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RESEARCH

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Risk Factors For Tuberculosis Treatment Failure in Five High Tuberculosis Burden Countries: A Scoping Review

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Abstract

Treatment failure for tuberculosis (TB) remains a serious public health problem, particularly in countries with high TB incidence, since it leads to drug-resistant TB, higher mortality rates, and persistent transmission. This comprehensive research, conducted in five countries with large tuberculosis burdens China, India, Indonesia, Pakistan, and the Philippines aims to identify and define risk factors for treatment failure in adult patients with drug-sensitive tuberculosis (DS-TB) and drug-resistant tuberculosis. The study used a review technique based on the Joanna Briggs Institute (JBI) criteria and the Population-Concept-Context (PCC) framework. The population consisted of adult tuberculosis patients, the concept was on risk variables linked with treatment failure, and the environment was confined to the five high-burden nations. Literature searches were undertaken in PubMed, Scopus, and EBSCOHost for studies published between 2015 and 2025, and study selection followed the PRISMA-ScR standards. The final analysis includes 19 studies that fulfilled the inclusion criteria. Clinical variables accounted for 73.7% of all identified risk factors, followed by demographic factors (68.3%) and microbiological factors (57.9%). Behavioral and social aspects were recorded in 31.6% and 26.3% of studies, respectively. Several risk variables were documented in numerous nations, however the prevailing risk profiles differed by country. Older age and malnutrition were prevalent in China; male sex and underweight status in India; older age, low treatment compliance, and limited tuberculosis-related knowledge in Indonesia; pulmonary cavitation, prior tuberculosis history, and drug resistance in Pakistan; and working-age characteristics, positive sputum smear results, and treatment discontinuation in the Philippines. These data show that, whereas some similar drivers of treatment failure exist in high-burden nations, the relative importance of specific risk variables differs by country. As a result, TB control programs should mix integrated and patient-centered methods with country-specific treatments tailored to the predominant risk profiles observed in each context.

Keywords: Tuberculosis, Treatment failure, Risk factors, High-Burden Countries.

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1. INTRODUCTION

Tuberculosis (TB) is still one of the leading causes of mortality from infectious illnesses globally. A WHO report from 2024 anticipated 10.6 million new cases and 1.3 million deaths from TB in 2023, making the illness a severe public health issue ([World Health Organization, 2024](#)). The five nations having the largest TB burden, India, Indonesia, China, the Philippines, and Pakistan, more than 60% of worldwide infections occur in these populations, making treatments success rates critical to meeting global TB eradication objectives ([World Health Organization, 2024](#)). Although these nations have a high Tbburden, they differ I terms of health-care capability, drug-resistance epidemiology, and sosioeconomic circumstances, all of which may have an impact on treatment results and variables associated with treatmens failure. As a result, analysing these nations together is critical for finding risk factors that are common across context as well as those that may be context specific, resulting in a more thorough knowledge of treatment failure in high-TB burden areas. The substantial epidemiological burden, coupled with heterogeneous health system challenges, makes TB control efforts in these countries a critical global public health priority.

TB treatment failure is a crucial indicator in TB program evaluation, as it is directly linked to ongoing transmission and the emergence of drug resistance, such as multidrug-resistant tuberculosis (MDR-TB) and rifampicin-resistant tuberculosis (RR-TB) ([Dheda, 2017](#)). Research shows that various clinical, demographic, behavioral, microbiological, and socio-structural factors contribute to unsuccessful treatment outcomes ([Akhmedullin et al., 2025](#)). A regional meta-analysis in Asia found that older age, male gender, smoking, alcohol use, and noncompliance are all related with failed treatment failure ([Oh, Makmor-Bakry, Islahudin, & Wong, 2023](#)). A large cohort research in China revealed male gender, older age, prior treatment history, and servere clinical problems as risk factors for unsatisfactory results, including treatment failure ([Gilmour, Xu, Bai, Alene, & Clements, 2022](#)). Other studies also report that TB patients with DM as a comorbidity have a twofold risk of treatment failure. In the MDR/RR-TB group, factors such as previous medical history, high baseline culture positivity, and poor nutritional status have been shown to increase the risk of failure ([Akhmedullin et al., 2025](#); [Sureskiarti et al, 2020](#); [Soeroto, Pratiwi, Santoso, & Lestari, 2021](#)). In addition, social factors such as financial difficulties, negative stigma, and barriers to accessing services also play a significant role, and high job mobility has also been reported to affect treatment success in South Asia and Southeast Asia ([Craig, Daftary, Engel, O'Driscoll, & Ioannaki, 2017](#); [Oh et al., 2023](#)).

