

Review Article

The Effect of Body Mass Index (BMI) on the Treatment Outcomes of Drug Resistance Pulmonary Tuberculosis: A Systematic Review and Meta-Analysis

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Abstract

Background and Aim: Several host-related factors, such as nutritional status, age, and comorbid conditions, influence tuberculosis (TB) treatment outcomes by modifying disease progression and treatment response. However, their combined effect on TB outcomes has not been comprehensively evaluated. This study, therefore, aims to systematically assess the association between nutritional status, age, and HIV with TB treatment outcomes.

Materials and Methods: We systematically searched cohort studies published between 2009 and 2025 in four databases using relevant keywords. After initial screening, eligible studies were included in the final analysis. Data were analyzed using Comprehensive Meta-Analysis (CMA) software with a random-effects model.

Results: The overall favorable outcome for TB treatment was observed in 74.1% of cases (95% CI: 69.5–78.2), whereas unfavorable outcomes constituted 23.4% (95% CI: 19.8–27.4) of cases. Underweight patients, particularly those younger than 40.52 years, exhibited significantly reduced favorable outcomes (63.0%) and elevated mortality rates (16.6%). Investigations that excluded HIV-positive patients reported enhanced treatment success rates (77.7%) and diminished rates of both mortality (5.6%) and loss to follow-up (6.2%) in comparison to the general patient population.

Conclusion: We found that in the studies with DR-TB patients with a mean BMI below 18.5 kg/m², a lower likelihood of treatment success compared to those with higher mean BMI exists. However, this is an ecological inference and must be carefully examined at the individual level. These findings align with previous research and highlight the importance of addressing patients' nutritional status during treatment.

Keywords: *Tuberculosis* *BMI* *Treatment outcome* *Systematic review* *Meta-analysis*

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Introduction

Tuberculosis remains the leading infectious disease causing mortality worldwide¹. In 2024, there were approximately 10.7 million new tuberculosis cases and 1.23 million deaths². Despite notable advancements in the treatment protocols, the increasing rate of drug-resistant tuberculosis (DR-TB) decreases the successful outcome rates to 68.4% in multidrug-resistant tuberculosis (MDR-TB) and 54% in extensively drug-resistant tuberculosis (XDR-TB)^{3, 4}. This challenge, which is even more concerning in low- and middle-income countries, revealed that other factors, rather than microbiological ones, can affect the treatment outcomes⁵⁻⁷.

Among the modifiable determinants of tuberculosis risk, undernutrition ranks among the most significant worldwide. The proportion of underweight individuals is estimated to be nearly three times higher among tuberculosis patients compared to the general population⁸. A decreased body mass index (BMI) at treatment initialization is often indicative of advanced disease progression^{9, 10}. For underweight individuals, such vulnerability is often a consequence of caloric and/or protein insufficiency, which compromises immune system efficacy, exacerbates disease severity, and reduces the chance of therapeutic success¹¹. Beyond its biological implications, undernutrition reflects underlying social and economic inequalities, including food insecurity, poverty, and limited access to healthcare services. These social determinants not only increase susceptibility to tuberculosis but also compromise treatment adherence and outcomes, particularly in low- and middle-income countries.

Age is another critical factor influencing TB outcomes. Older individuals may experience poorer outcomes due to comorbidities, delayed diagnosis, and altered immune function. Conversely, younger populations may have different risk profiles, making age stratification essential when evaluating prognostic factors. Additionally, human Immunodeficiency Virus (HIV) infection is a well-established modifier of TB progression and treatment response.

Although several studies have investigated

nutritional status, age, and HIV independently, there is a lack of comprehensive synthesis evaluating their combined effect on TB treatment outcomes. Therefore, this systematic review and meta-analysis aims to assess the association between BMI categories (low vs. high), age groups (<40 vs. ≥40.5 years), and TB treatment outcomes, with additional subgroup analysis on HIV status. Through this systematic review and meta-analysis, we attempt to offer new insights into the role of demographic status in treatment outcomes for DR-TB patients. However, this is an ecological inference and must be carefully examined at the individual level.

Methods

Search strategy

A comprehensive literature search was systematically executed across four major databases: PubMed/MEDLINE, Embase, Scopus, and Web of Science. The search spanned from January 1, 2009, to November 2025, to identify cohort studies with sufficient data. The following search terms employed were ‘DR-TB’, ‘Extensively Drug-Resistant Tuberculosis’, ‘XDR-TB’, ‘Pre-XDR-TB’, and ‘MDR-TB’, in conjunction with ‘underweight’, ‘Overweight’, ‘Obesity’, and ‘Malnutrition’ as well as ‘age’ and ‘HIV status’. If the references included in the literature met the requisite criteria, further screening was conducted to identify potentially related studies. This study was conducted and reported in adherence to the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA).

