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Research Article

Treatment Outcomes and Interrelated Factors among Patients with Drug-Susceptible Tuberculosis in Ethiopia from Espousal of "New Post-2015 End TB Strategy" to End of 2023: A Systematic Review and Meta-Analysis

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Abstract

Introduction: Tuberculosis is a communicable disease that is a major public health problem throughout the world by infecting one-third of the world's population and the world's second leading cause of death from a single infectious agent.

Objective: to assess the overall favourable treatment outcome and to identify all potential predictors associated with unfavourable treatment outcome among patients with drug susceptible tuberculosis in Ethiopia from espousal of "new post-2015 end TB strategy" to end of 2023.

Methods: Published literatures were conducted in this systematic review and meta-analysis. Original studies were identified through a computerized systematic search using PubMed, Google Scholar, Science Direct, Cochrane library, CINAHL and Scopus. The quality of studies was assessed using the Joanna Briggs Institute critical appraisal checklist. Heterogeneity across studies was assessed using Cochran's Q test and I^2 statistic.

Results: in a systematic search, a total of 988 articles were identified. Of these, 43 observational studies were eligible for systematic review and meta-analysis. It was found that 35,046 patients reported treatment outcomes. The treatment success rate varies from 30.3% to 95.6%. The overall pooled TB treatment success rate from espousal of new post-2015 end TB strategy up to end of 2023 in Ethiopia was 82.4% (with 95% CI of 79.04% to 85.7%). Based on subgroup analysis by region, the success rate was 90.5% in Addis Ababa, 84.2% in Afar, 82.5% in Amhara, 89.9% in Harari, 82.4% in Southern region, 95.5% in Sidama, 80.2% in Oromia, 55.4% in Southwest Ethiopia and 80.6% in Tigray. Predominantly, pulmonary TB patients (smear -/+), older age, TB/HIV co-infection, HIV positive, retreatment, distance from the health facility and rural residence were the most frequently identified factors associated with unfavourable TB treatment outcome.

Conclusion: This study revealed that the overall TB treatment success rate in Ethiopia was below the threshold of the Global End TB strategy target (≥90%). They're had regional disparities in treatment success rate in Ethiopia. Pulmonary TB patients (smear -/+), older age, TB/HIV co-infection, HIV positive, retreatment, distance from the health facility and rural residence were associated with unfavourable TB treatment outcome. To enhance treatment success rate, there should be special consideration for regions which had low TB treatment success rate and for patients with TB/HIV co-infection, older age, rural residence and HIV positive.

Keywords: Drug susceptible; Tuberculosis; Treatment; Outcome; Success rate; Ethiopia.

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Introduction

Tuberculosis (TB) is a communicable disease that is a major public health problem throughout the world by infecting one-third of the world's population [1-3] and its bacterium is one of the most destructive pathogens on the planet [4]. In 2022, tuberculosis was the world's second leading cause of death from a single infectious agent, after coronavirus disease (COVID-19), and caused almost twice as many deaths as HIV/AIDS [3]. It is the eighth 8th, the 5th and the 1st cause of death among the top ten causes of death in Africa, Ethiopia and southern region respectively [3,5,6]. In WHO African region, TB accounts for 23% of new case and 31% of TB-related deaths, despite making up only 15% of the world's population [7]. In Ethiopia, TB killed over 19,000 people in 2022. The WHO estimates that about 30 percent of TB cases go undetected by the healthcare system in Ethiopia, resulting in unnecessary deaths [4]. According to World health organization among the top 30 high burden countries, Ethiopia ranked 12th in TB incidence, and among the high Multi-Drug-Resistant TB (MDR-TB) high burden counties, ranked 24th, becomes 3rd among African countries [3,8,9].

Tuberculosis places its heaviest burden on the world's poorest and most vulnerable, further aggravating existing inequalities [10]. People affected by TB face costs and suffer income loss equivalent on average of more than 50 per cent of their income [10,11]. Almost all countries including Ethiopia committed to accelerate the fight to end TB epidemic by 2035 by endorsing the new post-2015 global End TB strategy [11] and Ethiopia has aligned this National TB Strategic Plan within the framework of National Health Sector Transformation Plan (HSTP) [12]. This strategy aims to end the global TB epidemic with targets to reduce TB deaths by 95% and new cases by 90% between 2015 and 2035 [11]. The global strategy also targeted to make sure that no family has burdened with TB catastrophic expenses [11,13,14]. World Health Organization recommends the DOTS strategic plan to scale up TB prevention and control as well as to improve TB treatment success rates and case detection rate [1]. It is adopted in Ethiopia since 1997 after successful piloting with the development of the first combined tuberculosis and leprosy prevention and control program [15,16].

Effective treatment of Tuberculosis (TB) patients is one of the basic measures of tuberculosis infection prevention and control strategy [12,16,17]. Scrutinizing tuberculosis treatment outcomes and their potential risk factors is an important indicator of the performance of a country's TB control program [17,18]. Tuberculosis treatment outcomes are the final results of anti-TB drugs which are mutually exclusive and only one outcome should be assigned per patient per treatment course [7,16,19,20]. The intentions of tuberculosis treatment are: to cure the patient from tuberculosis, to prevent death from tuberculosis disease and its late effects, to prevent relapse of tuberculosis, to prevent the development of acquired drug resistance, and to decrease tuberculosis transmission [3,16,21]. Without treatment the death rate from TB is high that is about 70% of individuals with sputum smear-positive pulmonary TB died within 10 years of being diagnosed, as did about 20% of people with smear-negative pulmonary TB whereas with treatment about 85% of people with TB can be cured [22,23]. The success rate of TB treatment is 88% worldwide but it is 89% both in Africa and Ethiopia respectively [3,24] and 85.5% in Southern Nation Nationality and Peoples' Region (SNNPR) [25] which is below the threshold [11,26,27]. Among patients with unsuccessful treatment outcome, nearly 50% were died and the rest were failures and defaulters [3,28].

