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Drug-susceptible tuberculosis treatment success and associated factors in Ethiopia from 2005 to 2017: a systematic review and meta-analysis

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ABSTRACT

Objectives The main aim of this study was to assess the overall tuberculosis (TB) treatment success in Ethiopia and to identify potential factors for poor TB treatment outcome.

Design A systematic review and meta-analysis of published literature was conducted. Original studies were identified through a computerised systematic search using PubMed, Google Scholar and Science Direct databases. Heterogeneity across studies was assessed using Cochran's Q test and I^2 statistic. Pooled estimates of treatment success were computed using the random-effects model with 95% CI using Stata V.14 software.

Results A total of 230 articles were identified in the systematic search. Of these 34 observational studies were eligible for systematic review and meta-analysis. It was found that 117 750 patients reported treatment outcomes. Treatment outcomes were assessed by World Health Organization (WHO) standard definitions of TB treatment outcome. The overall pooled TB treatment success rate in Ethiopia was 86% (with 95% CI 83%_88%). TB treatment success rate for each region showed that, Addis Ababa (93%), Oromia (84%), Amhara (86%), Southern Nations (83%), Tigray (85%) and Afar (86%). Mainly old age, HIV co-infection, retreatment cases and rural residence were the most frequently identified factors associated with poor TB treatment outcome.

Conclusion The result of this study revealed that the overall TB treatment success rate in Ethiopia was below the threshold suggested by WHO (90%). There was also a discrepancy in TB treatment success rate among different regions of Ethiopia. In addition to these, HIV co-infection, older age, retreatment cases and rural residence were associated with poor treatment outcome. In order to further improve the treatment success rate, it is strategic to give special consideration for regions which had low TB treatment success and patients with TB with HIV co-infection, older age, rural residence and retreatment cases.

Strengths and limitations of this study

- This study includes articles from different regions of the country which support the representativeness of the evidence obtained at the country level.
- In addition to this, inclusion of more than 30 articles for both quantitative and qualitative synthesis was considered as the major strength of this study.
- The variation in the study design used among the included studies and the inclusion of only observational studies were considered as the major drawback of this study.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by a bacteria called *Mycobacterium tuberculosis*. It is a preventable and curable disease mainly transmitted through air from person to person. Majorly, it affects the lungs, but it can also damage other organs in the body.[1] Common symptoms of active lung TB are cough with sputum and blood, chest pains, weakness, weight loss, fever and night sweats.[1 2]

TB is the ninth leading cause of death globally and the leading cause from a single infectious agent, ranking above HIV/AIDS. In 2016, it was responsible for an estimated 1.3 million and 374 000 TB deaths among HIV-negative and HIV-infected people, respectively.[3] It is also the number one cause of death among HIV-infected individuals with an estimated two-fifth deaths among HIV-infected individuals being due to TB.[1]

Ethiopia is among the countries where TB is highly prevalent. WHO prepared three lists of countries based on the burden of TB, TB/HIV co-infection and multidrug-resistant TB (MDR-TB). Accordingly, Ethiopia is among the 14 countries where there is high burden of TB, TB/HIV co-infection and MDR-TB. Even though the incidence of TB decreased by 54% and mortality because of TB decreased by 72% in the country in 2015,[4] 4000 deaths among HIV-infected individuals and 26 000 deaths among HIV-negative individuals still occurred in 2016.[3] The decline in the incidence and mortality could in part be attributed to improvement in the