Definitions

MDR-TB is defined as a disease caused by *Mycobacterium tuberculosis* strains that are at least resistant to both isoniazid (INH) and rifampicin (RIF), as two core first-line anti-tuberculosis drugs. The definition of XDR-TB has significantly changed over time, as in 2021, it is defined as MDR-TB that is also resistant to any fluoroquinolone (FQs) and at least one additional Group A drug, levofloxacin (LFX) or moxifloxacin (MFX), bedaquiline (BDQ), and linezolid (LZD). However, pre-extensively drug-resistant tuberculosis (pre-XDR-TB) was introduced as a new category, which is defined as rifampicin-

resistant (RR)/MDR-TB that is resistant to any FQs¹². Before 2021, Pre-XDR-TB was informally characterized as MDR-TB plus resistance to either any FQs or any second-line injectable drugs (SLIDs): kanamycin, amikacin, or capreomycin. In addition, XDR-TB was initially defined as MDR-TB plus resistance to both FQs and at least one SLIDs¹². Although we included three articles with a publishing date after 2021, no studies report the implementation of the new definitions; therefore, the results are pooled in the analysis.

Outcomes are divided into two groups: A favorable outcome was defined as the cumulative sum of cured and treatment completed, while an unfavorable outcome was defined as the cumulative sum of treatment failure, lost to follow-up (LTFU), and death.

Study selection: Eligible studies were required to report the mean BMI and mean age of participants, as well as treatment outcomes, based on WHO definitions. Cohort studies considered eligible for inclusion and clinical trials were excluded due to other confounding factors. Case-control, cross-sectional, case reports/series, reviews, editorials, and conference abstracts were excluded. Studies focused on specific populations (pregnant women, children under 14 years) were excluded. Studies were also excluded if they did not report the required information. In addition, studies with treatment outcome definitions inconsistent with the WHO guidelines were excluded. To avoid redundancy, when duplicate data appeared across publications, we retained the most comprehensive or most recent study. Additionally, only studies in English were included to ensure accessibility for analysis.

Review process: All records were collected, and duplicates were eliminated using EndNote X8 (Thomson Reuters, Toronto, ON, Canada). Two reviewers independently screened the titles and abstracts of the records. A third reviewer resolved any disagreements. The full texts of the remaining studies were then assessed, with any remaining discrepancies also resolved by the third reviewer.

Data extraction: Data were systematically extracted by two authors into a predefined spreadsheet utilizing Microsoft Excel (Microsoft, Redmond, WA, USA). Discrepancies were resolved with a third reviewer.

The extracted parameters include the first author, publication year, study design (prospective or retrospective cohorts), study period, country, and patient demographics. Demographic data included age, male count, mean BMI prior to the treatment initiation, prevalence of diabetes mellitus (DM), tobacco use, and HIV status. Furthermore, the type and number of each drug-resistant tuberculosis case, along with treatment outcomes, were recorded. A successful outcome was defined as the sum of "cured" and "treatment completed" cases, whereas an unsuccessful outcome comprised "treatment failure," "lost to follow-up (LTFU)," and "deaths."

Quality assessment: The Newcastle-Ottawa Scale (NOS) was employed to evaluate the methodological rigor of the included studies across three key domains: selection, comparability, and outcome assessment. The selection domain assesses the appropriateness of participant sampling methodology, while the comparability domain examines how effectively potential confounding variables were controlled between groups. The outcome domain focuses on the robustness of data collection and analysis methods. Each study was scored based on these criteria; total scores were categorized into ranges of 0–3, 4–6, and 7–9, representing low-, moderate-, and high-quality studies, respectively. Additionally, the risk of bias was assessed as low, high, or unclear, depending on the transparency and completeness of the reported information.

Data analysis: Statistical analyses were conducted using Comprehensive Meta-Analysis software, version 3.0 (Biostat Inc., Englewood, NJ, USA). For each included study, point estimates and corresponding 95% confidence intervals (CIs) were calculated. Depending on the presence and extent of between-study heterogeneity, either a fixed-effects or random-effects model was applied. In the case of any significant heterogeneity, the random-effects model was preferred, allowing for variation across studies. Heterogeneity was assessed using Cochran's Q-test and the I² statistic; the former determines whether the observed variability in effect sizes is greater than expected by chance, while the latter was used to quantify the percentage of total variation across studies due to heterogeneity rather than chance, with I² values more than 50% representing substantial