Tuberculosis can affect anyone, anywhere and anybody sties, but about 90% of people who developed TB are adults and more predominant in men than women in all age groups. In 2022, 55% of people who developed TB were men and 33% were women. Almost 90% of cases each year are in 30 high tuberculosis burden countries [3,29,30]. Ethiopia is implementing patient-centered equitable and quality TB treatment to address the gaps in treatment success [9,16] since TB treatment success rate is one of the ten priority indicators in achieving the targets of the End TB strategy [11,31-33] at the latest by 2025.The Global Plan End TB developed by Stop TB Partnership also aimed to achieve three 90-(90)–90 TB control program targets, that is, reach 90% of all people who need TB treatment, including 90% of people in key populations, and achieve at least 90% TB treatment success rate [34]. Even though there had been a systematic review and meta-analysis on the assessment of the overall TB treatment outcomes before the year 2017 in Ethiopia [35], there is no a recent systematic review on the evaluation of the overall progress of drug-susceptible TB treatment outcomes from espousal of "new post-2015 End TB strategy" to 2023. Hence, this study is aimed to get durable evidence from the available literatures regarding favourable treatment outcome among patients with drug-susceptible TB and to identify all potential predictors that are associated with unfavourable TB treatment outcomes in Ethiopia from espousal of "new post-2015 End TB strategy" to end of 2023.

Methods and Materials

Search Strategy and Information Source

A systematic review and meta-analysis were conducted to estimate the overall favourable tuberculosis treatment outcome among patients with drug susceptible TB in Ethiopia. This review and meta-analysis were conducted according to the guideline of Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) [36]. The articles searching were conducted systematically from the electronic databases including; PubMed, Google Scholar, Science Direct, Cochrane library, CINAHL and Scopus. The search will be conducted using the keywords; tuberculosis, treatment outcome. The search will be conducted using the keywords; tuberculosis, treatment outcome and predictors /risk factors/determinants. The search string for PubMed; ("tuberculosis"[MeSH Terms] OR ("TB"[AllFields]) AND ("treatment outcome" [MeSHTerms] OR ("treatment"[AllFields] AND "outcome"[All Fields]) OR "treatment outcome" [All Fields] OR ("treatment"[All Fields] AND "outcomes"[All Fields]) OR "treatment outcomes"[All Fields]) AND associated [All Fields] AND factors [All Fields] AND ("Ethiopia"[MeSH Terms] OR "Ethiopia"[All Fields]).

Eligibility Criteria

Observational studies (cross-sectional, cohort and case-control) with baseline measures for the outcome of interest (favourable TB treatment outcome), published studies conducted in Ethiopia and written in English were included. References from the selected studies were also cross checked to confirm that no relevant studies were excluded. Qualitative studies, studies that focus on treatment

outcome of patients with MDR-TB, studies that focus on both MDR-TB cases and drug-susceptible TB cases together, studies where full articles were no longer accessed and studies done outside Ethiopia were excluded from this review (Figure 1).

Study Selection and Data Extraction

We were followed a step-wise approach to select the eligible studies. Primarily, all the studies identified from the whole search were exported to EndNote X7 citation manager, and we were removed the duplicates. In the next step, we have screened the articles by title and abstract.

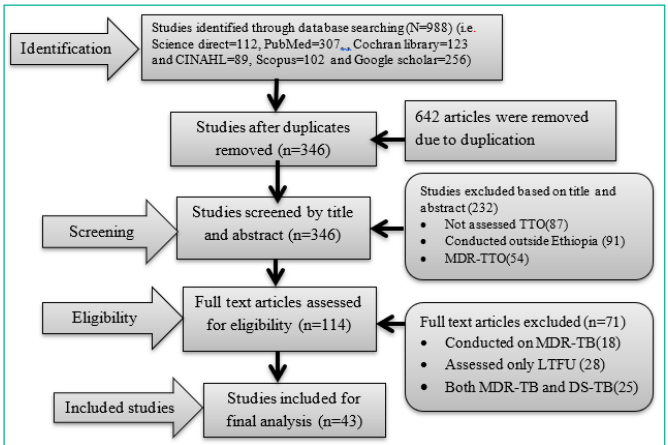

Figure 1: PRISMA flow diagram showing the selection of studies for a systematic review on tuberculosis treatment success in Ethiopia, 2024(TTO; tuberculosis treatment outcome, MDR-TTO; multidrug resistance tuberculosis treatment outcome, MDR-TB; multidrug resistance tuberculosis, LTFU; lost to follow up, DS-TB; drug susceptible tuberculosis).

