

Magnitude and Determinants of Unsuccessful Tuberculosis Treatment Outcomes in Ethiopia: A Systematic Review and Meta-Analysis

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Abstract:

Objective: Unsuccessful treatment outcomes of tuberculosis (TB), including treatment failure, death, and loss to follow-up, pose significant challenges to TB control programs. This systematic review and meta-analysis aimed to assess the magnitude and determinants of unsuccessful TB treatment outcomes in Ethiopia.

Material and Methods: A comprehensive literature searches were conducted using databases such as PubMed, Scopus, and Google Scholar. Observational studies published between 2000 and 2024 that reported on TB treatment outcomes in Ethiopia were included. The pooled magnitude of unsuccessful TB treatment outcomes was estimated using a random-effects model. Subgroup analysis, and meta-regression, and publication bias assessments were also conducted in order to explore potential sources of heterogeneity.

Results: The overall pooled magnitude of unsuccessful TB treatment outcomes in Ethiopia was 17% (95% confidence interval (CI): 15%–20%). Significant heterogeneity was observed between studies ($I^2=98.49\%$, $p\text{-value}<0.01$). Subgroup analysis revealed that unsuccessful outcomes were higher among patients with multidrug-resistant TB (31.7%) and those co-infected with Human Immunodeficiency Virus (HIV) (24.5%). Older age >45 years (HR: 1.82; 95% CI: 1.25–2.65), HIV co-infection (HR: 2.10; 95% CI: 1.23–3.58), and retreatment (HR: 1.67; 95% CI: 1.13–2.47) were significant predictors of unsuccessful outcomes.

Conclusion: Unsuccessful treatment outcome in Ethiopia is high. Multi-drug resistance TB and HIV co-infection had significant impact on TB treatment outcome. Therefore, the findings underscore the need for targeted interventions that address the key determinants of unsuccessful TB treatment outcomes in Ethiopia, particularly among high-risk populations such as multidrug-resistant TB (MDR-TB) patients and those co-infected with HIV.

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Keywords: meta-analysis, Ethiopia, systematic review, tuberculosis, unsuccessful treatment outcome

Introduction

Tuberculosis (TB) remains one of the world's most pressing public health challenges, particularly in low- and middle-income countries. Ethiopia, ranking seventh among the 30 highest TB-burden countries globally, faces significant challenges in controlling the disease and achieving successful treatment outcomes¹. The World Health Organization (WHO)² defines unsuccessful TB treatment outcomes as a composite of treatment failure, loss to follow-up, and death. These outcomes not only represent individual patient tragedies but also signify broader systemic challenges in TB control programs.

According to the Ethiopia National TB Program (NTP), the country has adopted standard treatment regimens, including a six-month regimen for drug-susceptible TB (DS-TB) and longer, more complex regimens for drug-resistant TB (DR-TB), such as multidrug-resistant TB (MDR-TB) and rifampicin-resistant TB (RR-TB); these regimens include combinations of first-line drugs for DS-TB and second-line drugs³. Ethiopia's TB data reporting relies on a mix of paper-based systems and a case-based digital platform introduced in recent years. However, issues with the completeness and accuracy of the surveillance system limit its utility for studying the magnitude and determinants of unsuccessful treatment outcomes⁴. Even though the healthcare system includes a tiered structure of hospitals providing primary, general, and specialized care, with contributions from private and Non-Governmental organization (NGO)-run facilities in TB diagnosis and management, health centers in Ethiopia play a critical role in TB treatment through contact tracing, case investigation, and provision of diagnosis and treatment, and most health centers lack doctors but are staffed with trained health officers or nurses who oversee TB care⁵.

In Ethiopia, while progress has been made in expanding access to TB diagnosis and treatment services, the country still struggles with a high burden of the disease and lower treatment success rates^{6,7}. Unsuccessful treatments lead to prolonged infectiousness, increasing the risk of community transmission and potentially fueling the spread of drug-resistant TB strains⁸. This not only escalates the cost of TB management but also strains the already limited healthcare resources of the country. Studies have reported varying rates of unsuccessful outcomes across different regions of the country, ranging from 9%⁹ to 39%¹⁰. However, these individual studies often have a limited geographical scope or focus on specific patient populations, making it challenging to ascertain the true national picture. The lack of a comprehensive, country-wide assessment of unsuccessful TB treatment outcomes hampers the ability of health authorities to accurately gauge the effectiveness of current TB control strategies and allocate resources efficiently. Therefore, this review and meta-analysis were aimed to assess the magnitude and determinants of unsuccessful treatment outcomes in the adult population in Ethiopia.

Material and Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement's reporting guidelines were followed in the reporting of this systematic review and meta-analysis.

Eligibility criteria

The PICO (Population, Intervention, Comparison, Outcome) framework for the described focus can be summarized as follows:

Population: Adult patients with active TB in Ethiopia, excluding children, prisoners, and miners.