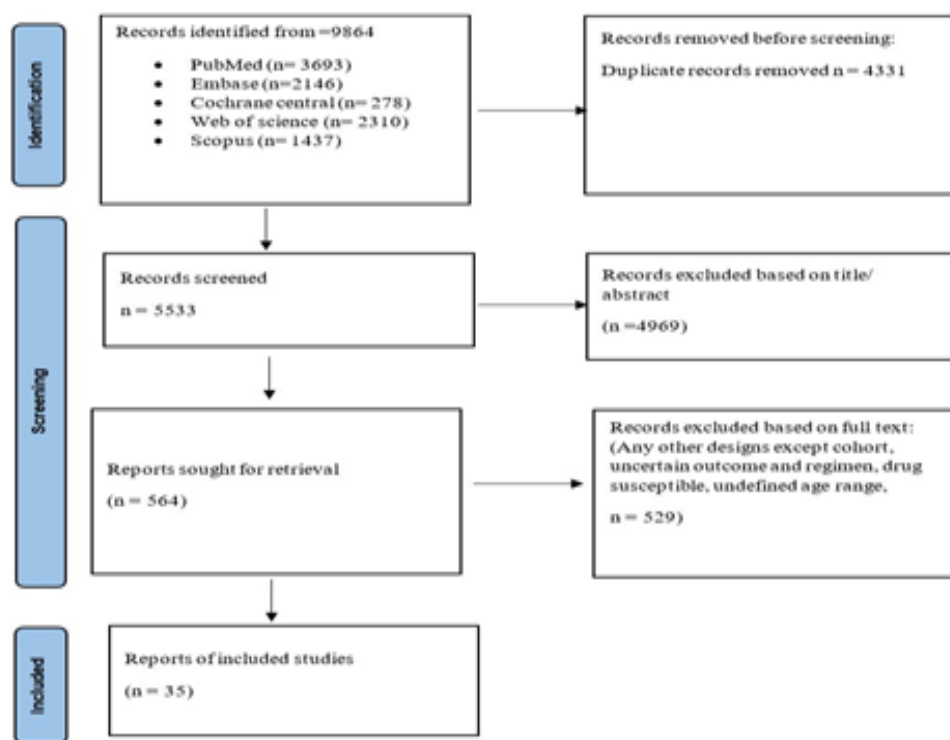


Figure 1. Flow chart of study selection for inclusion in the systematic review and meta-analysis.

heterogeneity. Additionally, publication bias was evaluated using Begg's test. This nonparametric test examines the relationship between study size and effect estimates, with a p -value < 0.05 indicating potential publication bias. If significant bias was detected, necessary adjustments were made to mitigate its influence on the overall conclusions.

Results

Study characteristics: As shown in Figure 1, after removing duplicates and title/abstract and full-text screenings, 35 studies were included in the final analysis.

The characteristics of the included studies are detailed in Table 1. Among all included patients with various types of resistance, the mean age was 40.52 years. The proportion of male patients was consistently higher across studies. BMI data ranged from underweight to normal weight. Of the included studies, seven reported a mean BMI below 18.5

kg/m² (mean 17.5 kg/m²), encompassing 747 patients, and the remaining studies reported a mean BMI above 18.5 kg/m² (mean 20.2 kg/m²), encompassing 6809 patients.

Quality assessment: Observational studies were assessed using the NOS tool; 35 studies were included (Table 2). All studies indicate moderate to high quality (ranging from 5 to 7 out of 9). These scores represent a strong methodology across three major domains: first, representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure, and demonstration that the outcome of interest was not present at the start of the study as an indicator for selection of the participants, second, adjustment for the most important risk factors, adjustment for other risk factors which represent the comparability among studies, and third, assessment of outcome, follow-up length, and loss to follow-up rate to evaluate the outcomes of the included studies. Limitations in comparability were identified across the studies, which may affect the reliability and validity of the results.