Then, full-text assessment was conducted for the remaining articles. Finally, we have included the articles that passed the full-text review in the final analysis. We used "PICOSS" criteria to review the studies (Participants; Drug susceptible tuberculosis patients, Intervention; Anti-TB treatment, Comparator; no, Outcome; Successful treatment outcome, Study design: observational studies and study setting; across Ethiopia).The included studies' characteristics (author, year of publication, study design, study area sample size, number of treatment outcomes (successful treatment outcomes; cured, completed and unsuccessful treatment outcomes; lost to follow up, treatment failure, died, not-evaluated, moved to MDR) (Tables 1–3). The quantitative data were extracted from the included studies and stored in Microsoft Excel 2010 by one author.

Quality assessment: Two reviewers (MG and BB) evaluated the quality of the original articles independently using the Joanna Briggs Institute (JBI) critical appraisal checklist which is freely available at (https://jbi.global/critical-appraisal-tools). The checklist consists of 8, 10, and 11 questions for cross-sectional, case control and cohort studies respectively with Yes (Y), No (N), Unclear (U) or Not Applicable (NA) responses. Each of them equally scored and summed up to give 100%. The quality of the studies was scored to have high,

Table 1: The characteristics of included studies for the final analysis.

S.N	Authors	Year of Publication	Study period	Study Design	Study area	Sample size	Quality score
1	D. Zenbaba et al [70]	2021	2014-2019	Retrospective cohort	Oromia	1257	72.7%
2	Asebe et al [71]	2015	2011-2013	Retrospective cohort	SNNPR	1156	90.9%
3	Balcha T etal [72]	2015	2010-2013	Prospective cohort	Oromia	439	81.8%
4	Belayneh etal [46]	2015	2009-2011	Cross-sectional	Tigray	342	87.5%
5	Berhan et al [27]	2023	2017-2021	Cross-sectional	Amhara	400	75%
6	Birlie et al [73]	2015	2008-2012	Retrospective cohort	Amhara	810	72.2%
7	Ejeta et al [47]	2015	2009-2013	Cross-sectional	Oromia	1175	87.5%
8	Moges et al [48]	2015	2007-2011	Cross-sectional	Amhara	181	75%
9	Mokenen D.et al [49]	2015	2011-2014	Cross-sectional	Amhara	990	100%%
10	Tesfahuneygn et al [50]	2015	2007-2012	Cross-sectional	Tigray	4275	87.5%
11	Ali et al [51]	2016	2012-2013	Cross-sectional	Addis Ababa	575	100%
12	Asres et a1 [52]	2016	2008-2014	Cross-sectional	SNNPR	846	75%
13	Belayneh et al [74]	2016	2009-2013	Retrospective cohort	Amhara	403	72.7%
14	Gebreegziabher S et al [75]	2016	2014-2015	Prospective cohort	Amhara	706	81.8%
15	Gebremariam et al [53]	2016	2008-2014	Cross-sectional	Oromia	1649	87.5%
16	Gebrezgabiher et al [54]	2016	2010-2014	Cross-sectional	SNNPR	1537	87.5%
17	Mekonnen et al [55]	2016	2011-2014	Cross-sectional	Amhara	949	100%
18	H.T. Adane et al. [29]	2023	2020-2021	Prospective cohort	Addis Ababa	267	72.7%
19	Tefera et al [56]	2016	2009-2013	Cross-sectional	Amhara	1280	100%
20	Tilahun et al [76]	2016	2009-2013	Retrospective cohort	Addis Ababa	491	90.9%
21	Workneh et al [77]	2016	2013-2015	Prospective cohort	Amhara	1314	81.8%
22	Zenebe T et al [57]	2016	2011-2013	Cross-sectional	Afar	380	87.5%
23	Debash et al [31]	2023	2014-2021	Retrospective cohort	Amhara	552	81.8%
24	Sinshaw et al [58]	2017	2010-2016	Cross-sectional	Amhara	308	87.5%
25	Wondale et al. [78]	2017	2004-2014	Retrospective cohort	SNNPR	1172	72.7%
26	Teshome et al [59]	2017	2012-2015	Cross-sectional	Southwest Ethiopia	188	87.5%
27	Worku et al [79]	2018	2008-2016	Retrospective cohort	Amhara	985	90.9%
28	Tola et al [68]	2019	2012-2017	Cross-sectional	Harari	1236	75%
29	Tola et al. [60]	2019	2012-2017	Cross-sectional	Harari	356	75%
30	Tesema et al [61]	2020	03/2016-12/2016	Cross sectional	Oromia	281	100%
31	Woldesemayat et al [82]	2021	2011-2016	Retrospective cohort	SNNPR	731	81.8%
32	Amante et al [84]	2015	2007-2012	Case-control	Oromia	976	90%
33	Zerihun et al [28]	2023	2017-2019	Cross-sectional	Addis Ababa	636	100%
34	Getie et al [63]	2020	2013-2018	Cross-sectional	Amhara	270	87.5%
35	Fentie et al [83]	2020	2014-2018	Retrospective cohort	Addis Ababa	352	72.7%
36	Mamo et al [62]	2020	2015-2019	Cross-sectional	Oromia	373	75%
37	Mengesha et al [85]	2022	2016-2019	Cross-sectional	SNNPR	400	75%
38	Tadele et al [64]	2022	2014-2018	Cross-sectional	Amhara	1084	87.5%
39	S. Zewudie et al [65]	2021	2011-2018	Cross-sectional	Southwest Ethiopia	1651	87.5%
40	Tsegaye et al [69]	2019	2013-2017	Cross-sectional	Sidama	1122	100%
41	Agazhu et al [30]	2023	2015-2019	Cross-sectional	SNNPR	347	87.5%
42	Alemu et al [80]	2021	2015-2019	Retrospective cohort	SNNPR	604	90.9%
43	G. Fekadu et al [81]	2020	2013-2019	Retrospective cohort	Oromia	506	81.8%