Intervention/exposure: Presence of specific risk factors influencing TB treatment outcomes.

Comparison: Patients with unsuccessful TB treatment outcomes who did not exhibit the specific risk factor under investigation.

Outcome: Unsuccessful treatment outcomes (e.g., treatment failure, loss to follow-up, death).

Eligible study designs included retrospective cohort and cross-sectional studies, while single case reports and studies without primary outcomes were excluded. Only studies conducted in Ethiopia between 2000 and 2024 and published in English were included. Additionally, studies that remained inaccessible after 2 unsuccessful attempts to contact the primary or corresponding author via email were excluded from the review.

Data sources and search strategy

A thorough and systematic search was carried out across several electronic databases (PubMed/MEDLINE, CINAHL, Embase, Google Scholar, and Science Direct) in order to find any relevant studies on TB treatment outcomes. Alongside the database search, reference lists of the selected studies were manually reviewed to uncover any additional relevant articles. The search process was independently conducted by 2 authors (SM and BAL), using specific search terms: A combination of controlled vocabulary and free-text keywords was used, including terms such as “Tuberculosis” OR “TB,” “Treatment outcome” OR “Unsuccessful outcome” OR “Treatment failure” OR “Mortality” OR “Loss to follow-up,” “Determinants” OR “Risk factors” OR “Associated factors,” and “Ethiopia.” The Boolean logic applied was: (“Tuberculosis” OR “TB”) AND (“Treatment outcome” OR “Unsuccessful outcome” OR “Treatment failure” OR “Mortality” OR “Loss to follow-up”) AND (“Determinants” OR “Risk factors” OR “Associated factors”) AND “Ethiopia.” Filters included

language (English), study type (observational studies), and population (human studies). The search was supplemented with manual screening of references from included studies and a grey literature search using similar keywords.

Screening, selection process and data extraction

The study screening and selection process was conducted systematically. Articles were imported into EndNote, and duplicates were removed. Two independent reviewers screened titles and abstracts based on predefined eligibility criteria, then extracted data using Microsoft Excel. Initial discrepancies were addressed by both reviewers by extracting data from the first 3 articles for comparison. One reviewer then extracted the data, while the second verified it, with a third author resolving any disputes. Relevant study information, such as authors, study area, year, design, and sample size were extracted using a standardized Excel sheet, and disagreements were resolved through discussions.

Risk of bias assessment

We used the Newcastle–Ottawa Scale (NOS) for observational studies in order to have 2 independent reviewers carefully evaluate the integrity and possible bias of the studies that were part of our review. The selection of study groups, group comparability, and determining the outcomes of interest were the 3 areas in which the NOS assessed bias risk. By allocating up to 4 stars for the “Selection” category, 2 for “Comparability,” and 3 for the “Outcome” category, this framework facilitated a thorough evaluation.

Data synthesis and analysis

A narrative synthesis was used to describe the study characteristics and key findings. Meta-analysis, conducted using Stata version 17, calculated the overall prevalence of unsuccessful TB treatment outcomes and associated risk factors. Effect sizes from the primary studies were log-

transformed to determine HRs, and forest plots were used to display pooled estimates. Heterogeneity was assessed using the I^2 statistic, Cochran's Q, and chi-square tests, with heterogeneity levels classified as low (I^2 : 0–25%), moderate (I^2 : 25–50%), or high (I^2 : $\geq 50\%$). Subgroup analyses and meta-regression were performed to investigate potential sources of heterogeneity, considering variables such as study setting, region, design, publication year, and sample size. Publication bias was evaluated using Begg's and Egger's tests, which assess asymmetry in funnel plots.

Results

Selection of studies

A comprehensive literature search identified 185 articles, including 75 from PubMed, 65 from Google Scholar, and 42 from Web of Science and EMBASE. After removing duplicates and screening titles, 80 articles were excluded. Abstract screening of 105 records led to the exclusion of 67 articles that did not meet the inclusion criteria. Full-text reviews were conducted on 38 articles. After review,

31 articles met the inclusion criteria and were included in the final analysis. Articles were excluded for lacking primary outcomes ($n=3$), unclear outcomes ($n=2$), or non-extractable data ($n=2$) (Figure 1).

Characteristics of the studies

This systematic review included 31 studies conducted in different regions of Ethiopia between January 2000 and September 2024, involving a total of 8,113 participants. The majority of the studies (21 studies) used a retrospective cohort design, while 9 were cross-sectional^{6,7,10–16}. In terms of setting, 8 were in health centers^{9,12,15–20}, 5 included both hospitals and health centers^{10,13,21–23}, and the rest of the 17 studies were carried out in hospitals. The studies were predominantly from the Amhara region (9 studies), followed by Addis Ababa (5 studies), Oromia (5 studies), and Southern Ethiopia (6 studies). Sample sizes ranged from 136 to 9493 study participants across the different studies (Table 1).