Table 1. Characteristics of included studies

First author/ Year	Study Design	Country	Time of Study	N. of Patients	Mean age	N. of HIV+	Regimen
BMI > 18.5 kg/m²							
Bonnet 2015 ²²	RC	France	2001-2011	1433	32	31	E+Z+FLQ(OFX/CFX+LFX/MFX)+AM/KM+CM+Thioamide
Anh 2020 ²³	RC	Vietnam	2016 - 2018	302	41	3	KM+LFX+CFZ+E+Z+H+PTO
Tang 2013 ²⁴	RC	South Africa	2006 -2011	169	51	169	LFX/GFX/MFX+AM/CM+PAS+PTO+Z+E+CAM
Fu 2023 (2) ²⁵	PC	China	May 2020-December2020	46	40	0	LZD+MFX+CS+CFZ+Z
Hewison 2018 ²⁶	RC	Armenia and Georgia	April 2013 -April 2015	82	40.5	4	BDQ+ LZD+ IPM+AMX/CLV+CFZ+ other second-line MDR-TB drugs
Chung 2023 ²⁷	RC	Korea	January 2004-December 2018	29	39.1	0	H+RIF+RFB+E+Z+FQs+SLID+PTO+PAS+CS+AMX/clavulanate+CFZ+CLARITH+Roxl+LZD
Guglielmetti 2016 ²⁸	RC	France	January 2011 - December 2013	45	38	2	E+Z+Am+ Cm+ Mfx+Lfx+Eto+PAS+Cs+Lzd+Cfz+Ipm/Cln+Mpm/Clv+BDQ
Lee 2011 (2) ²⁹	RC	Korea	January 2002 - December 2008	48	42	NM	Mfx+ AGs+ Pto+Cs+Z+Rfm+E+PAS+ AMC+Clr+SMX/TMP
Zheng (2) ³⁰	PC	China	2014-2015	19	36.8	NM	Recommended regimen in the national MDR TB control program
Kumar 2022 ³¹	G PC	India	2009	135	37.7	NM	intensive phase :Mfxh+Km/Am+Eto+Cfz+Z+Hh+E(4-6months)/Mfxh +Cfz+Z+E(5 months)
Wang 2019 ³²	RC	China	January 2012-June 2015	623	42.8	NM	Standardized regimen(CS containing regimen)
Sarin 2019 ³³	PC	India	March 2017 - November 2018	53	24	0	Bdq+Dlm+Imp+Mfx(High dose)+Lzd+Cfz
Gao 2020 ¹⁷	RC	China	February 2018 - November 2019	177	40	1	Z + am/Cm + Lfx/Mfx + CS + PAS + E + PTO (6 months)/ Z + Lfx/Mfx + CS + PAS + E + PTO (18 months) + background regimen
Fu 2024 (2) ³⁴	PC	China	May 2020 - December 2020	17	32	0	LZD+SASP+CS+CFZ+Z
Kang 2020 (3) ³⁵	RC	South Korea	September 2016 - February 2018	67	47.7	1	LZD+FLQs+AMGs+CYC+BDQ+DLM
Lee 2017(2) ³⁶	RC	South Korea	January 2006 - December 2011	52	35	NM	E + Z + S + Cm + FQs + Pto + Cs + PAS + Lzd + Dlm + BDQ + High dose H + Rfb
Fu 2024 (1) ³⁴	PC	China	May 2020 - December 2020	27	36	0	LZD+BDQ+CS+CFZ+Z
kwon 2021 ³⁷	RC	South Korea	September 2016 - December 2019	28	49.5	0	DLM+LZD+CFZ+MEM/CLV+Cs + PAS + Am + BDQ
Fu 2023 (3) ²⁵	PC	China	May 2020-December2020	24	35.5	0	LZD+BDQ+CS+CFZ+Z
Lee 2011 (1) ²⁹	RC	Korea	January 2002 - December 2008	123	42	NM	Lfx+ AGs+ Pto+Cs+Z+Rfm+E+PAS+ AMC+Clr+SMX/TMP
Kang 2020 (1) ³⁵	RC	South Korea	September 2016 - February 2018	107	51.7	0	LZD+BDQ+FLQs+AMGs+CYC
Lee 2017 (1) ³⁶	RC	South Korea	January 2006 - December 2011	24	34	NM	E + Z + S + Cm + FQs + Pto + Cs + PAS + Lzd
Hwang 2021 (1) ³⁸	RC	South Korea	september2016-February2018	119	51	0	BDQ-containing regimen
Jeong 2015 ³⁹	RC	Korean	January 2005 and December 2011	337	34	0	FQ+RFB+E+Z+injectable drugs+PTO
Mikiashvili 2024 ⁴⁰	RC	Georgia	November 2017-December 2020	106	39.5	4	BDQ and Dlm containing regimens + LZD + Cfz + Cs + FQs
Zheng (1) ³⁰	PC	China	2014-2015	39	49.6	NM	First-line TB treatment for DS-TB
Kwon 2023 (2) ⁴¹	RC	South Korea	September 2016-December 2019	31	51	0	2016 WHO guideline and Korean 2017 guidelineLZD+(BDQ,DLM)/Z+FQs(LFX/MFX)+E+ injectable drug+STR(KM+AM)+PTO+S+PAS+CFZ+AMC