medium and low quality if the overall quality score was >80%, 60–80% and <60%, respectively [37]. The reviewers independently assessed the methodological quality, quality of reported data (extractable data to calculate treatment successful and unsuccessful rate), outcomes stratified on the types of TB (drug-susceptible TB, MDR-TB or both drug-susceptible TB and MDR-TB) and clear data research design of the included studies. Any disagreements were resolved by consensus.

Data analysis and synthesis: The necessary data were extracted from the studies using Microsoft Excel V.2010, and the extracted data were exported to STATA V.17 software for analysis. The articles were summarized by tables and forest plot. Heterogeneity between studies was assessed by using Cochran's Q test and I2 statistics with 95% CI. The I2 statistic measures the proportion of observed variance between trials that is not due to chance (rather due to real differences across studies populations and interventions).

The I2 value less than 30% was interpreted as low evidence of heterogeneity, between 30% and 60% was moderate heterogeneity and I2 more than 60% was interpreted as evidence of substantial heterogeneity [38]. Meta-regression was used to explore whether study characteristics explained heterogeneity. Publication bias was assessed qualitatively by visual inspection of funnel plots and quantitatively by Egger's test. Sensitivity analysis was performed to assess the influence of individual studies on the overall estimate and P < 0.05 was considered statistically significant.

Table 2: Descriptions of overall TB treatment outcomes of the included studies.

S.N	Authors	STO	UTO	TSR (%)	Cured	Completed	LTFU	TF	Died	NE
1	D. Zenbaba et al [70]	1126	131	89.6	NR	NR	NR	NR	66	0
2	Asebe et al [71]	814	144	70.4	262	552	97	4	43	198
3	Balcha Tetal [72]	349	59	79.5	NR	NR	32	0	27	31
4	Belayneh etal [46]	242	100	70.7	43	199	7	5	88	0
5	Berhan et al [27]	356	44	89	77	279	15	6	23	0
6	Birlie et al [73]	685	68	84.6	103	582	2	6	60	57
7	Ejeta et al [47]	832	181	82	170	662	84	2	95	162
8	Moges et al [48]	127	13	90.7	36	91	9	3	1	41
9	Mokenen D.et al [49]	853	96	89.9	NR	NR	NR	NR	NR	30
10	Tesfahuneygn et al [50]	3853	215	94.7	491	3362	76	13	126	207
11	Ali et al [51]	526	49	91.5	106	420	15	7	27	0
12	Asres et a1 [52]	695	88	88.8	162	533	41	1	46	0
13	Belayneh et al [74]	318	29	91.6	76	242	7	2	20	56
14	Gebreegziabher S et al [75]	656	49	93	310	346	11	10	28	0
15	Gebremariam et al [53]	1437	94	93.3	421	1016	28	7	59	115
16	Gebrezgabiher et al [54]	1310	227	85.2	181	1129	171	4	52	0
17	Mekonnen et al [55]	853	96	89.9	132	721	28	21	47	0
18	H.T. Adane et al [29]	251	16	94.0	94	157	4	1	7	4
19	Tefera et al [56]	1016	129	88.7	203	813	23	4	102	135
20	Tilahun et al [76]	420	14	85.5	NR	NR	3	2	9	55
21	Workneh et al [77]	1228	86	93.5	317	911	14	15	57	0
22	Zenebe T et al [57]	320	52	86	128	192	34	1	17	8
23	Debash et al [31]	518	34	93.8	64	454	7	6	21	0
24	Sinshaw et al [58]	238	70	77.3	32	206	37	2	31	0
25	Wondale et al. [78]	868	304	74.0	154	714	107	1	119	77
26	Teshome et al [59]	57	131	30.3	18	39	20	NR	24	87
27	Worku et al [79]	672	74	90.1	126	546	NR	5	69	239
28	Tola et al [68]	1143	93	92.5	376	767	30	15	48	0
29	Tola et al. [60]	309	47	86.8	107	202	7	13	27	0
30	Tesema et al [61]	227	54	80.8	90	137	36	4	14	0
31	Woldesemayat et al [82]	675	56	92.3	165	510	20	13	18	5
32	Amante et al [84]	646	330	66.2	NR	NR	100	18	212	0
33	Zerihun et al [28]	550	86	84.9	211	339	46	21	19	0
34	Getie et al [63]	218	52	80.7	NR	NR	15	14	15	8
35	Fentie et al [83]	333	19	94.6	95	238	4	2	13	0
36	Mamo et al [62]	320	53	85.8	91	229	10	3	18	22
37	Mengesha et al [85]	342	58	85.5	110	232	37	8	13	0
38	Tadele et al [64]	742	342	68.5	217	525	36	69	52	185
39	S. Zewudie et al [65]	1327	324	80.4	376	951	7	NR	39	238
40	Tsegaye et al [69]	1037	85	95.6	284	753	29	3	53	0
41	Agazhu et al [30]	275	72	79.3	85	190	8	48	16	0
42	Alemu et al [80]	544	90	90.1	134	410	NR	NR	NR	NR
43	G. Fekadu et al [81]	412	94	81.4	72	340	20	32	42	0