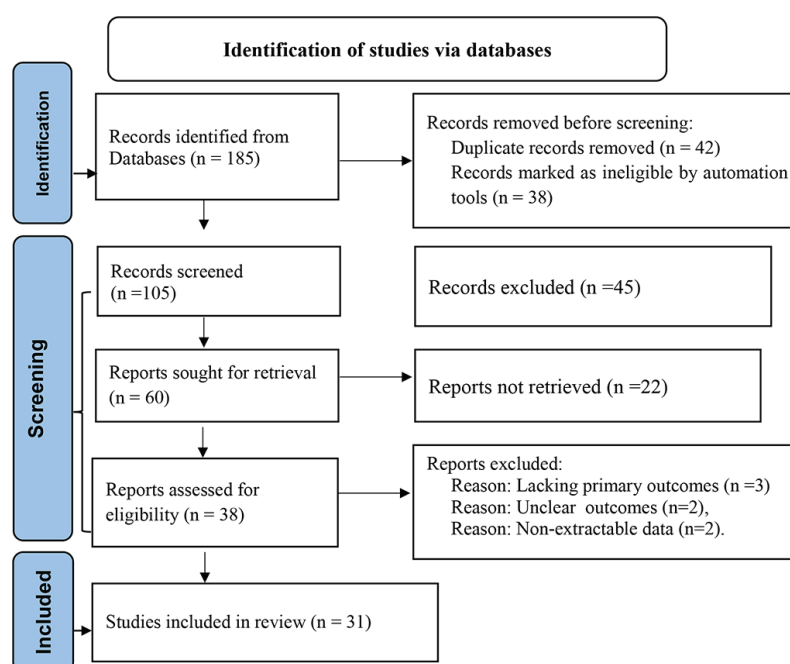


Figure 1 Selection of studies of PRISMA flow diagram

Table 1 Characteristics of the studies included in the review

Studies	Publication year	Study Region	Study Design	Study Setting	Types of TB	Sample Size	Event
(Asres et al., 2016) ³⁵	2016	Oromia	Retrospective cohort	Hospital	PTB	790	95
(Wondale et al., 2017) ²⁸	2017	Southern Ethiopia	Retrospective cohort	Hospital	PTB	1172	305
(Berhe et al., 2012) ¹²	2018	Tigray	Cross-sectional	Health center	PTB	407	45
(Ejeta et al., 2018) ¹³	2016	Gambella	Cross-sectional	Both	PTB	4144	493
(Sahile et al., 2021) ⁹	2021	Addis Ababa	Retrospective cohort	Health center	PTB	456	40
(Beza et al., 2013) ¹⁸	2013	Amhara	Retrospective cohort	Health center	PTB	827	119
(Gebrezgabiher et al., 2016) ³⁶	2016	Southern Ethiopia	Retrospective cohort	Hospital	PTB	1537	227
(Getahun et al., 2013) ²⁰	2013	Addis Ababa	Retrospective cohort	Health center	PTB	6450	1116
(Jemal et al., 2015) ³⁷	2015	Amhara	Retrospective cohort	Hospital	PTB	2970	1031
(Lindtjørn & Madebo, 2001) ¹⁰	2001	Southern Ethiopia	Cross-sectional	Both	PTB	239	93
(Tadesse & Tadesse, 2014) ¹⁵	2014	Amhara	Cross-sectional	Health center	PTB	1305	159
(Sintayehu et al., 2014) ³⁸	2014	Southern Ethiopia	Retrospective cohort	Hospital	PTB	2043	90
(Woldeyohannes et al., 2015) ²³	2015	Oromia	Retrospective cohort	Both	PTB	31,198	4524
(Woldeyohannes et al., 2021) ³⁹	2021	Oromia	Retrospective cohort	Hospital	MDR-TB	406	116
(Kassa et al., 2019) ⁴⁰	2019	Amhara	Retrospective cohort	Hospital	MDR-TB	332	118
(Birhane et al., 2023) ²¹	2023	Somalia	Retrospective cohort	Both	PTB	589	170
(Mamo et al., 2021) ¹⁴	2021	Oromia	Cross-sectional	Hospital	PTB	351	31
(Limenh et al., 2024) ²²	2024	Amhara	Retrospective cohort	Both	PTB	362	42
(Debash et al., 2023) ⁴¹	2023	Amhara	Retrospective cohort	Hospital	PTB	552	34
(Zerihun et al., 2023) ¹⁶	2023	Addis Ababa	Cross-sectional	Health center	PTB	636	97
(Wakjira et al., 2022) ⁷	2022	Oromia	Cross-sectional	Hospital	MDR-TB	136	42
(Berhan et al., 2023) ²⁷	2023	Amhara	Retrospective cohort	Hospital	PTB	400	44
(Agazhu et al., 2023) ¹¹	2023	Southern Ethiopia	Cross-sectional	Hospital	PTB	347	72
Getie & Alemnew ⁴²	2020	Amhara	Retrospective cohort	Hospital	PTB	270	52
Abdilahi et al., 2024 ⁴³	2024	Somalia	Retrospective cohort	Hospital	TB/HIV	194	20
(Alem & Gebre-Selassie, 2017) ¹⁷	2027	Addis Ababa	Retrospective cohort	Health center	PTB	6178	1235
(Fentie et al., 2020) ¹⁹	2020	Addis Ababa	Retrospective cohort	Health center	PTB	352	18
((Teferi et al., 2021) ⁴⁴	2021	Southern Ethiopia	Retrospective cohort	Hospital	PTB	232	41
(Tola et al., 2019) ⁴⁵	2019	Harar	Retrospective cohort	Hospital	PTB	1236	93
(Meseret Tadele et al., 2022) ⁶	2022	Amhara	Cross-sectional	Hospital	PTB	1084	152