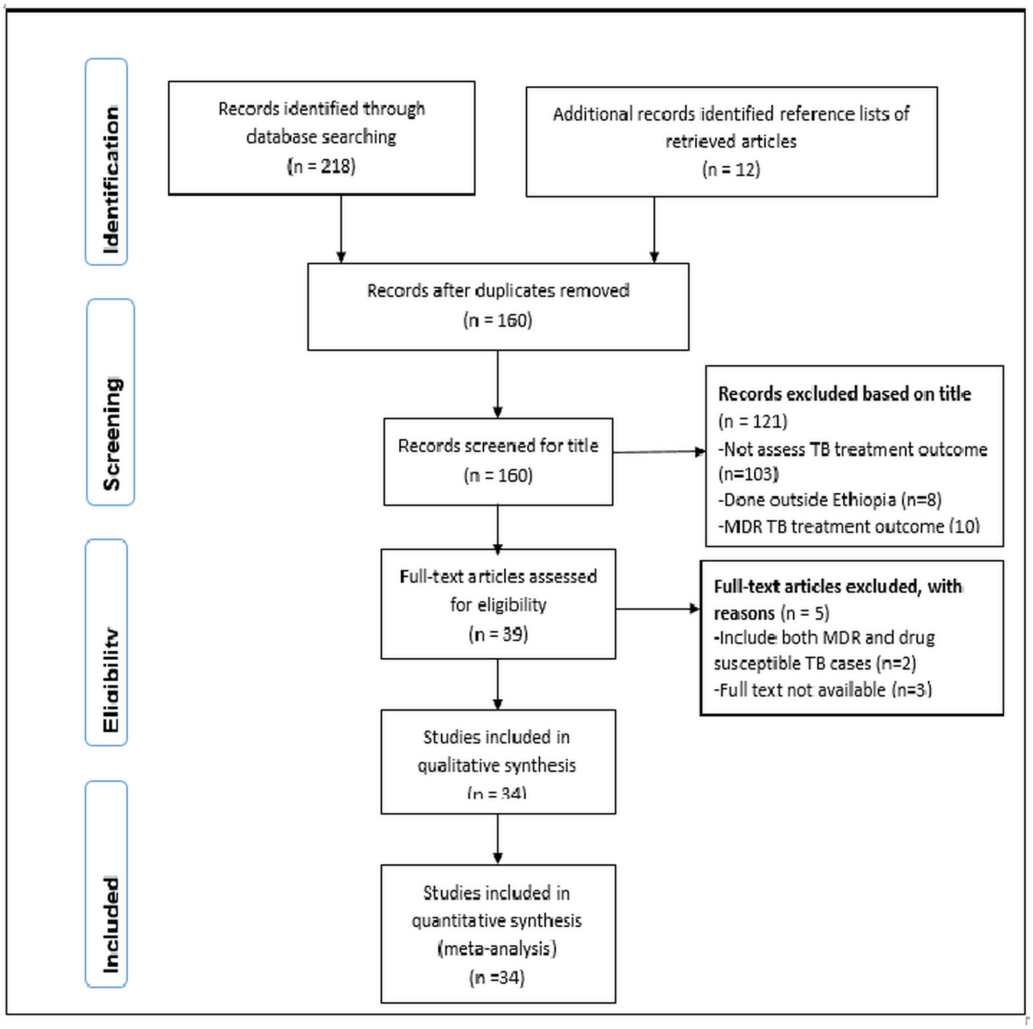

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram showing the selection of studies for a systematic review on tuberculosis treatment success in Ethiopia, 2017. MDR, multidrug resistant; TB, tuberculosis.

TB detection rate,[4] provision of isoniazid preventive therapy for HIV-infected individuals[5] and early initiation of antiretroviral therapy (ART),[6] a community-based package involving health extension workers.[7]

Since the discovery of the first anti-TB drug, streptomycin, in 1943[8] and the few drugs that followed (isoniazid, rifampicin, ethambutol and pyrazinamide), drug development for drug-susceptible TB has lagged.[8 9] As a result, the same anti-TB drug regimen that was first introduced half a century ago is being used today in the management of active, drug-susceptible TB.[10] A 6-month course of four anti-TB drugs is used as a standard treatment for active, drug-susceptible TB disease. Isoniazid and rifampicin serve as the backbone of this regimen, with ethambutol and pyrazinamide given in the first 2 months of treatment.[1 3 11] However, treatment success could be compromised by poor adherence mainly due to the long treatment period and the development of drug-resistant TB ultimately from the inadequate treatment of active TB.[9 11] In Ethiopia, this four-drug, 6-month and 9–12-month regimen is also recommended as a first-line drug for the treatment of active drug-susceptible pulmonary TB and extrapulmonary TB (EPTB), respectively.[12]

Currently, the global TB treatment success rates were 83% for drug-susceptible TB, 78% for HIV-associated TB, 54% for MDR-TB and 30% for extensively drug-resistant TB.[3] The WHO Global Plan aimed to achieve three 90-(90)–90 TB control program targets at least by 2025, such as; 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.[13]