S.N: Serial Number; STO: Successful Treatment Outcome; UTO: Unsuccessful Treatment Outcome; TSR: Treatment Success Rate; LTFU: Lost To Follow Up; TF: Treatment Failure; NE: Not Evaluated; NR: Not Reported; SNNPR: Southern Nation Nationality People's Region

Results

Selection and search results: A total of 988 articles were identified through an electronic search strategy. Among these articles 642 were found to be duplicated. Then, 346 articles were checked based on the title and abstract and 232 were found to be irrelevant (of these, 87 were not assessed TB treatment outcome, 91 were conducted outside Ethiopia and 54 were conducted only MDR-TB treatment outcome. Finally, 114 articles were assessed based on their full text. Among these, 71 were excluded and 43 articles were selected for inclusion in the meta-analysis (Figure 1). Additional studies weren't obtained after retrieving the references of all the 43 full text reviewed articles. Among the reviewed articles from 2015 to 2023, the highest pooled TB treatment success rate showed in 2019 and the lowest was in 2017. There is an up and down movement of TB treatment success rate from the espousal of new post-2015 End TB strategy. Apart from the year 2019(91.9%), the success rate is below the threshold of the Global End TB strategy indicators (Figure 2).

Study Characteristics

Studies included in this review were conducted in different regions of Ethiopia published from 2015 to the end of 2023.From a total of 988 articles obtained through electronic search, 43 were found to be eligible and were included in this study. Twenty-six (60.5%) of the included studies were cross-sectional in nature [24,39-64], 16(37.2%) of the studies were cohort studies [65-80], and 1 (2.33%)

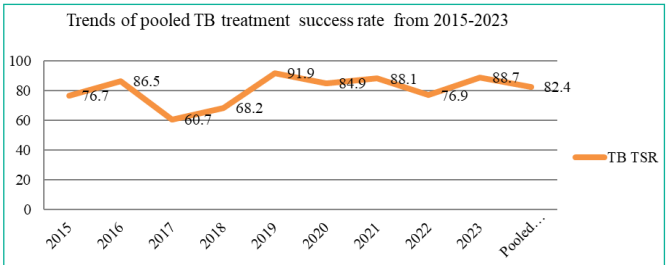

Figure 2: Trends of pooled TB treatment success rate across each year with overall pooled TB treatment success rate from the espousal of new post-2015 End TB strategy to end of 2023 in Ethiopia.

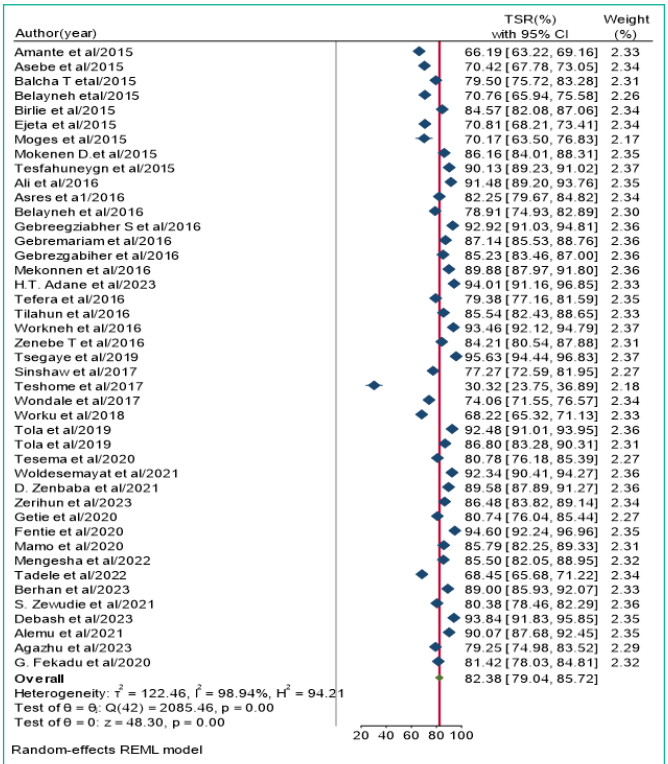

Figure 3: A Forest plot displaying pooled estimate of TB treatment success rate from espousal of new poest-2015 End-TB strategy to end of 2023 in Ethiopia.

was a case-control study [81]. Regarding the study area, 5 studies were conducted in Addis Ababa [44,55,71,72,80], 14 in Amhara region [24,41,42,48,49,51,57,58,68-70,73,74,76), 8 in Oromia region [40,46,54,56,65,67,78,81], 8 in Southern Nations, Nationalities and People (SNNP) [45,47,60,61,66,75,77,79], 2 in Harari region [53,63], 2 in Tigray region [39,43], 1 in Sidama region [64], 1 in Afar region [50] and 2 in southwest region [52,59]. The study period ranged from 1 year to 10 years. These studies were conducted among 35,046 participants. The smallest and largest sample sizes were 181 [41] and 4275 [43], respectively with an average sample size of 827 (Table1). This review was concerned only about participants whose final treatment outcome were ascertained and hence excluded those participants who were on treatment during the study periods.