TB=tuberculosis, MDR-TB=multi-drug resistant tuberculosis, PTB=pulmonary tuberculosis, TB/HIV=tuberculosis/human immunodeficiency virus co-infection

Quality assessment and risk of bias

The Newcastle-Ottawa Scale (NOS) evaluates bias risk across 3 domains: study group selection, group comparability, and outcome ascertainment. Most studies excelled in the selection domain, scoring 4 stars for clearly defined inclusion and exclusion criteria, which minimized selection bias. However, 2 studies^{7,24} scored 3 stars due to unclear eligibility criteria, potentially compromising population representativeness. In the comparability domain,

5 studies^{23,25-28} earned 2 stars for effectively controlling confounding factors, reducing confounding bias. The remaining studies^{12,18,19,29} received one star, indicating inadequate control for confounders. For the outcome domain, most studies received 3 stars for high-quality outcome assessment. However, 3 studies^{6,7,10-16} scored 2 stars, as their cross-sectional design introduced potential bias in outcome measurements, limiting their ability to establish temporal relationships between variables.

Magnitude of unsuccessful TB treatment outcomes

The overall magnitude of unsuccessful TB treatment outcomes in Ethiopia was 17% (95% confidence interval (CI) CI: 15%–20%). A significant heterogeneity between studies was observed ($I^2=98.49\%$, p -value<0.01); the included studies had a wide range of proportions of unsuccessful TB treatment outcomes, from 9%⁹ to 39%¹⁰ (Figure 2).

Investigating heterogeneity & publication bias

Subgroup analysis based on study setting revealed variations in unsuccessful outcomes across healthcare facilities and regions in Ethiopia. The highest pooled unsuccessful treatment outcome was in Oromia at 21.2% (95% CI: 15.8%–26.7%) from 6 studies, followed by Tigray at 20.2% (95% CI: 11.1%–29.2%). Cross-sectional studies reported a higher unsuccessful treatment outcome at 19% (95% CI: 15.3%–22.6%). The unsuccessful treatment

outcome was the highest among MDR-TB patients, 31.7% (95% CI: 27%–36.3%). These findings indicate that both geographic region and TB type contribute to the observed heterogeneity in estimates. Meta-regression analysis was conducted in order to explore any potential sources of heterogeneity, focusing on study-level characteristics like sample size and publication year. Both factors were found to be non-significant predictors of the pooled estimate, indicating that they did not contribute to heterogeneity. Regarding publication bias, Begg's test (Kendall's score=129, SE=58.83, p -value=0.02) and the funnel plot (supplementary material) suggested evidence of bias, while Egger's test (intercept=6.73, SE=1.44, p -value<0.01) also indicated some small-study effects and significant publication bias. However, the trim and fill method showed no imputed studies, with no change in the pooled estimate (Table 2).

