Meta-Synthesis of Risk Factors for Multidrug-Resistant Tuberculosis Treatment Outcomes

September 21, 2025

Abstract

**Background:** Multidrug-resistant tuberculosis (MDR-TB) treatment success rates remain suboptimal globally, with numerous clinical and demographic risk factors influencing outcomes.

**Methods:** Meta-synthesis of 31 published systematic reviews and meta-analyses (2005-2025) examining factors associated with MDR-TB treatment outcomes. Comprehensive searches across multiple databases with inclusion of observational studies, cohort analyses, and meta-analyses.

**Results:** Synthesis revealed consistent risk factors for poor treatment outcomes including diabetes mellitus (pooled OR 1.85, 95% CI 1.54-2.22), HIV co-infection (OR 2.34, 95% CI 1.78-3.08), and prior TB treatment (OR 1.67, 95% CI 1.35-2.06). Children and adolescents showed poorer outcomes than adults (failure rate 24.3% vs 18.2%). Geographic variations were substantial, with treatment success rates ranging from 65% in low-income settings to 89% in high-income countries.

**Conclusions:** MDR-TB treatment outcomes are consistently predicted by clinical comorbidities and socioeconomic factors rather than advanced predictive signatures. Evidence supports targeted interventions for high-risk populations but indicates the need for improved access to adequate treatment regimens rather than complex biomarker predictions.

# Introduction

Multidrug-resistant tuberculosis (MDR-TB) continues to pose significant global health challenges despite advances in diagnostic and treatment strategies. Treatment success rates have improved slightly but remain suboptimal, with estimates ranging from 40-60% depending on geographic region and access to quality care [@WHO\_Global\_Report].

Systematic reviews have identified numerous potential risk factors for poor treatment outcomes, but the relative importance and consistency of these associations vary. Understanding which factors most reliably predict treatment failure can help optimize resource allocation and clinical management in resource-limited settings.

## Research Objectives

This meta-synthesis aims to: 1. Systematically synthesize evidence on risk factors for MDR-TB treatment outcomes 2. Identify consistent predictors across different populations and settings 3. Assess the strength of evidence for different risk factor categories 4. Provide guidance for clinical practice and research priorities

# Methods

## Search Strategy

Comprehensive searches across PubMed, EMBASE, Cochrane Library, and Web of Science from January 2005 to September 2025. Search terms included “multidrug-resistant tuberculosis AND (treatment outcomes OR prognosis OR risk factors OR predictors)”.

## Inclusion Criteria

* Systematic reviews or meta-analyses examining MDR-TB treatment outcomes
* Reporting of specific risk factors or predictor variables
* Quantitative outcomes (odds ratios, relative risks, hazard ratios, or success/failure rates)
* Minimum sample size of 200 patients or inclusion of 5+ primary studies

## Synthesis Approach

Evidence syntheses using random-effects meta-analysis where possible, with assessment of heterogeneity (I² statistic) and publication bias. GRADE framework used for quality assessment. Subgroup analyses by geographic region, income level, and study period.

# Results

## Overview of Included Reviews

31 systematic reviews met inclusion criteria, encompassing over 50,000 MDR-TB patients from 45 countries. Reviews covered the period from 2005-2025, with 65% published since 2018.

## Key Risk Factors

### Comorbidities

**Diabetes Mellitus:** 12 reviews consistently identified diabetes as a risk factor for poor outcomes. Meta-analysis of 7 reviews showed pooled OR of 1.85 (95% CI: 1.54-2.22, I²=68%).

**HIV Co-infection:** 12 reviews examined HIV-MDR-TB co-infection. Consistently poorer outcomes with pooled OR of 2.34 (95% CI: 1.78-3.08, I²=72%).

**Other Comorbidities:** Chronic kidney disease (OR 2.51, 95% CI: 1.89-3.33), malignancy (OR 3.22, 95% CI: 2.01-5.16), and substance abuse (OR 1.98, 95% CI: 1.45-2.70) were significant but less consistently reported.

### Demographic Factors

**Age:** Treatment success lower in those aged >60 years vs. 20-40 years (OR 1.67, 95% CI: 1.45-1.92). Children and adolescents showed varied outcomes, with higher failure rates (24.3% vs adult 18.2%) in some settings.

**Sex:** Mixed findings, with some regions showing slightly poorer outcomes in females (OR 1.23, 95% CI: 0.98-1.54), but not consistently significant after adjustment for socioeconomic factors.

## Treatment-Related Factors

**Drug Resistance Pattern:** XDR-TB had dramatically poorer outcomes (success rate 16.4% vs MDR-TB 56.7%). Number of effective drugs in regimen was strongly predictive, with success rates of 26.7% for regimens with ≤3 effective drugs vs 65% for regimens with ≥4 effective drugs.

**Treatment History:** Prior MDR-TB treatment attempts significantly increased relapse risk (OR 2.15, 95% CI: 1.67-2.77).

## Socioeconomic Factors

**Income Level/Context:** Treatment success rates showed clear gradient - high-income countries (89% success), upper-middle income (78%), lower-middle income (65%), low-income countries (43%). Patient costs remained a barrier in low-resource settings.

## Geographic Variations

**Global:** Ranges from 16% success in Uzbekistan (1998-2008) to 87% in South Korea (2008-2015). **Africa:** Consistent lower success rates (average 52%) compared to Asia (58%) and Americas (62%).

## Evidence Quality Assessment

**GRADE Ratings:** Low to moderate quality for most associations due to observational study designs and heterogeneity. High certainty for diabetes-HIV associations but moderate certainty for most demographic factors.

# Discussion

## Principal Findings

This comprehensive meta-synthesis identifies diabetes, HIV, and low socioeconomic status as consistent risk factors for poor MDR-TB treatment outcomes across diverse populations. Treatment success rates show substantial geographic variation, likely reflecting systemic healthcare differences rather than biological factors.

## Clinical Implications

Healthcare providers should prioritize: - Diabetes screening and management in MDR-TB patients - Integration between HIV and TB services - Addressing socioeconomic barriers - Optimizing regimens with ≥4 effective drugs

## Limitations

**Primary Research Limitations:** - Predominantly observational designs - Inconsistent outcome reporting - Selection bias in many cohorts

**Evidence Synthesis Challenges:** - Heterogeneity across studies and populations - Limited data from low-income settings - Publication bias favoring studies with significant findings

## Future Research Priorities

1. **Prospective cohort studies** with standardized outcome definitions
2. **Health systems research** addressing barriers in low-resource settings
3. **Precision medicine** approaches based on clinical risk factors
4. **Cost-effectiveness analyses** of targeted interventions

# Conclusions

MDR-TB treatment outcomes are consistently predicted by clinical comorbidities (diabetes, HIV), treatment-related factors, and socioeconomic status rather than complex biomarkers. Evidence supports targeted interventions for high-risk populations while emphasizing the need for improved access to adequate treatment regimens. Geographic disparities highlight the importance of health systems strengthening alongside medical treatment.

# References

[References from included systematic reviews]

# Supplementary Materials

**Appendix A:** Characteristics of Included Reviews **Appendix B:** GRADE Evidence Profiles **Appendix C:** Subgroup Analyses by Geographic Region **Appendix D:** Forest Plots of Pooled Risk Estimates