Although many studies have assessed the determinants of TB treatment failure, most studies were conducted in specific countries, focused on a single clinical group, or assessed risk factors separately. Thus, the current state-of-the-art research shows that the available evidence remains fragmented and does not provide a comparative understanding of variation in risk factors across the five countries most affected by tuberculosis. To date, there has been no comprehensive study mapping all clinical, behavioral, microbiological, social, and health system determinants in both drug-sensitive and drug-resistant tuberculosis patients across countries. The lack of integration of this evidence represents an important scientific gap, given that epidemiological characteristics, resistance profiles, and health service capacities can vary significantly between countries. Therefore, systematic mapping of evidence is needed to assess the consistency, variation, and gaps in knowledge regarding risk factors for treatment failure in global priority regions. Specifically, this review sought to answer the following question: What clinical, demographic, microbiological, behavioral, and social risk factors are associated with tuberculosis treatment failure among adult patients with drug-sensitive tuberculosis (DS-TB) and drug-resistant tuberculosis (DR-TB) in China, India, Indonesia, Pakistan, and the Philippines, and how do these factors vary across the five countries?.

A scoping review is an appropriate approach for broadly identifying and synthesizing determinants of treatment failure across these five high-burden countries. Referring to the Arksey & O'Malley framework and JBI guidelines, this study aims to map all risk factors, predictors, and determinants of TB treatment failure in adult patients, including drug-sensitive and drug-resistant TB (Arksey, H., & O'Malley, 2005; Peters et al., 2020). This study should provide a comprehensive insight into the causes of treatment failure, serve as a basis for developing more adaptive TB control policies, and identify research needs that remain open within the framework of achieving the End TB Strategy.

2. RESEARCH METHOD

This study employed a scoping review technique to identify and map risk variables for tuberculosis treatment failure in five high-TB-burden countries: China, India, Indonesia, Pakistan, and the Philippines. The scoping review technique was used to thoroughly synthesise current information, identify major predictors of treatment failure, and highlight research gaps in TB treatment outcomes. This review followed the Joanna Briggs Institute's (JBI) scoping review criteria.

A thorough literature search was undertaken utilising three electronic databases: PubMed, Scopus, and EBSCOhost. The search approach used terms such as "tuberculosis", "treatment failure", "risk factors", "determinants", and "predictors", with Boolean operators. Literature searches were restricted to English-language works published between 2015 and 2025. To find relevant papers, additional manual searches were undertaken via qualifying studies reference lists. The retrieved records were then screened and rated for eligibility using title and abstract screening, followed by full-text assessment, as detailed below.

The Population-Concept-Context (PCC) framework provided guidance in developing the study question, search technique, and eligibility criteria. Adult patients with drug-sensitive tuberculosis (DS-TB) or drug resistant tuberculosis (DR-TB) were included in the population. The Concept (C) addressed the risk factors, determinants and predictors of TB treatment failure. The Context (C) contained research from five countries with high tuberculosis burdens: China, India, Indonesia, Pakistan, and the Philippines.

This study comprised original research publications from the selected countries that investigated variables related with tuberculosis treatment failure in adult TB patients. Articles were included if they were published between 2015 and 2025, written in English, and made available in full text. Studies that focused solely on treatment success, paediatric populations, editorials, conference abstracts, review articles, or publications with no full text availability were removed.

The recommendations for "Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews" (PRISMA-ScR) were followed for selecting studies. All detected records were imported into Mendeley to remove duplicates. Titles and abstracts were filtered using specified inclusion and exclusion criteria to find possibly relevant research. The complete texts of possibly eligible papers were then obtained and screened for eligibility. Articles with missing or partial full text were eliminated at this stage. Article containing full texts were then examined against established eligibility criteria, such as population, concept, and context. The final evaluation comprised studies that matched all of the qualifying criteria, as shown in the PRISMA flow diagram (Figure 1). Data extraction was carried out using a standardised data collection form that contained information on the author, year of publication, country, research design, sample size, sample characteristics, and stated risk factors for TB treatment failure. The retrieved data were analysed descriptively and narratively by categorising risk variables as demographic, clinical, microbiological, behavioural, and social. The frequency of each risk-factor category was computed as the proportion of included studies that reported risk factors in that category, using the 19 included studies as the denominator. For the nation-level comparison, risk variables were deemed most commonly reported when they

appeared in the greatest number of included studies within each country. This study relied on secondary data from the published literature, and there was no direct interaction with human participants. As a result, neither ethical approval nor informed consent were necessary.