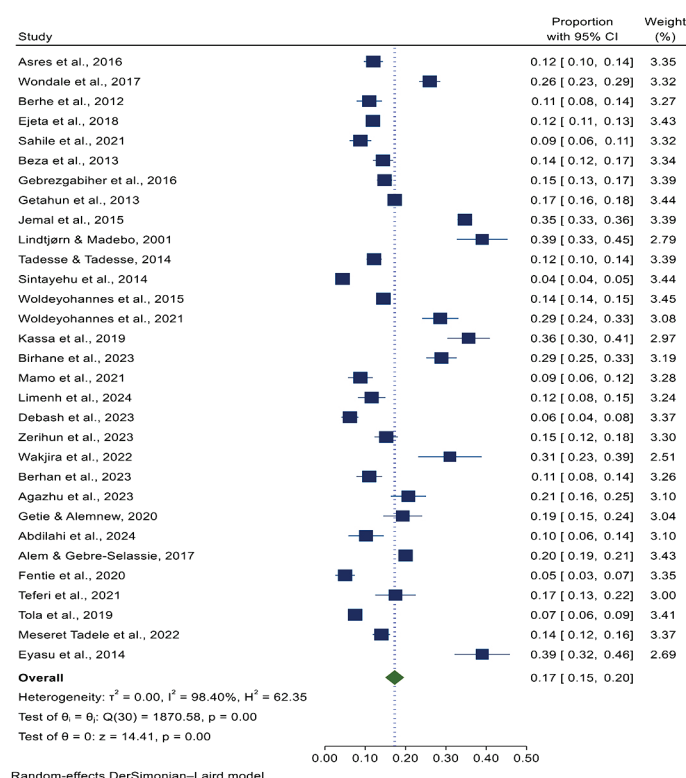


Figure 2 Magnitude of unsuccessful Tuberculosis (TB) treatment outcome in Ethiopia

Table 2 Subgroup analysis by group level variables

Group	No. of studies	Effect size (proportion)	95% confidence interval	
			LCI	UCI
Study region				
Addis Ababa	5	0.134	0.087	0.180
Amhara	9	0.176	0.103	0.249
Gambella	1	0.119	0.109	0.129
Harar	1	0.075	0.060	0.090
Oromia	6	0.212	0.158	0.267
Somalia	2	0.196	0.013	0.379
Southern Ethiopia	6	0.202	0.111	0.292
Tigray	1	0.110	0.080	0.140
Study design				
Cross-sectional	10	0.190	0.153	0.226
Retrospective cohort	21	0.164	0.134	0.195
Study setting				
Both	5	0.198	0.158	0.237
Health center	8	0.131	0.097	0.164
Hospital	18	0.187	0.137	0.238
Type of TB				
MDR-TB	3	0.317	0.270	0.363
PTB	26	0.154	0.130	0.179
TB/HIV	2	0.245	-0.037	0.527

LCI=lower confidence interval, UCI=upper confidence interval, TB=tuberculosis, MDR-TB=multi-drug resistant tuberculosis, PTB=pulmonary tuberculosis, TB/HIV=tuberculosis/human immunodeficiency virus co-infection

Determinants of unsuccessful treatment

outcomes

Older age

Nine studies identified a significant association between an age above 45 years and unsuccessful TB treatment outcomes with heterogeneity ($I^2=90.02\%$) (HR: 1.82; 95% CI: 1.25–2.65) (Figure 3).

HIV co-infection

A meta-analysis was conducted in 14 studies using a random-effects meta-analysis to pool the effect sizes due to heterogeneity between studies ($I^2=93.45\%$). The analysis indicated a significant association between HIV co-infection and unsuccessful TB treatment outcome (HR: 2.10; 95% CI: 1.23–3.58) (Figure 4).

Extra-pulmonary TB (EPTB)

The effect of extrapulmonary TB was evaluated in 8 studies, and a random-effects meta-analysis was employed to pool the effect sizes due to heterogeneity between studies ($I^2=90.98\%$). Based on the analysis, EPTB was associated with a 78% increased risk of unsuccessful TB treatment (HR: 1.78; 95% CI: 1.33–2.39) (Figure 5).

Retreatment

Six studies were used to assess the effect of retreatment using a random-effects method to pool the effect sizes due to heterogeneity between studies ($I^2=83.94\%$). The analysis indicates that retreatment was associated with a 67% higher risk of unsuccessful treatment outcome as compared to new cases (HR: 1.67; 95% CI: 1.13–2.47) (Figure 6).