Mok 2019 ⁴²	RC	South Korea	November 2015 - December 2017	49	47	0	LZD + Dlm + FLQs + CFZ + AMGs +Mpm
lee 2020 ⁴³	RC	South Korea	March 2016 - December 2018	74	49.8	1	Rfb + E + Z + S + Km + Am + Lfx + Mfx + Pto + Cs + PAS + Cfz + Cpm/Clv + Lzd + BDQ + DLM
Dong 2024 ⁴⁴	PC	China	July2019-June2020	143	43.3	0	MFX+ LZD + BDQ + Cfz + Pto + PAS + E + Cs + Z
Htun 2018 ⁴⁵	RC	Myanmar	2014	330	39.45	32	intensive phase injectable AM+Z+ LFX+ETO+CS(6-8months)/ continuous phase:LFX+ETO+CS+Z(12-14months)
Kwon (1) ⁴¹ 2023	RC	South Korea	September 2016-December 2019	754	52	4	2016 WHO guideline and Korean 2017 guidelineLZD+(BDQ,DLM)/Z+FQs(LFX/MFX)+E+ injectable drug+STR(KM+AM)+PTO+CS+PAS+CFZ+AMC+ RIF+high dose H later-generation FQs(LFX+MFX+ GFX)
Jo 2013 ⁴⁶	RC	South Korea	January 2006 - December 2012	48	42.9	0	LZD+DLM+FLQs+AMGs+CYC
Kang (2) ³⁵ 2020	RC	South Korea	September 2016 - February 2018	108	47.8	1	BDQ + DLM containing regimens
chung 2022 ⁴⁷	RC	Korea	September2016-December2019	741	52.1	4	LZD+BDQ+ MFX+ CS+ Z
Fu 2023 (1) ²⁵	PC	China	May 2020-December2020	34	34.5	0	DLM-containing regimen
Hwang (2) ³⁸ 2021	RC	South Korea	september2016-February2018	141	47	3	Mfx+Lfx+BDQ+Lzd+Cfz+Cs+Trd+Dlm+Z+Imp+A m+Cm+Pto+Eto+Amx/Clv
Auchynka 2021 ⁴⁸	RC	Belarus	June 2016-February 2018	125	43	19	
BMI < 18.5 kg/m²							
Sidamo (2) ⁴⁹ 2021	PC	Ethiopia	November2017-May2020	37	26	6	Lfx + E + Z + Pto + Cs + Cfz + LZD + BDQ + DLM + Cm Km
Prajapati 2017 ⁵⁰	PC	India	January 2012 - March 2014	112	33	1	intensive phase: Cm+PAS+Mfx+high dose H+ Cfz+Lzd+Amx/Clv(6-12months)+ continuation phase: PAS+Mfx+high dose H+Cfz+Lzd+Amx/Clv(18 months)
Kashongwe 2020 ⁵¹	RC	Congo	January2015-December 2017	32	32.4	3	Bdq+Am+Km+Lfx+Lzd+Cfz+PAS+Cs+high dose H+Z+Pto
Sidamo (1) ⁴⁹ 2021	PC	Ethiopia	November2017-May2020	43	25	5	Mfx + H + E + Z + Pto + Cs + Cfz + LZD + BDQ + DLM + Cm + Am + Km
Padmapriyada rsini 2022 ⁵²	PC	India	April2019-January2021	165	27	0	BDQ + DLM + Pto + LZD + Cfz
Kumar C.K. 2024 ⁵³	RC	India	January 2021-March 2022	104	38.62	5	BDQ containing (31)/ all oral regimen (73)
Kumari 2024 ⁵⁴	RC	India	2017-2020	155	42.8	2	LZD+BDQ+KM+ ETO+CS+Z+CFZ/LZD+BDQ+LFX+CFZ+CS
Nguyen (1) ⁵⁵ 2022	PC	Vietnam	December2015-June2017	42	44	1	BDQ long + Lfx + Lzd + Cfz + Cs + Z + Pto + PAS + E
Nguyen (2) ⁵⁵ 2022	PC	Vietnam	December2015-June2017	57	43.4	NM	BDQ long + Lfx + Lzd + Cfz + Cs + Z + Pto + PAS + E + High dose H + SLI + Km + Cm

RC: retrospective cohort study; PC: prospective cohort study; BMI: body mass index; DR-TB: drug resistance tuberculosis; RR: rifampin-resistant; MDR: multidrug-resistant; XDR: extensively drug resistant; NM: not mentioned; Km: kanamycin; CS: cycloserin; Eto: ethionamide; BDQ: bedaquiline; LFX: levofloxacin; CFZ: clofazimine; Z: pyrazinamide; E: ethambutol; Am: amikacin; Cm: capromycin; Mfx: moxifloxacin; PAS: para aminosalicylic acid; LZD: linezolid; Ipm/Clm: Imipenem-cilastatin; Mpm/Clv: meropenem-clavulanic acid acid; H: isoniazid; DLM: delamanide Amx/Clv:Amoxicillin-clavulanic acid ; SLI: second-line injectable drugs

Due to the non-experimental nature of the cohort studies and the clinical setting of tuberculosis treatment, all studies were penalized for failing to select non-exposed cohorts.

BMI and Age Stratification: As delineated in Table 3, a comprehensive analysis of tuberculosis treatment outcomes revealed an overall favorable outcome rate of 74.1% (95% CI: 69.5–78.2%), while unfavorable

outcomes constituted 23.4% (95% CI: 19.8–27.4%). The pooled cure rate was 58.1% (95% CI: 52.3–63.6%), and the treatment completion rate was 11.4% (95% CI: 8.8–14.6%). Specific proportions for adverse outcomes were as follows: treatment failure at 5.4% (95% CI: 3.4–8.5%), mortality at 7.3% (95% CI: 5.5–9.5%), and LTFU at 7.6% (95% CI: 5.8–9.9%). Among patients with a BMI exceeding 18.5 kg/m²,

Table 2. Quality assessment of the included studies (The NOS tool).