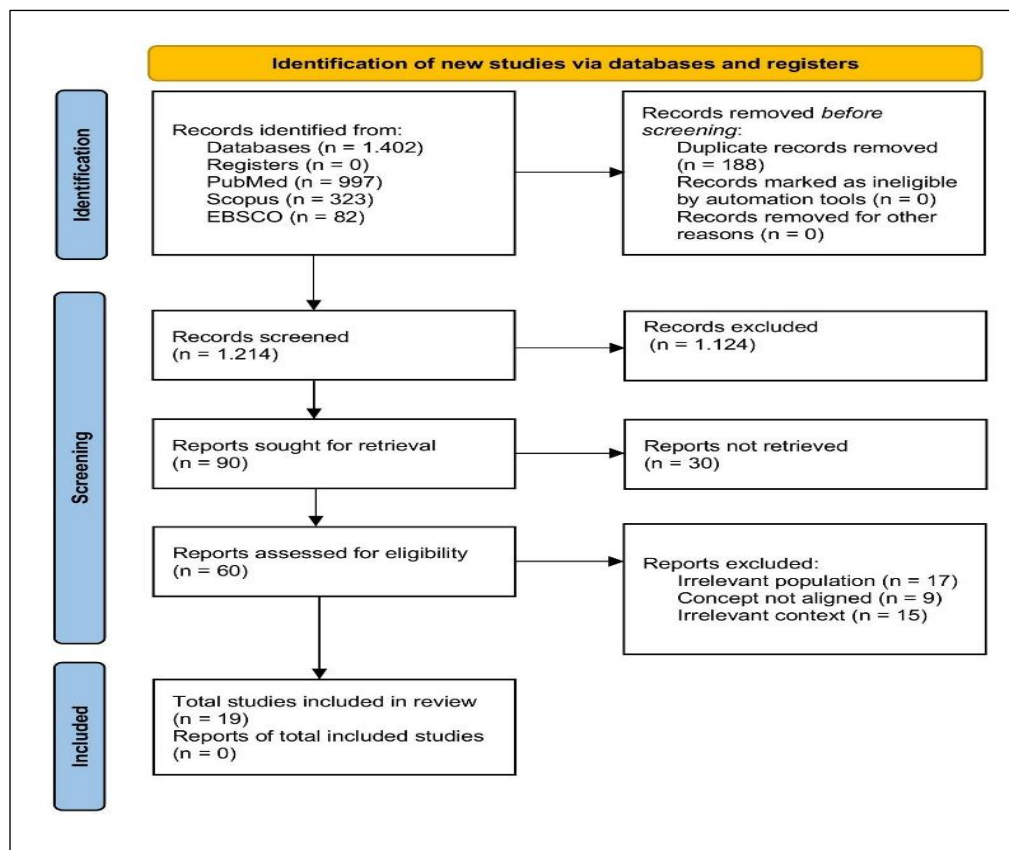


Figure 1 PRISMA Flow Diagram

3. RESULTS AND DISCUSSION

A standardised data collection form was used to capture information from all of the studies included in the review. The authors' names, year of publications, country, research design, sample characteristics, and stated risk factors for TB treatment failure were all gathered. The extracted data were analyzed descriptively and synthesized narratively. Risk factors were categorized into five groups: clinical, demographic, microbiological, behavioral, and social. A total of 19 studies met the inclusion criteria and were included in the final analysis.

