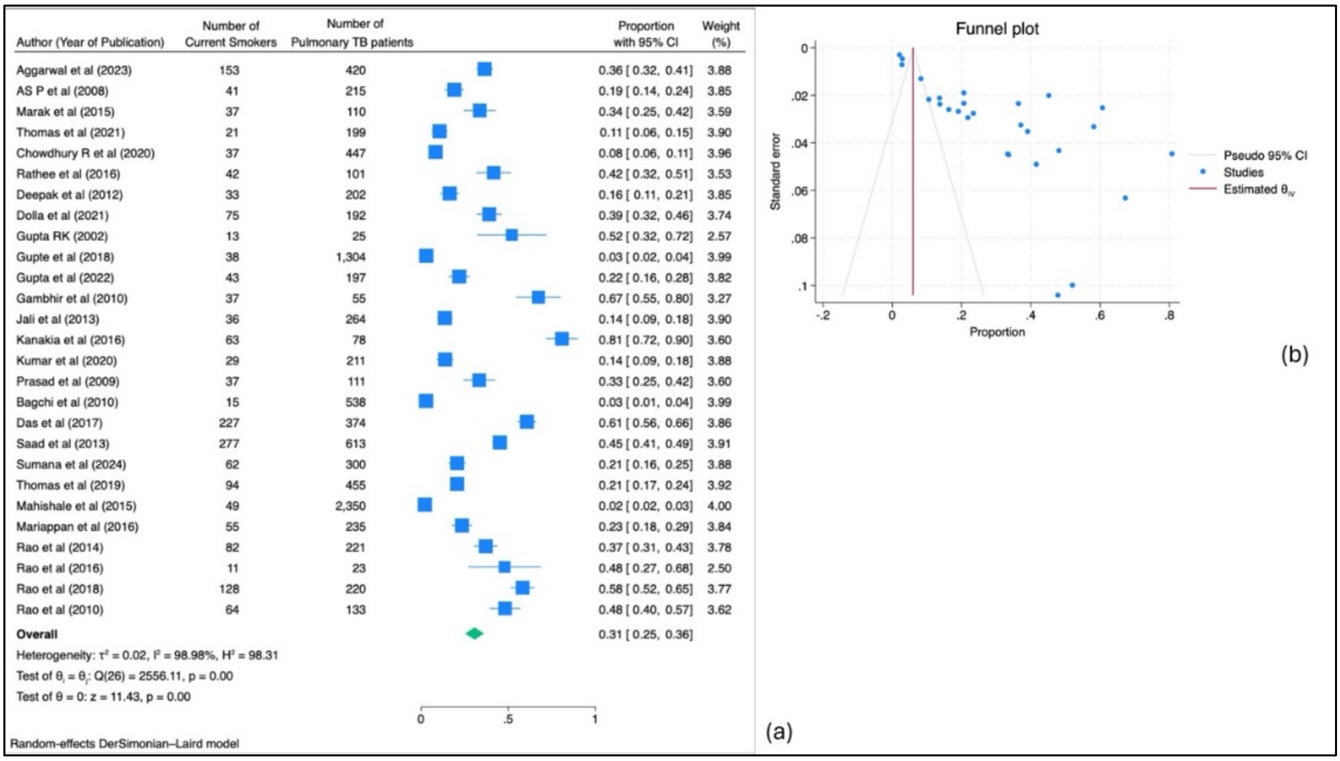

Figure 2. a) Forest plot of smoking prevalence among pulmonary TB patients; b) funnel plot for publication bias in smoking prevalence among PTB patients.