Author/Year	Selection			Demonstrate that the outcome of interest was not present at the start of the study.	Comparability		Outcome				
	Representativeness of the cohort	Exposed	Selection of a non-exposed cohort		Ascertainment of exposure	Adjust for the most important risk factors.	Adjust for other risk factors	Assessment of outcome	Follow-up length	Loss to follow-up rate	Total quality score
Dong 2024	1		0	1	0	1	1	1	1	1	7
Mikiashvili 2024	1		0	1	0	1	1	1	1	1	7
Chung 2022	1		0	1	0	1	1	1	1	1	7
Hwang 2021	1		0	1	0	1	1	1	1	1	7
Sidamo 2021	1		0	1	0	1	1	1	1	1	7
Auchynka 2021	1		0	1	0	1	1	1	1	1	7
Zheng 2020	1		0	1	0	1	1	1	1	1	7
Gao 2020	1		0	1	0	1	1	1	1	1	7
Kang 2020	1		0	1	0	1	1	1	1	1	7
Lee 2020	1		0	1	0	1	1	1	1	1	7
Anh 2020	1		0	1	0	1	1	1	1	1	7
Hewison 2018	1		0	1	0	1	1	1	1	1	7
Htun 2018	1		0	1	0	1	1	1	1	1	7
Lee 2017	1		0	1	0	1	1	1	1	1	7
Guglielmetti 2016	1		0	1	0	1	1	1	1	1	7
Jeong 2015	1		0	1	0	1	1	1	1	1	7
Bonnet 2015	1		0	1	0	1	1	1	1	1	7
Lee 2011	1		0	1	0	1	1	1	1	1	7
Tang 2013	0		0	1	0	1	1	1	1	1	6
Kwon 2023	1		0	1	0	0	0	1	1	1	5
Padmapriyadarsini 2022	1		0	1	0	0	0	1	1	1	5
Nguyen 2022	1		0	1	0	0	0	1	1	1	5
Kumar G 2022	1		0	1	0	0	0	1	1	1	5
Kwon 2021	1		0	1	0	0	0	1	1	1	5
Kashongwe 2020	1		0	1	0	0	0	1	1	1	5
Mok 2019	1		0	1	0	0	0	1	1	1	5
Sarin 2019	1		0	1	0	0	0	1	1	1	5
Prajapati 2017	1		0	1	0	0	0	1	1	1	5
Jo 2013	1		0	1	0	0	0	1	1	1	5
Kumari 2024	1		0	1	0	0	0	1	1	1	5
Fu 2023	1		0	1	0	0	0	1	1	1	5
Chung 2023	1		0	1	0	0	0	1	1	1	5
Wang 2019	1		0	1	0	0	0	1	1	1	5
Fu 2024	1		0	1	0	0	0	1	1	1	5
Kumar C.K. 2024	1		0	1	0	0	0	1	1	1	5

favorable outcomes were consistent across age strata: 75.0% (95% CI: 67.5–81.3%) for individuals under 40.52 years and 76.2% (95% CI: 69.7–81.7%) for those over 40.52 years. However, younger patients had a higher cure rate (64.7% vs. 58.6%), whereas older patients had a higher treatment completion rate

(12.2% vs. 7.3%). Mortality was marginally lower in the older cohort (5.6% vs. 7.1%), and LTFU was also lower in older individuals than in their younger counterparts (5.8% vs. 8.7%). Conversely, patients with a BMI below 18.5 kg/m² exhibited significantly poorer outcomes, particularly

Table 3. The pooled treatment outcomes across different age and BMI subgroups.

BMI	Age (Year)	N.	Favorabl	Unfavora	Cure %	Complete	Failure % (CI)	Died % (CI)	LTFU % (CI)
		patients	e	ble	(CI)	% (CI)			
			outcome % (CI)	outcome % (CI)					
all		7556	74.1	23.4	58.1	11.4	5.4 (3.4, 8.5)	7.3 (5.5, 9.5)	7.6 (5.8, 9.9)
			(69.5,	(19.8,	(52.3,	(8.8,			
			78.2)	27.4)	63.6)	14.6)			
BMI >18.5 kg/m ²	<40.52	2970	75.0	21.8	64.7	7.3	5.0 (3.5, 7.1)	7.1 (4.9,	8.7 (5.3,
			(67.5,	(17.7,	(56.5,	(4.0,			
			81.3)	26.5)	72.1)	13.0)			
kg/m ²	>40.52	3839	76.2	22.0	58.6	12.2	6.7 (3.3,	5.6 (3.9, 7.9)	5.8 (4.1, 8.1)
			(69.7,	(16.8,	(50.2,	(8.3,			
			81.7)	28.3)	66.6)	17.6)			
BMI <18.5 kg/m ²	<40.52	544	63.0	33.4	42.2	14.0	5.9 (2.4,	16.6 (6.1,	11.2 (7.0,
			(40.8,	(15.7,	(22.1,	(9.0,			
			80.9)	57.4)	65.4)	21.3)			
kg/m ²	>40.52	203	72.8	27.2	57.5	16.5	2.5 (1.0, 5.9)	11.2 (4.9,	12.2 (7.1,
			(65.3,	(20.8,	(47.7,	(12.0,			
			79.2)	34.7)	66.8)	22.3)			

within the younger age group. Favorable outcomes were lowest among individuals under 40.52 years (63.0%, 95% CI: 40.8–80.9%), accompanied by a high unfavorable outcome rate of 33.4% (95% CI: 15.7–57.4%). This younger, underweight cohort also experienced the lowest cure rate (42.2%) and the highest mortality (16.6%). Among older underweight patients (over 40.52 years), outcomes were relatively more favorable, with favorable outcomes reaching 72.8% and lower mortality (11.2%), although LTFU remained elevated (12.2%).