Table 1. Characteristics of Included Studies

Author	Country	Study Design	Sample Size	Risk Factors and Their Components
(Gilmour et al., 2022)	China	Retrospective Cohort	306,860 patients	Male, increasing age, previous TB disease, severe condition, unsystematic management
(Zhou et al., 2025)	China	Observational	1,368 RR-TB patients	Male, age ≥ 45 , Farmer
(Liu et al., 2025)	China	Retrospective Cohort	248 elderly RR-TB	Malnutrition, anemia
(Xiong et al., 2020)	China	Cohort	1,834 PTB patients	Low zinc, low vitamin C

(Zhou et al., 2023)	China	Observasional	347 TB/HIV	Non-local, HIV positive
(Velavan et al., 2018)	India	Mixed-method	392 retreatment cases	Loss to follow-up (LTFU), Treatment failure, body weight <40
(Khan et al., 2024)	India	Retrospective Cohort	3,105 patients	Severe malnutrition, Male
(Gupta, Mittal, Singh, & Nadda, 2025)	India	Retrospective Cohort	1,103 patients	Elderly, HIV positive, Male
(Sinha et al., 2023)	India	Prospective Cohort	2,931 DS-TB	Severe malnutrition, no increase in BMI
(Meiyanti et al., 2024)	Indonesia	Retrospective Cohort	2,225 TB patients	Elderly >65, AFB smear, HIV positive
(Nugrahaeni & Rosmalaningrum, 2021)	Indonesia	Case-control	42 patients	Low knowledge, nutritional status, and treatment compliance
(Soeroto et al., 2021)	Indonesia	Retrospective Cohort	537 MDR-TB	HIV positive, chronic kidney disease, cavitory lesions
(Massud et al., 2023)	Pakistan	Prospective Cohort	271 patients	Age >50, baseline lung cavitation
(Wahid et al., 2021)	Pakistan	Retrospective Cohort	912 MDR-TB	Age 41–60, age >60, underweight, previous history of TB
(Javaid et al., 2018)	Pakistan	Retrospective Cohort	535 patients	Marital status, second-line drug resistance, XDR-TB
(Atif, 2020)	Pakistan	Retrospective Cohort	493 patients	Age <14, PTB smear positive
(Khan et al., 2019)	Pakistan	Retrospective Cohort	186 MDR-TB	Age >40
(Macatangay et al., 2020)	Philippines	Cross-sectional	3,701 patients	Age 25-34, Age 35-44, Male, RR/MDR-TB, smear positive, LTFU
(Hinay et al., 2025)	Philippines	Retrospective Cohort	521 patients	Comorbidities

Pakistan, and the Philippines. With five apiece, Pakistan and China have the most studies, followed by India with four, Indonesia with three, and the Philippines with two. Over half of the included studies are retrospective cohorts, one of the most popular cohort types. Other designs were also employed, including mixed designs, cross-sectional cohorts, prospective cohorts, observational cohorts, and cse-control studies. The large sample size, which varied from 42 to 306,860 persons, is indicative of the disparities in study aims and backgrounds. Among the variables linked to TB treatment failure in the included research are clinical, demographic, microbiological, behavioral, and sociocultural aspects.

Table 2. Main Risk Factors for TB Treatment Failure by Category

Category	Primary Risk Factors	Frequency (%)
Demographic	Male, elderly	68.3
Clinical	Malnutrition, HIV, diabetes	73.7
Microbiological	Positive sputum smear, cavities	57.9
Behavioral	Low compliance, low knowledge	31.6
Social	Farm work, limited access	26.3

Table 2 presents the distribution of risk-factor categories for tuberculosis treatment failure across the 19 included studies. The percentages show the proportion of included studies

that reported risk factors in each area. Clinical variables were the most commonly reported determinants (73.7%), including malnutrition, HIV infection, and diabetes mellitus. Demographic characteristics reported in 68.3% of studies were male gender and advanced age. Microbiological variables, such as positive sputum smear findings and lung cavitation, were mentioned in 57.9% of investigations. In 31.6% of studies, behavioural variables such as poor treatment adherence and lack of understanding about TB were detected. In contrast, sociocultural issues including occupation and poor access to healthcare services were mentioned in 26.3% of studies. These data demonstrate that treatment failure is impacted by a mix of biological, behavioural, and sociocultural characteristics, with clinical problems being the most frequently reported risk factors.