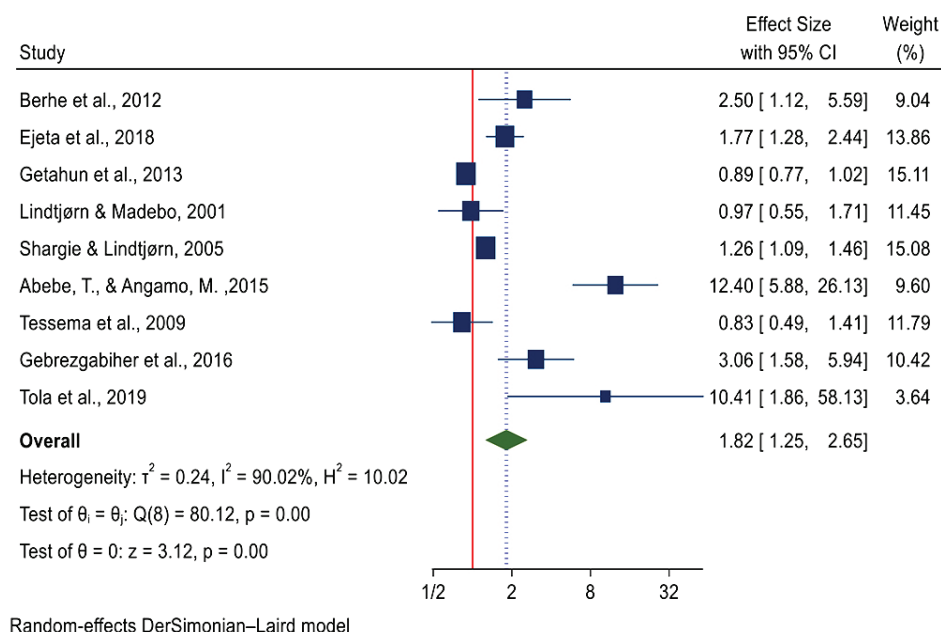


Figure 3 Age >45 years and unsuccessful Tuberculosis (TB) treatment outcome

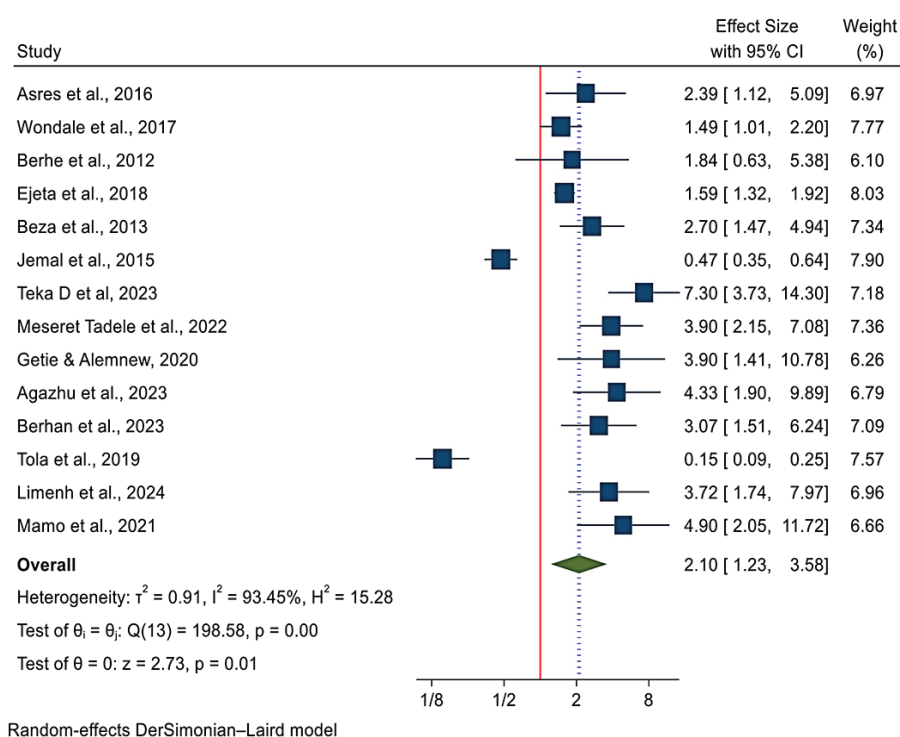


Figure 4 Human immunodeficiency virus (HIV) co-infection and unsuccessful Tuberculosis (TB) treatment outcome