Tuberculosis treatment outcomes in Ethiopia: This systematic review showed that tuberculosis treatment success rate varies from 30.32% [52] to 95.6% [64]. The following table shows the detailed description of cure, treatment completed, lost to follow up, treatment failure, died and not evaluated from individual included studies (Table 2).

Factors significantly associated with unfavourable treatment outcomes: Different demographic and clinical characteristics were stated from the reviewed studies which had a significant association with unfavourable TB treatment outcome ($p<0.05$). Among these, the most frequently stated were old age, TB/HIV co-infection, retreatment case, being rural residence and sputum smear positive pulmonary TB (Table 3).

Table 3: Independent predictors which had a significant association with unfavourable TB treatment outcomes.

S.N	Authors	Identified factors*
1	D. Zenbaba et al [48]	PTB+, EPTB, transferred in and being HIV positive
2	Asebe et al [49]	The age group 45–64 years
3	Balcha Tetal [50]	Low mean upper arm circumference (MUAC)
4	Belayneh etal [51]	Having low baseline CD4 count (<200cells/L) and WHO stage IV
5	Berhan et al [23]	HIV positive and sputum negative PTB
6	Birlie et al [52]	Old age, low baseline body weight and TB/HIV co-infected
7	Ejeta et al [53]	HIV co-infection and being sputum smear positive PTB
8	Moges et al [54]	Not reported
9	Mokenen D.et al [55]	TB/HIV co-infection, ages>45 years and being PTB+/-
10	Tesfahuneygn et al [56]	TB/HIV co-infection, being retreatment and being PTB+/-
11	Ali et al [57]	HIV co-infection with TB
12	Asres et a1 [58]	Advanced age, being rural residence and being HIV positive
13	Belayneh et al [59]	Not reported
14	Gebreegziabher S et al [60]	Being HIV positive
15	Gebremariam et al [61]	TB/HIV co-infection
16	Gebrezgabiher et al [62]	Being rural residence, EPTB, PTB− and 55–64years old
17	Mekonnen et al [63]	Being HIV positive and Smear positive PTB
18	H.T. Adane et al [64]	Diabetes mellitus
19	Tefera et al [65]	Not reported
20	Tilahun et al [66]	TB/HIV co-infected patients and age < 1year
21	Workneh et al [67]	TB with DM and HIV-positive
22	Zenebe T et al [68]	Age, sex, and HIV positive
23	Debash et al [69]	Retreatment and HIV positive
24	Sinshaw et al [70]	Being rural residence, baseline wt.<43.7kg and treatment side effect
25	Wondale et al. [71]	TB/HIV co-infection
26	Teshome et al [72]	WHO clinical stage III and IV and being HIV positive
27	Worku et al [73]	No significant associated factor
28	Tola et al [74]	TB/HIV co-infection, retreatment, PTB+ and history of opportunistic infection
29	Tola et al. [75]	Age groups> 54 years old
30	Tesema et al [76]	Distance >5km, ages>24years and being seropositive for HIV
31	Woldesemayat et al [77]	Pre-treatment weight and being HIV positive
32	Amante et al [78]	Lack of person to be contacted at a time of treatment interruption and HIV+
33	Zerihun et al [79]	Not having TTS, HIV positive, co-morbidities and smoking history
34	Getie et al [80]	Older age, female sex, and being HIV positive
35	Fentie et al [81]	Being extra-PTB and HIV positive
36	Mamo et al [82]	HIV positive and age >40 years
37	Mengesha et al [83]	Distance≥10km, no family support and bedridden base line function
38	Tadele et al [84]	HIV status, educational status and being rural residence
39	S. Zewudie et al [85]	Being rural residence and HIV status
40	Tsegaye et al [86]	Being rural residence, HIV positive and EPTB
41	Agazhu et al [87]	HIV positive, age>60years and unmarried
42	Alemu et al [88]	Being rural residence, retreatment and chronic diseases
43	G. Fekadu et al [89]	Being single, PTB-EPTB and retreatment

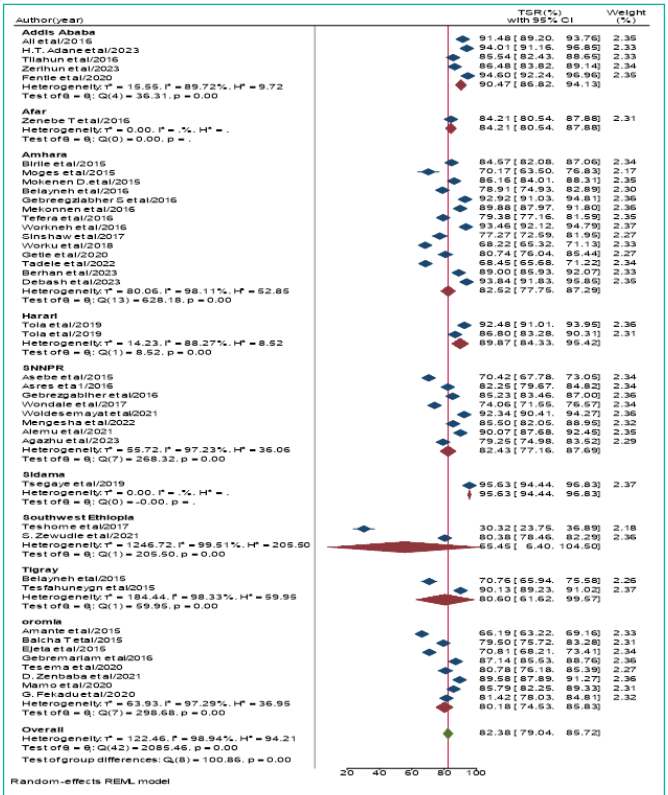

Figure 4: A forest plot displaying a subgroup analysis pooled estimate of TB treatment success rate by region from espousal of new poest-2015 End-TB strategy to end of 2023 in Ethiopia.