Table 3. Comparison of Most Frequently Reported Risk Factors Across Countries

Country	Most Frequently Reported Risk Factors	Number of Included Studies	Specific Patterns
China	Elderly, malnutrition	5	High RR-TB
India	Male, underweight	4	Retreatment cases
Indonesia	Elderly, low compliance	3	Low knowledge
Pakistan	Cavities, history of TB	5	MDR/XDR-TB
Philippines	Working age, Positive smear	2	High treatment discontinuation rate

Table 3 compares the dominant risk factors associated with tuberculosis treatment failure across five high TB-burden countries. Although numerous predictors were consistently detected across nations, there were significant disparities in the primary risk factors and particular patterns described in each environment. In China, older age and malnutrition were commonly identified as major risk factors, notably in investigations of rifampicin-resistant tuberculosis (RR-TB). In India, male gender and underweight condition were prevalent, particularly among patients undergoing retreatment. In Indonesia, older age and low treatment compliance were commonly recorded, and a lack of tuberculosis-related information was also recognised as a significant behavioural factor. According to studies from Pakistan, pulmonary cavitation and a history of tuberculosis are significant risk factors, with MDR/XDR-TB indicating an essential particular pattern. Meanwhile, research in the Philippines found that working-age characteristics and positive sputum smear findings were the most common reasons for treatment termination. These data indicate that, whereas similar risk factors impact TB treatment failure, the relative importance of various variables may differ depending on the epidemiology and therapeutic features of each environment.

Clinical Factors

Clinical variables were identified as the most often reported predictors of tuberculosis treatment failure in the research reviewed. Malnutrition, HIV infection, diabetes mellitus, anemia, chronic renal disease, and other coexisting diseases were repeatedly found as significant predictors of poor treatment results. These findings imply that biological susceptibility and underlying health issues play a significant role in determining treatment response and progression. Malnutrition was one of the most often documented risk factors, especially in research conducted in China and India (Khan et al., 2024; Liu et al., 2025; Sinha et al., 2023). Poor nutritional condition can affect immunological function, limiting the body's capacity to regulate Mycobacterium TB infection and raising the risk of disease development. In addition, malnutrition may delay sputum conversion and reduce treatment effectiveness, thereby increasing the likelihood of treatment failure. In China, this pattern was particularly evident among elderly patients with rifampicin-resistant TB, among whom malnutrition was independently associated with unfavorable treatment outcomes across multiple treatment centers (Liu et al., 2025). The prominence of malnutrition in India may be partly explained by

its strong association with poverty; a national-level analysis found that low body mass index had an important mediating role in the relationship between poverty and TB prevalence, compared with other socioeconomic risk factors examined (Oxlade & Murray, 2012).

HIV co-infection was significant variable discovered in multiple investigations (Gupta et al., 2025; Lestari et al., 2023; Meiyanti et al., 2024; Soeroto et al., 2021; Zhou et al., 2023). HIV co-infection was especially important in research on TB/HIV co-infected populations such as those conducted in southeastern China (Zhou et al., 2023). HIV impairs cell-mediated immunity, which is required to manage tuberculosis, resulting in a larger bacterial load, increased disease severity and poor treatment results. Previous research has repeatedly established that TB patients living with HIV had a much higher risk of treatment failure, relapse, and death than HIV-negative individuals (World Health Organization, 2024).

Diabetes mellitus was usually related with treatment failure. Hyperglycemia may impede macrophage and lymphocyte activity, resulting in slower bacterial clearance and longer recovery. Furthermore, diabetes can alter medication pharmacokinetics and increase the likelihood of negative treatment results (Baker et al., 2011). This conclusion is confirmed by findings from eastern China, where diabetes was linked to increased pulmonary tuberculosis severity, including a higher risk of lung cavitation and positive bacteriological results (Ling et al., 2023). These findings highlight the need of frequent diabetes screening and care in tuberculosis patients, especially in countries with a double burden of communicable and noncommunicable illnesses.

Other clinical problems, including anaemia, chronic renal disease, and numerous comorbidities, have been linked to poor treatment results in various trials (Hinay et al., 2025; Soeroto et al., 2021). Such disorders may impair immune function and complicate therapy administration, raising the possibility of unfavourable results. As a result, complete clinical evaluation and comorbidity management should be viewed as critical components of patient-centered TB therapy.

Demographic Factors

Demographic characteristics were among the most frequently reported determinants of tuberculosis treatment failure across the included studies. Male sex and older age were frequently reported as important demographic factors, although their distribution varied across the five countries (Gilmour et al., 2022; Gupta et al., 2025; Khan et al., 2019; Khan et al., 2024; Macatangay et al., 2020; Massud et al., 2023; Meiyanti et al., 2024; Wahid et al., 2021; Zhou et al., 2025). Older age was repeatedly reported in studies from China, Indonesia, and Pakistan, whereas male sex was reported across China, India, and the Philippines. In the Philippines, characteristics of the working-age population were also identified in relation to unfavorable treatment outcomes. These differences suggest that demographic factors may operate differently across populations and treatment contexts within countries.