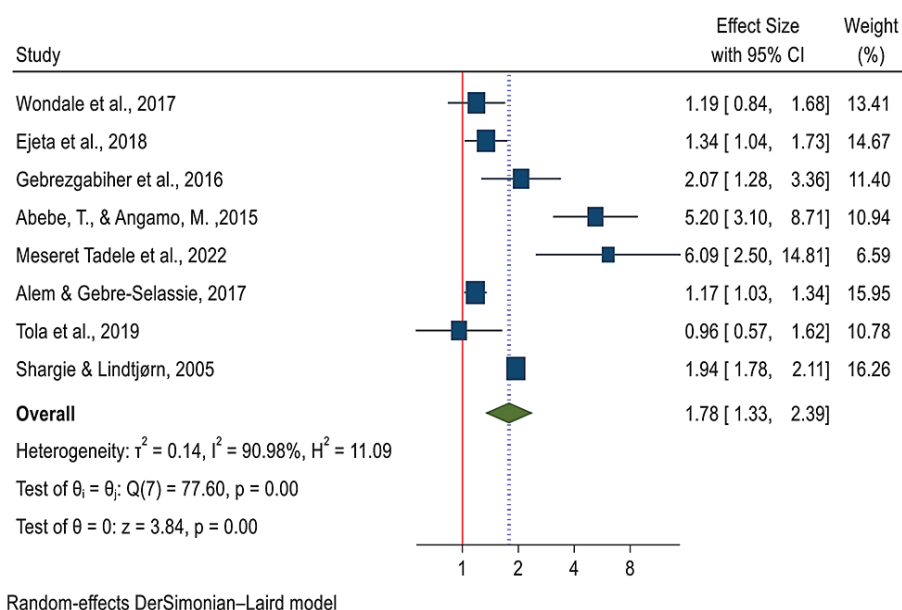


Figure 5 Extrapulmonary Tuberculosis (TB) and unsuccessful treatment outcomes

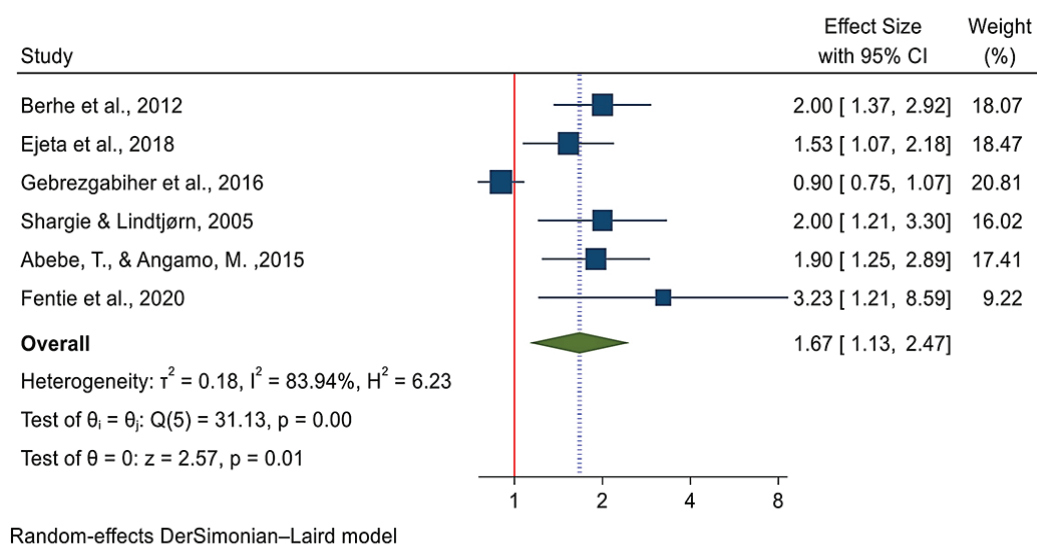


Figure 6 Retreatment and unsuccessful Tuberculosis (TB) treatment outcome

Discussion

The present systematic review and meta-analysis revealed that the overall magnitude of unsuccessful TB treatment outcomes in Ethiopia was 17% (95% CI 15%–20%). This finding reflects a notable proportion of patients who did not complete treatment successfully, encompassing treatment failure, default, or death. The observed heterogeneity across studies suggests substantial variability in the proportion of unsuccessful outcomes reported. Factors contributing to this heterogeneity may include geographical disparities, age, HIC infection, and types of healthcare institutions. When compared to studies conducted in other African countries, the magnitude of unsuccessful TB treatment outcomes in Ethiopia appears consistent with some regions while differing significantly from others. For instance, a systematic review in Africa reported an overall unsuccessful treatment outcome rate of 21%³⁰, similar to the pooled estimate in Ethiopia. However, the current report was higher than other African countries and global studies. For example, a report from China³¹ reported an unsuccessful treatment outcome of 1.8% of patients, and 11.5% was reported from Saudi Arabia³². These discrepancies may be attributed to differences in the healthcare systems, patient adherence, and the burden of TB–HIV coinfection across different regions. The subgroup analysis further elucidates the sources of heterogeneity. Geographical variations within Ethiopia are evident, with the Oromia region reporting the highest poor treatment outcome at 21.2%. These variations highlight the importance of addressing local healthcare challenges, particularly in resource-limited settings, in order to improve TB treatment outcomes. Moreover, subgroup analysis based on the type of TB shows that MDR–TB patients had the highest unsuccessful treatment outcome at 31.7%. This finding is consistent with global trends, where MDR–TB patients often have worse treatment outcomes due to the complexity of treatment regimens, higher pill burden, and the potential for adverse drug reactions¹.

Another report also found that unsuccessful outcome rates among MDR–TB patients were higher than those of pulmonary TB²⁵. These findings highlight the need for tailored interventions targeting MDR–TB patients in order to improve their treatment success rates.