Meta-Analysis

The overall estimate of TB treatment success rate: The overall drug-susceptible TB treatment success rate in Ethiopia from the espousal of the new post-2015 End TB strategy to the end of 2023 is 82.38% (95% CI 79.04% to 85.72%). There was a significant degree of heterogeneity across the included studies on the outcome of interest (P<0.001) (Figure 3). The true variability among 43 studies other than chance was 98.9 % (I2=98.9) and the between study variance was 122.46 % (τ2=122.46%).

Subgroup analysis by region: The sub group analysis based on the study area showed that Addis Ababa (90.5%, 95% CI; 86.82% to 94.13%), Afar (84.2%, 95% CI; 80.54% to 87.88%), Amhara (82.5%, 95% CI; 77.75% to 87.29%), Harari (89.9%, 95% CI; 84.33% to 95.42%), Southern region (82.4%, 95% CI; 77.16% to 87.69%), Sidama (95.6%, 95% CI; 94.44% to 96.83%), Oromia (80.2%, 95% CI; 74.53% to 85.53%), Southwest Ethiopia (55.4%, 95% CI; 6.4% to 104.5%) and Tigray (80.6%, 95% CI; 61.62% to 99.59%) had TB treatment success rate (Figure 4). There was a significant heterogeneity among studies conducted in each region, that is, Addis Ababa (I2=89.7%, p<0.001), Amhara (I2=98.1%, P<0.001), Harari (I2=88.2%, P<0.001), Southern Nation Nationality and People Region (SNNPR) (I2=97.2%, P<0.001), South west Ethiopia (I2=99.5%, p<0.001), Tigray (I2=98.3%, P<0.001) and Oromia region (I2=97.2%, p<0.001). Publication bias assessment: The funnel plot showed that there is symmetry between the studies and no significant publication bias was seen, or small study effect was insignificant that is neither the funnel plot nor the egger tests showed evidence of significant publication bias (P=0.71) (Figure 5).

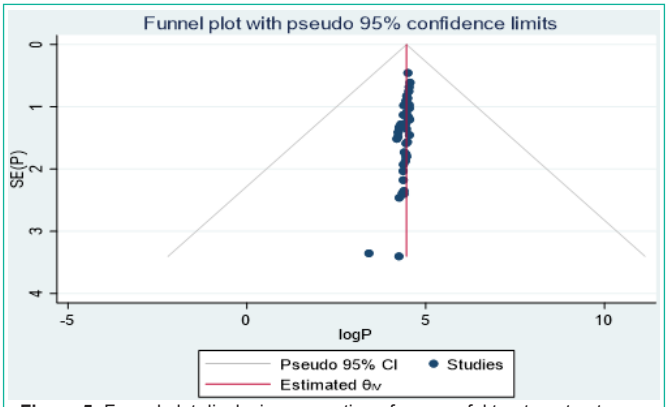

Figure 5: Funnel plot displaying proportion of successful treatment outcome among drug susceptible TB patients from the espousal of new post-2015 End TB strategy to end of 2023 in Ethiopia (P; proportion of successful treatment outcome).

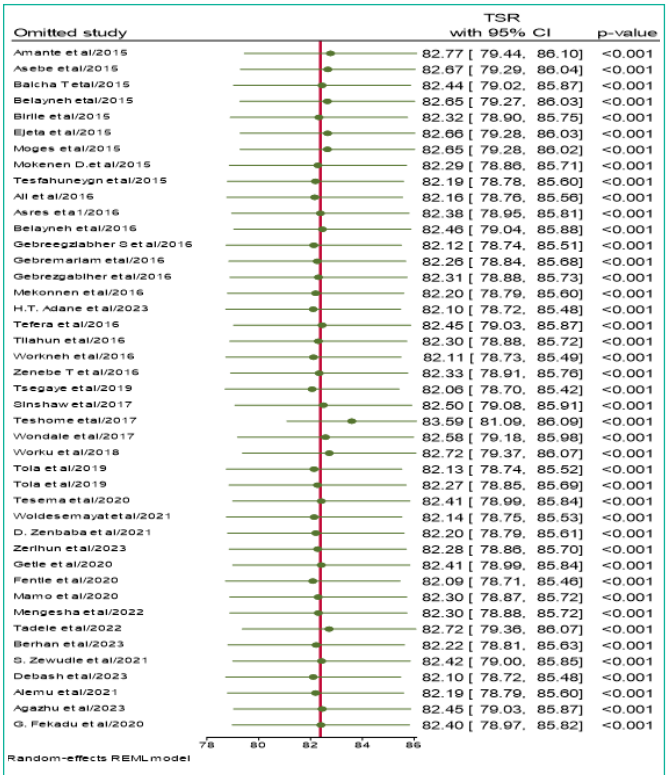

Figure 6: Results of leave-one-out method in sensitivity analysis for pooled estimate of successful treatment outcome among drug susceptible TB patients in Ethiopia.