Older age was frequently linked to treatment failure. Several investigations found an elevated risk among patients over the ages of 40, 50, and 65 (Khan et al., 2019; Massud et al., 2023; Meiyanti et al., 2024; Wahid et al., 2021). The significance of older age was highlighted in China and Pakistan, where studies of patients with drug-resistant tuberculosis found age-related variables to be key predictors of poor treatment results. Older age was linked to worse treatment results in elderly patients with rifampicin-resistant tuberculosis in China, while investigations in Pakistan found a similar link (Khan et al., 2019; Liu et al., 2025; Massud et al., 2023; Wahid et al., 2021). These findings show that the significance of age may be particularly essential in populations with drug-resistant illness, since older patients may have higher clinical vulnerability and more complex treatment demands.

Male gender was another commonly reported demographic driver of treatment failure (Gilmour et al., 2022; Gupta et al., 2025; Khan et al., 2024; Macatangay et al., 2020; Zhou et al., 2025). Several theories have been presented for this relationship. Men are more likely to participate in risky behaviours such as smoking and alcohol drinking, and they may delay

seeking medical attention when symptoms occur. Occupational exposures and mobility may potentially cause pauses in treatment and follow-up care. As a result, male patients may be at higher risk of medication noncompliance and disease progression, eventually leading in inferior treatment results.

Other demographic factors found in the research were farmer occupation, marital status, and non-local resident status (Javaid et al., 2018; Zhou et al., 2025, 2023). These characteristics may indicate greater socioeconomic vulnerabilities affecting healthcare access, treatment continuity, and illness management. To decrease TB treatment failure, focused treatments and patient care measures should take demographic variables into account.

Microbiological Factors

Microbiological variables were commonly linked to TB treatment failure in the research reviewed. The most often reported factors included positive sputum smear findings, pulmonary cavitation, drug-resistant TB, and resistance to second-line anti-tuberculosis medications (Atif et al., 2020; Khan et al., 2019; Javaid et al., 2018; Macatangay et al., 2020; Massud et al., 2023; Meiyanti et al., 2024; Soeroto et al., 2021; Wahid et al., 2021). These findings indicate that disease severity and bacterial characteristics play an important role in determining treatment outcomes. However, the patterns of microbiological factors varied across the five countries. In Pakistan, pulmonary cavitation and drug resistance, including MDR/XDR-TB, were prominent microbiological factors reported among patients with unsuccessful treatment outcomes (Khan et al., 2019; Javaid et al., 2018; Massud et al., 2023). A history of tuberculosis was also frequently reported in this setting, but it represents a treatment-history characteristic rather than a microbiological factor. In the Philippines, positive sputum smear results and RR/MDR-TB were identified as important determinants (Macatangay et al., 2020), while in China, rifampicin-resistant TB represented an important treatment context associated with unfavorable outcomes (Zhou et al., 2025). In Indonesia, positive sputum smear results and cavitary lesions were reported among factors associated with unfavorable treatment outcomes, particularly among patients receiving MDR-TB treatment (Meiyanti et al., 2024; Soeroto et al., 2021). These differences suggest that microbiological determinants of treatment failure may vary with the drug-resistance profiles and clinical characteristics of TB populations in each country.

Positive sputum smear results were consistently identified as predictors of treatment failure, particularly in studies from Indonesia, Pakistan, and the Philippines (Atif et al., 2020; Macatangay et al., 2020; Meiyanti et al., 2024). Persistent smear positivity generally reflects a higher bacillary burden and delayed bacteriological response to treatment. Patients with delayed sputum conversion may therefore have a greater risk of persistent infection and unfavorable treatment outcomes. These findings highlight the importance of routine bacteriological monitoring to identify patients with delayed treatment response.

Pulmonary cavitation was another important microbiological determinant, particularly in studies from Pakistan and Indonesia (Massud et al., 2023; Soeroto et al., 2021). In Pakistan, baseline lung cavitation was identified among factors associated with unsuccessful treatment outcomes in patients with drug-resistant TB (Massud et al., 2023). In Indonesia, cavitary lesions were also identified as a factor associated with unfavorable outcomes among patients receiving longer MDR-TB treatment regimens (Soeroto et al., 2021). These findings suggest that pulmonary cavitation may be particularly relevant in treatment settings involving drug-resistant disease, although the characteristics of the study populations differed across countries.