The analysis demonstrated that individuals aged over 45 years were significantly more likely to experience unsuccessful TB treatment outcomes. This association has been consistently reported in previous studies. For instance, a report conducted in Nigeria³³ found that older age was associated with a higher risk of treatment failure and death. The reasons for this may include the presence of comorbidities, a weakened immune system, and delayed healthcare-seeking behavior among older adults. The current review indicated HIV co-infection was strongly associated with unsuccessful TB treatment outcomes. Our findings are in line with other research that has repeatedly shown HIV to be a strong predictor of poor TB treatment outcomes because HIV infection compromises the immune system, which worsens TB progression and lowers treatment success rates. TB–HIV co-infection has been a major problem in sub-Saharan Africa, where HIV is prevalent, increasing death and treatment failure rates. Furthermore, the current study emphasizes how critical it is to improve access to TB preventive therapy for people living with HIV and to boost antiretroviral therapy (ART) adherence among TB–HIV co-infected patients. Global trends also show this, with TB–HIV co-infection being identified as a primary cause of subpar TB treatment results globally¹. Patients with extrapulmonary TB had a 78% increased risk of unsuccessful treatment outcomes. This finding aligns with studies from other African countries, where EP–TB is associated with worse outcomes due to the difficulty in diagnosing and treating these cases³³. These findings underscore the need for improved diagnostic and treatment strategies for EP–TB patients in order to reduce the risk of unsuccessful outcomes. Moreover,

EP-TB frequently necessitates sophisticated diagnostic techniques like imaging and biopsies, which may not be easily accessible in resource-constrained environments like Ethiopia, in contrast to pulmonary TB, which is simpler to identify with sputum-based testing. Because the clinical symptoms of EP-TB may be less obvious than those of pulmonary TB, patients may put off obtaining therapy or finishing it, which increases the chance of unsatisfactory treatment results in these individuals. Retreatment was another significant determinant of unsuccessful TB treatment outcomes. Patients undergoing retreatment are often those who previously defaulted, failed treatment, or relapsed, and they typically face higher risks of drug resistance and treatment failure. This pattern has been observed across various studies, both in Africa and globally. A study in Kenya³⁴ found that retreatment cases had a significantly higher risk of treatment failure compared to new cases. Similarly, global studies have reported higher unsuccessful treatment outcomes among retreatment cases, particularly in settings with high MDR-TB prevalence³¹. These findings suggest the need for enhanced follow-up and support for patients undergoing retreatment in order to improve their chances of successful outcomes. Future efforts should focus on strengthening healthcare systems, particularly in regions with high TB-HIV co-infection and MDR-TB prevalence, and enhancing patient support mechanisms to reduce treatment failure, default, and mortality.

Limitations of the study

The majority of the included studies were facility-based cohort studies, which may overestimate mortality rates compared to community-based populations. Additionally, publication bias could have influenced the results, favoring significant associations. Study heterogeneity, likely due to unmeasured characteristics not accounted for in the analysis, and the small sample size for certain predictors, limits the generalizability of the findings.

Conclusion

This review highlights a significant burden of unsuccessful TB treatment outcomes in Ethiopia, with a pooled estimate of 17%. The analysis reveals that factors such as older age, HIV co-infection, extrapulmonary TB, and retreatment are major determinants of unsuccessful treatment outcomes. Addressing these determinants through targeted interventions and strengthening healthcare systems is crucial to improving TB treatment success and reducing mortality and treatment failure rates in Ethiopia and similar settings. Future efforts should focus on strengthening healthcare systems, particularly in regions with high TB-HIV co-infection and MDR-TB prevalence, and enhancing patient support mechanisms to reduce treatment failure, default, and mortality. Moreover, the influence of socioeconomic factors or region-specific interventions on TB treatment outcomes should be investigated.

Ethics approval and consent to participate

Not applicable to this section because it was conducted using secondary data.

Data Availability

All data analyzed during this study are included in this published article.

Authors' Contributions

SM and BAL were responsible for developing the protocol and were involved in various aspects of the study, including designing the study, selecting the eligible studies, extracting the data, and performing the statistical analyses. SM, AFG, and BAL contributed to drafting the initial versions of the manuscript and revising the manuscript. SM prepared and edited the final draft of the manuscript, which was subsequently read and approved by all the author.

Conflict of interest

The authors declare that they have no competing interests.

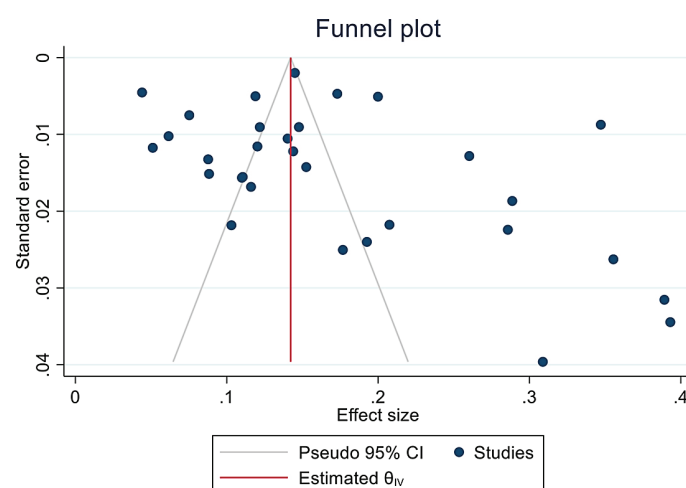
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Supplementary Figure 1 Funnel plot of publication bias