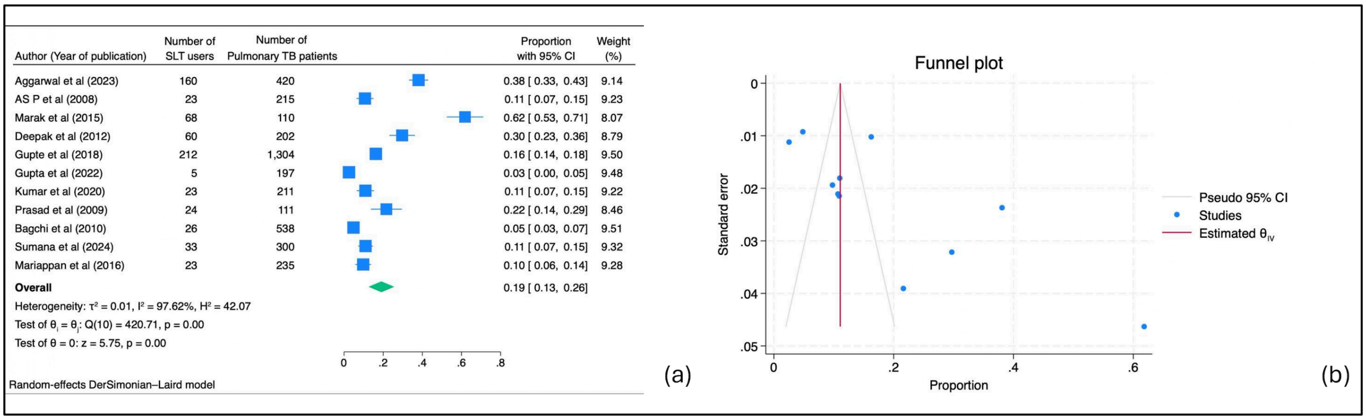

Figure 3. a) Forest plot of smokeless tobacco prevalence among pulmonary TB patients; b) funnel plot for publication bias in SLT prevalence among PTB patients.

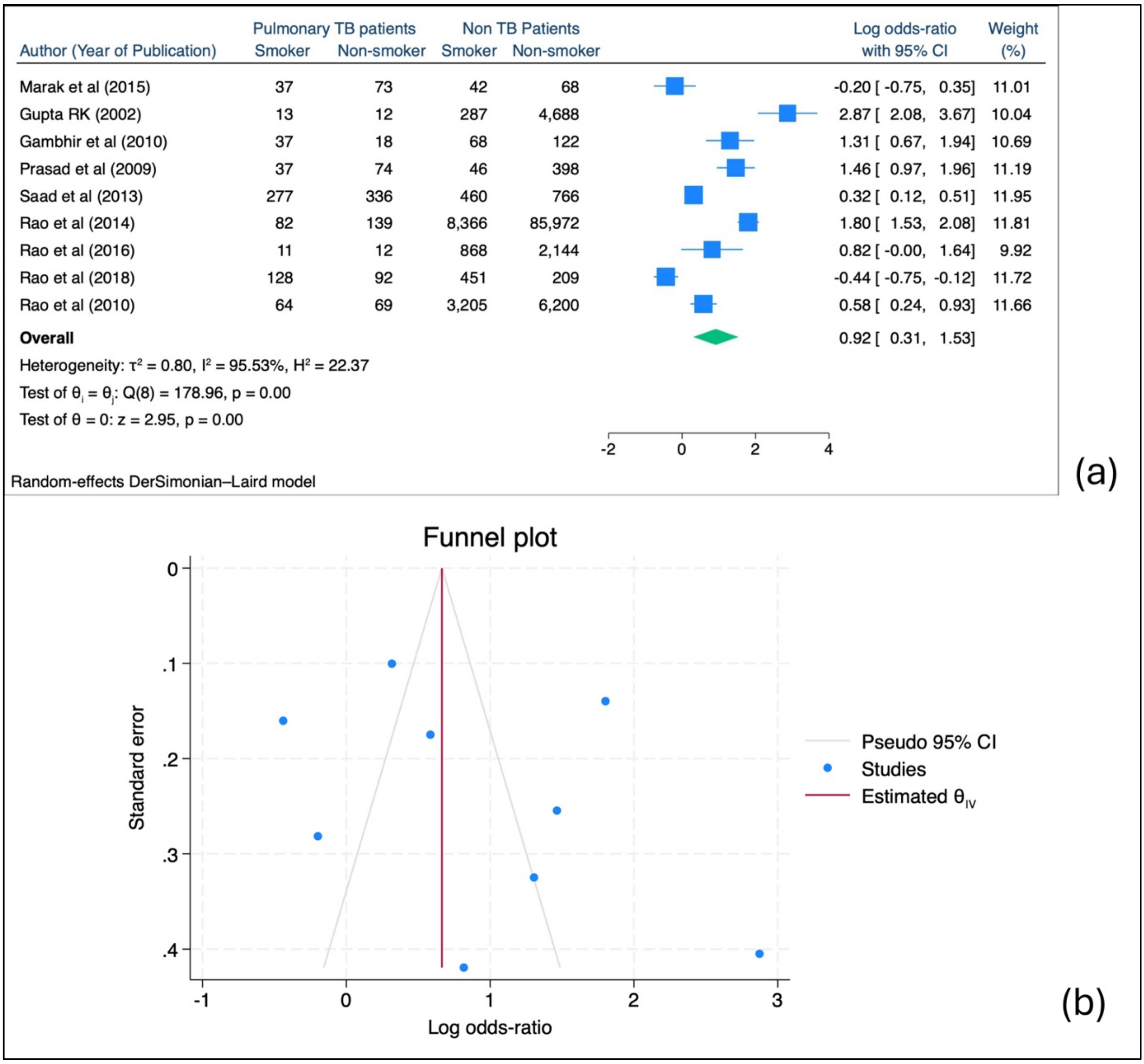

Figure 4. a) Forest plot of odds ratios for smoking in PTB patients vs non TB participants; b) funnel plot of odds ratios for smoking in PTB patients vs non TB participants.