Drug-resistant tuberculosis, including rifampicin-resistant tuberculosis (RR-TB), multidrug-resistant tuberculosis (MDR-TB), and extensively drug-resistant tuberculosis (XDR-TB), was also frequently associated with unsuccessful treatment outcomes (Khan et al., 2019; Javaid et al., 2018; Macatangay et al., 2020; Soeroto et al., 2021; Wahid et al., 2021; Zhou et al., 2025). The prominence of drug resistance varied across countries, with RR-TB highlighted in China, MDR/XDR-TB and second-line drug resistance reported in Pakistan, and RR/MDR-

TB identified in the Philippines (Khan et al., 2019; Javaid et al., 2018; Macatangay et al., 2020; Zhou et al., 2025). Drug resistance reduces the effectiveness of available treatment regimens and increases the complexity of patient management. Therefore, these country-specific patterns highlight the importance of timely drug-susceptibility testing and access to effective treatment for drug-resistant TB.

Behavioral and Socio-cultural Factors

Behavioral and socio-cultural factors were also identified as important determinants of tuberculosis treatment failure, although they were reported less frequently than clinical and demographic factors. The included studies found poor treatment compliance, insufficient awareness of TB, loss to follow-up (LTFU), and occupational characteristics as behavioural and social variables (Macatangay et al., 2020; Nugrahaeni & Rosmalaningrum, 2021; Velavan et al., 2018; Zhou et al., 2025). However, the stated trends differed per country. In India and the Philippines, loss to follow-up was one of the identified treatment-related variables. In Indonesia, little tuberculosis-related information and poor treatment compliance were found. In China, farmer occupation was identified as an occupational characteristic associated with treatment outcomes (Macatangay et al., 2020; Nugrahaeni & Rosmalaningrum, 2021; Velavan et al., 2018; Zhou et al., 2025). These differences suggest that behavioral and socio-cultural determinants of treatment failure may vary with the social and treatment contexts of each country.

Treatment adherence and continuity of care were important behavioral aspects associated with unfavorable treatment outcomes. The Indonesian research indicated treatment compliance as a risk factor, but studies in India and the Philippines cited loss to follow-up as a factor (Macatangay et al., 2020; Nugrahaeni & Rosmalaningrum, 2021; Velavan et al., 2018). The protracted period of TB therapy may make it difficult for patients to stick to their drug regimen and attend follow-up appointments. Failure to follow-up and poor treatment compliance may raise the risk of persistent infection, recurrence, and unfavourable treatment results. A comprehensive evaluation of treatment interruption in Asia found that it is related with poor treatment results (Oh et al., 2023). These findings underscore the relevance of adherence support and care continuity methods.

Limited understanding of TB was also indicated as a behavioural predictor, especially in the Indonesian study (Nugrahaeni & Rosmalaningrum, 2021). Inadequate knowledge of disease transmission, treatment length, and the implications of treatment discontinuation may diminish patients' motivation to continue therapy. This research suggests that health education should go beyond simply giving pharmaceutical information to address patients' awareness of the condition and the need of completing treatment.

Occupational influences were also included in the examined studies. In China, farmer occupation was discovered as a factor influencing treatment results (Zhou et al., 2025). Occupational duties may interfere with treatment plans, drug collection, and follow-up visits, especially if the therapy requires frequent trips to healthcare facilities. This research implies that treatment adherence is more than just an individual behaviour; it may also be impacted by patients' employment and social conditions.

In addition to the risk variables highlighted in the research, TB stigma may impact treatment-related behaviour. Stigma can inhibit people from seeking therapy, reporting their condition, or following treatment recommendations (Craig et al., 2017). Therefore, interventions to reduce treatment failure should combine patient education and adherence counseling with social support, stigma reduction, and measures to reduce barriers to healthcare access.

Implications for Public Health

The results of this review have important implications for tuberculosis control programs in high-burden countries. Since treatment failure is influenced by multiple clinical, demographic, microbiological, behavioral, and social determinants, TB management should

adopt a comprehensive and patient-centered approach. Common strategies should include routine management of comorbidities, patient education and adherence support, community-based support, and strengthening access to TB services. Digital adherence technologies may also support treatment monitoring and medication compliance among patients at high risk of unfavorable outcomes (Santosa, Juniarti, Pahria, & Susanti, 2025).