Sensitivity analysis: The Meta leave-one-out method was conducted by eliminating each study step by step. As Shown in figure7, the pooled estimate was in the range from 82.06% (95% CI; 78.8-85.4) to 83.6% (95% CI; 81.1–86.1). The result showed that no studies were found to be outside the confidence bound of the pooled magnitude of TB treatment success rate. Therefore, it showed that all studies had nearly equal influence on the overall pooled magnitude of TB treatment success rate by excluding leave out one from meta-analysis (Figure 6).

Discussion

Analyzing TB treatment outcomes and their potential risk factors is an important indicator of the performance of a country's TB control

program [17,18]. The assessment of determinants at the start of TB treatment can improve treatment outcomes [82]. Tuberculosis (TB) treatment success rate is one of the ten priority indicators in achieving the targets of the End TB strategy [11,31-33]. This systematic review and meta-analysis was conducted mainly to estimate the pooled treatment success rate of patients with drug-susceptible TB in Ethiopia and this review identified 43 studies from the espousal of the new post-2015 End TB strategy to the end of 2023. All the studies included in this review were observational studies which were conducted in different parts of Ethiopia; Addis Ababa, Amhara, Oromia, Tigray, Southern region, Afar, Sidama, Harari and South west Ethiopia. We analyzed data for a total of 35,046 patients with drug-susceptible TB. All the included studies used Ethiopian guidelines for "clinical and programmatic management of TB, TB/HIV, DR-TB and Leprosy" to define TB treatment outcomes which were espoused from WHO [16,83].

The result of this review showed that the pooled estimate of TB treatment success rate from espousal of new post-2015 End TB strategy to end of 2023 among patients with drug-susceptible TB in Ethiopia is 82.4% (with 95% CI of 79.04% to 85.7%). It is lower than the targets of the End TB strategy as suggested by WHO (≥90%) [11]. Since treatment success rate is one of the priority indicators and targets of this strategy, all countries aimed to reach these targets at the latest by 2025 [11,31-33]. This study's result is relatively lower compared with a previous review done in Ethiopia which was 86% [35]. This might be due to drought, disputes, political instability and ethnic conflicts. According to the 2023 WHO global TB report, Ethiopia achieved a TB treatment success rate about 89% [3] and based on the subgroup analysis by year in this review, the pooled TB treatment success rate in 2023 was 88.7%.The overall result of this systematic review and meta-analysis was poor compared with the WHO report even if the pooled TB treatment success rate in the year 2023 from subgroup analysis by year consistent with the WHO global TB report. This might be an indication that Ethiopia is within the pathway of the Global End TB strategy treatment targets. However, there should be a collaborative effort among healthcare providers and policy makers in achieving both national and international treatment targets.

In this systematic review and meta-analysis, the TB treatment success rate was evaluated in the different regions of Ethiopia. The pooled estimate results showed that the lowest treatment success rate was appreciated in the South west Ethiopia (55.45% (95% CI; 6.4% to 104.5%)) [52,59] and the highest success rate was in Sidama region, that is, 95.6% (95% CI; 94.4% to 96.8%) [64] This might be due to the variations in health-seeking behaviour, the quality of healthcare facilities, the emphasis given by regional governments and policy makers towards TB infection prevention and control programmes. As a result, close supervision of each TB infection prevention and control program is required to achieve effective nationwide End TB strategy indicators and targets. Poor treatment adherence remains a major obstacle to fight against TB epidemic which in turn resulted in poor treatment outcomes [17,20,24,28,84-93]. The results of this review showed that different demographic and clinical characteristics were reported to have significant association with unfavourable TB treatment outcome in Ethiopia. Mainly pulmonary TB (+/-), old age, HIV co-infection, retreatment cases and being rural residence were most frequently identified predictors associated with unfavourable TB treatment outcome [24,40,43,44,47,50,60,65,68,70,74,77) (Table 3). In WHO African region, about 2.5 million people falling ill with TB. Among these, approximately 20% of new TB cases were reported among patient with HIV positive [7]. Being HIV-positive lowered the likelihoods of favourable treatment outcome [24,43,46-48,56,65,68,74,75,80]. This might be due to drug pill burden, forgetfulness, lack of close follow up, stigmatization and so on. In spite of such vital findings, this study is not without limitations; all the included studies were observational studies; there were differences in the study design among the studies; and studies included were limited to Addis Ababa, Amhara, Oromia, Tigray, Southern region, Afar, Sidama, Harari and South west Ethiopia. Therefore, interpretation of the results of this review should take into consideration of these limitations.

Conclusion and recommendations

The overall treatment success rate among patients with drug-susceptible TB in Ethiopia is below the Global End strategy target (≥90%). There are variations in TB treatment success rate among different regions of Ethiopia. Pulmonary TB (+/-), TB/ HIV co-infection, older age, retreatment cases and rural residence were the most frequently factors that had a significant association with unfavourable TB treatment outcome. To enhance the success rate of TB treatment, a special consideration should be given to regions that had a lower TB treatment success rate and for patients with pulmonary TB, TB/HIV co-infected patients, older patients, patients residing in rural areas and retreatment cases.

Author Statements

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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