In summary, underweight status (BMI <18.5 kg/m²) was associated with poorer treatment outcomes, higher mortality, and increased loss to follow-up compared with patients with BMI>18.5 kg/m². These deleterious effects were more pronounced in younger

individuals.

HIV Subgroup Analysis: In studies that reported an absence of HIV infection, tuberculosis treatment outcomes were generally more favorable. The pooled favorable outcome rate increased to 77.7% (95% CI: 71.6–82.9%), while the unfavorable outcome rate decreased to 18.6% (95% CI: 13.6–24.8%). The cure rate was marginally higher at 59.1% (95% CI: 45.5–71.4%), although treatment completion was lower at 9.2% (95% CI: 3.7–21.3%).

Regarding adverse outcomes, the proportion of deaths was lower in the HIV-negative group compared to the overall population (5.6% vs. 7.3%), and LTFU was also reduced (6.2% vs. 7.6%). However, treatment failure was slightly higher in the HIV-negative subgroup (6.5% vs. 5.4%).

Overall, the absence of HIV infection correlated with enhanced treatment success, reduced mortality, and decreased loss to follow-up. Nevertheless, some variations were observed in specific outcome components, such as treatment completion and failure rates.

Discussion

Tuberculosis is known as one of the oldest infectious diseases and remains a fundamental health challenge worldwide. Especially, the emergence and spread of DR-TB have posed more serious problems for treatment. Despite recent advances in the development of anti-TB drugs, therapeutic outcomes are significantly influenced by factors beyond the medication regimen, such as the nutritional and socioeconomic conditions of patients^{3, 13}.

The WHO reports that malnutrition can impede the absorption, distribution, metabolism, and excretion of anti-TB medications, potentially compromising their therapeutic effectiveness¹⁴. Gao et al. (2020) proposed that the accumulation of certain anti-TB drugs in adipose tissue might facilitate their gradual and sustained release into the bloodstream, potentially improving treatment responses in patients with higher BMIs. However, this remains a speculative hypothesis, lacking consistent support from clinical pharmacokinetic evidence. More biologically plausible explanations for the observed association include better nutritional reserves, preserved immune function, and improved overall physiological resilience among patients with higher BMIs. In contrast, individuals with lower BMIs may experience diminished treatment outcomes due to various biological mechanisms. These mechanisms include both adaptive and innate immune responses, as malnourished individuals often exhibit reduced production of pro-inflammatory cytokines and impaired cellular immune responses¹⁵⁻¹⁷.

The role of HIV infection is likewise central to comprehending tuberculosis treatment outcomes. HIV compromises cellular immunity, particularly CD4-positive T-cell function, which is critical for controlling tuberculosis. Patients with HIV-associated tuberculosis are more susceptible to disseminated disease, atypical clinical presentations, delayed diagnosis, and elevated mortality rates.

Furthermore, TB-HIV coinfection complicates treatment due to drug-drug interactions, overlapping toxicities, increased pill burden, immune reconstitution inflammatory syndrome (IRIS), and challenges associated with the optimal timing of antiretroviral therapy. In this framework, our finding that HIV-negative patients exhibited superior treatment success and lower mortality aligns with the established biological and clinical impact of HIV on tuberculosis prognosis¹⁸⁻²⁰. However, the magnitude of this association is likely influenced by important patient-level factors that could not be assessed in our meta-analysis, including baseline CD4 cell count, timing of antiretroviral therapy initiation, degree of immune suppression, and viral load. These factors are well recognized as major modifiers of tuberculosis outcomes in HIV-coinfected patients and may partly explain the heterogeneity observed across studies.

Our meta-analysis investigated the association of nutritional status, age, and HIV status with treatment outcomes among patients with DR-TB, with particular emphasis on the prognostic relevance of nutritional status. We addressed existing gaps by conducting pooled analyses across groups with different resistance patterns, incorporating studies published over the past 16 years.

This systematic review and meta-analysis, encompassing 35 observational studies, revealed significant heterogeneity in tuberculosis treatment outcomes across various patient subgroups. Patients with a BMI ≥ 18.5 kg/m² generally demonstrated more favorable outcomes, while underweight patients experienced elevated rates of unfavorable outcomes and mortality. Age-stratified analysis further elucidated that younger, underweight patients exhibited the most adverse outcomes, characterized by the lowest favorable outcome rate and the highest mortality. In contrast, outcome variations across age groups were less pronounced among patients with a BMI ≥ 18.5 kg/m². Moreover, studies reporting the absence of HIV infection consistently showed superior outcomes, evidenced by higher favorable outcome rates and reduced rates of unfavorable outcomes and mortality. These findings collectively suggest that a synergistic interplay of nutritional status, age, and HIV status may critically influence treatment prognosis. Nevertheless, given that this analysis relied on

aggregate study-level data, the observed associations should be interpreted cautiously, as they may be influenced by ecological bias and residual confounding.