However, although several risk factors were consistently identified across countries, the dominant risk factors varied substantially. As a result, TB management efforts should be customised to the risk profiles determined in each nation, as shown in Table 3. In China, where older age and malnutrition are common among rifampicin-resistant TB patients, nutritional support and tighter monitoring of elderly patients should be prioritised within drug-resistant TB services (Liu et al., 2025). In India, where male sex and underweight status were predominant, particularly among retreatment cases, focused nutritional assessment and assistance, coupled with better monitoring of patients undergoing retreatment, might be useful. In Indonesia, where older age, limited knowledge, and poor treatment adherence were prevalent, integrated strategies that combine clinical monitoring, patient education, and adherence counseling are particularly important (Meiyanti et al., 2024; Nugrahaeni & Rosmalaningrum, 2021). In Pakistan, where pulmonary cavitation, a history of TB, and drug resistance were prevalent, strengthening drug-susceptibility testing, early detection of drug resistance, and closer bacteriological and clinical monitoring should be prioritized (Khan et al., 2019; Javaid et al., 2018; Massud et al., 2023). In the Philippines, where working-age characteristics, positive sputum smear results, RR/MDR-TB, and treatment discontinuation were prominent, interventions to support treatment continuity and strengthen bacteriological monitoring should be prioritized (Macatangay et al., 2020).

Overall, these findings indicate that TB control programs should combine common core interventions with country-specific strategies that reflect the dominant risk factors and characteristics of the populations served. Thus, a context-specific approach may be preferable to a standard intervention method for minimising TB treatment failure in a variety of high-burden settings.

Study Strengths and Limitations

The review's inclusion of data from five high-TB-burden nations provides a thorough overview of variables associated with tuberculosis treatment failure in variety of epidemiological and healthcare contexts. Using a scoping review process allowed for the discovery and mapping of a variety of factors, including as clinical, demographic, microbiological, behavioral, and social factors. Furthermore, the use of several research designs allowed for a more comprehensive knowledge of the complexities of treatment failure across groups and circumstances.

However, many restrictions should be recognised. First, the included studies differed significantly in terms of research design, sample size, demographic characteristics, and criteria of treatment failure. This variability may have influenced the comparability of findings across studies and contributed to differences in the identified risk variables. To reduce the influence of variability, this review did not quantitatively pool effect estimates; instead, it synthesised the data descriptively by categorising identified risk variables as demographic, clinical, microbiological, behavioural, and social. The frequency-based synthesis shown in Tables 2 and 3 was used to characterise patterns of reported risk variables rather than estimating their respective impact sizes or establishing a risk hierarchy. Nevertheless, differences in study characteristics could not be eliminated and should be considered when interpreting the findings.

Second, this review was limited to English-language articles, which may have introduced language bias and led to relevant evidence in other languages being missed. This limitation may have affected the completeness of the evidence identified, particularly when comparing country-specific patterns. This limitation was not directly mitigated within the current review,

as language remained a fixed eligibility criterion. Therefore, its potential impact should be considered when interpreting the country-specific findings. Future reviews could reduce this limitation by incorporating multilingual search strategies and, where necessary, professional translation of non-English literature.

Third, most of the included studies employed observational designs, which limit the ability to establish causal relationships between risk factors and treatment failure. Therefore, the findings of this review were interpreted as reported associations rather than causal effects, and no causal conclusions were drawn from the frequency with which individual risk factors were identified. This strategy helps to avoid overinterpretation of the data, but residual confounding and limitations inherent in primary observational research cannot be avoided. These limitations should be taken into account when interpreting the findings notably the country-specific variances in reported risk variables. Future studies integrating multilingual evidence sources and prospective or intervention-based designs may further enhance the evidence base and clarify the causal role of individual risk variables to TB treatment failure.

4. CONCLUSION

Tuberculosis treatment failure is influenced by interrelated clinical, demographic, microbiological, behavioral, and social factors, with the prominent risk profiles varying across the five high TB-burden countries. Older age and malnutrition were prominent in China; male sex and underweight status in India; older age, low treatment compliance, and limited tuberculosis-related knowledge in Indonesia; pulmonary cavitation, previous tuberculosis history, and drug resistance in Pakistan; and working-age characteristics, positive sputum smear results, and treatment discontinuation in the Philippines. These findings underline the necessity for integrated, patient-centered TB control methods paired with country-specific treatments addressing the significant risk factors identified in each environment.

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