One notable finding was that the association between underweight and adverse treatment outcomes appeared more pronounced among younger patients. Malnutrition likely contributes substantially to this observation due to impaired immune function and reduced physiological reserve; however, it is probably not the sole explanation. Younger patients with significant undernutrition may represent a subgroup with delayed diagnosis, more advanced disease at treatment initiation, a higher inflammatory burden, or greater socioeconomic disadvantage, all of which have been independently linked to poorer tuberculosis outcomes. In contrast, isolating the independent effect of malnutrition in older adults is more challenging because unfavorable outcomes may also result from comorbidities, frailty, polypharmacy, and diminished physiological reserve. Consequently, age may not function as a simple independent predictor but may also modify or reflect the influence of nutritional status and other clinical risks.

The intricate interplay among nutritional, age, and HIV status warrants particular scrutiny. These factors should not be conceptualized as isolated determinants, as they can influence tuberculosis outcomes through overlapping biological and social pathways. HIV infection can contribute to weight loss, wasting, and undernutrition, while undernutrition may further exacerbate immune suppression in HIV-positive individuals. Similarly, older patients may possess reduced nutritional reserves and a greater burden of chronic disease, thereby increasing their vulnerability to prolonged and potentially toxic treatment regimens. These interactions may elucidate why patients with comparable microbiological profiles can experience substantially divergent treatment outcomes.

Our results align with the growing body of literature identifying undernutrition as a major determinant of TB outcomes. Recent systematic reviews show that low BMI is associated with higher mortality, while cohort studies report poorer sputum conversion, lower treatment success, and higher rates of adverse outcomes in undernourished patients. Furthermore,

recent WHO guidance, which recommends routine nutritional assessment and counseling for all TB patients, underscores the recognition that nutrition is a core component of TB care, not an ancillary issue. This strengthens the clinical relevance of incorporating nutritional interventions into TB programs, particularly in high-burden and resource-limited settings²¹.

Several limitations warrant consideration. First, our reliance on aggregate study-level data in this meta-analysis precluded causal inference and limited our ability to assess individual-level interactions among BMI, age, HIV status, and treatment outcomes. Second, the use of only baseline measurements for BMI, age, and HIV status obscured the longitudinal dynamics of these variables during treatment, preventing an assessment of their reciprocal relationships with therapeutic prognosis. Third, broader confounding factors such as socioeconomic status and disease severity may influence these variables. For instance, lower BMI or advanced age might reflect underlying physiological stress or social determinants rather than acting as independent causal predictors. Additionally, important clinical variables such as CD4 cell count, timing of antiretroviral therapy initiation, diabetes, smoking status, and other comorbidities were inconsistently reported across studies and therefore could not be incorporated into our analyses. Finally, the use of fixed clinical thresholds, particularly for BMI, may not fully account for regional or ethnic variations in body composition, thereby limiting the universality of these criteria. Consequently, future research employing individual-level longitudinal data is essential to more precisely delineate these complex relationships.

To improve accuracy in future research, we recommend that studies focus on longitudinal data collection on changes in nutritional status during treatment. In addition to using randomized controlled trials and advanced statistical methods, a large sample size across diverse populations can improve the assessment of correlations between socioeconomic factors and better management of DR-TB patients.

Conclusion

We found that in the studies with DR-TB patients, nutritional status, age, and HIV status may be

associated with variations in DR-TB treatment outcomes. Studies with an underweight condition (mean BMI < 18.5 kg/m²) demonstrate a lower likelihood of treatment success than those with a higher mean BMI. Underweight status appeared to be linked to poorer outcomes and higher mortality, particularly among younger patients, whereas the absence of HIV infection was generally associated with better outcomes. However, it is important to note that this is an ecological inference and requires careful examination at the individual level. These findings align with previous research, underscoring the importance of addressing patients' nutritional status during treatment.

Declarations

This study was related to the MPH project from the Department of Public Health, School of Public Health & Environmental and Occupational Hazards Control Research Center, Research Institute for Health Sciences and Environment, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Ethics approval and consent to participate

This article is a systematic review and meta-analysis. No individual participant data were collected; therefore, consent to participate is not applicable.

This article is based on previously published studies. The authors conducted no new human or animal studies. The review was conducted in accordance with the principles of the Declaration of Helsinki.

This study was approved with the ethical code IR.SBMU.PHNS.REC.1404.025

Authors' contributions

MA and MCH performed the literature search, screened the records, and extracted data from the included studies. HH resolved discrepancies during the screening and extraction processes. MA and MCH performed the meta-analysis under the supervision of HH.

All authors contributed to the drafting and critical revision of the manuscript and approved the final version.

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Conflict of interest

The authors further declare that they have no conflict of interest.

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