According to the WHO report, Ethiopia is among the four countries where treatment outcomes of more than 10% of TB cases were not evaluated and documented.[3] Even though there has been a recent systematic review on TB treatment outcome in Ethiopia,[14] it doesn't clearly assess the overall drug-susceptible TB treatment outcome independently and it also emphasis only on limited factors which associated with TB treatment outcome. In addition to this, there have also been several single studies published on TB treatment outcome in Ethiopia. However, there is a paucity of evidence regarding

Table 1 Tuberculosis (TB) treatment outcomes according to WHO and National Tuberculosis and Leprosy Control Programme (NTLCP) guidelines

Outcome	Definition
Cured	A patient with TB with bacteriologically confirmed TB at the beginning of treatment who was smear-negative or culture-negative in the last month of treatment and on at least one previous occasion.
Treatment completed	A patient with TB who completed treatment without evidence of failure, but with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because the tests were not done or because results are unavailable.
Treatment failed	A patient with TB whose sputum smear or culture is positive at month 5later during treatment.
Died	A patient with TB who dies for any reason before starting or during the course of treatment.
Defaulter	A patient who has been on treatment for at least 4 weeks and whose treatment was interrupted for eight or more consecutive weeks.
Not evaluated	A patient with TB for whom no treatment outcome is assigned. This includes cases 'transferred out' to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.
Treatment success	The sum of cured and treatment completed.

the overall drug-susceptible TB treatment success at the country level. Therefore, we aimed to get stronger evidence from the available literature regarding drug-susceptible TB treatment success and to identify all potential factors reported that are associated with poor TB treatment outcome in Ethiopia.

MATERIALS AND METHODS

Study design and search strategies

A systematic review and meta-analysis of published observational studies was conducted. Original studies providing information on the treatment outcomes of patients with TB were identified through a computerised systematic search using PubMed, Google Scholar and Science Direct databases. A combination of keywords and phrases like: 'tuberculosis OR TB', 'treatment OR management', 'Anti-TB', 'outcomes', 'treatment success', 'smear-positive', 'smear-negative', 'Extra-pulmonary-TB' and 'Ethiopia' were used to search articles in the databases (online supplementary file 1). The literature search, review and data extraction were performed from February to September 2017. Articles were retrieved up to 15 March 2017. Only those articles written in English language and conducted in Ethiopia were considered for this review.

Inclusion criteria

Observational studies fulfilling the following criteria were included in this study: studies reported as original articles; studies done on TB treatment outcomes; studies conducted in Ethiopia and written in English. References from the selected studies were also cross-checked to confirm that no relevant studies were excluded. Outcomes were reported according to the WHO definition of treatment success (cure or treatment completion), failure, default and death.[15]

Exclusion criteria

The following articles were excluded from this review: 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. The selection of articles for review was done in three stages: looking at the titles alone, then abstracts and then the full text (figure 1).

Definitions of TB treatment outcomes

To classify treatment outcomes of patients with TB, the WHO and National Tuberculosis and Leprosy Control Programme (NTLCP) guidelines' standard definitions were used[15 16] (table 1).

Data extraction and review process

All of the research articles that were identified from searches of the electronic databases were imported into the ENDNOTE software V.X5 (ThomsonThomson Reuters, USA) and duplicates were removed. Before data extraction had begun, full-length articles of the selected studies were read to confirm the fulfilment of the inclusion criteria. Then, data extraction was performed by three authors (MAS, MBA and EAM) independently. The selected studies were reviewed to extract data like: year of publication; author(s); study design; sample size; type of TB (smear-negative pulmonary TB (PTB^-), smear-positive pulmonary TB (PTB^+) and EPTB); HIV status; TB treatment outcomes; geographical location of the study area, and factors affecting TB-treatment outcome (p value of <0.05). When there was a disagreement in data extraction between the reviewers, it was resolved through discussion and mutual agreement between the investigators.

Methodological quality assessment

All reviewers (MAS, MBA, EAM, EAG and TMA) independently assessed the methodological quality of included studies by using the Newcastle-Ottawa Scale (NOS).[17 18] The studies which have at least five NOS criteria were considered to be high-quality studies (online supplementary file 2).

Statistical analysis and heterogeneity

Statistical analyses were carried out by using Stata V.14 (Stata Corp, College Station, Texas, USA) software[19] to estimate the pooled treatment success rate. Statistical heterogeneity between studies was evaluated using Cochran's Q test and the I^2 statistic.[20] Random-effects meta-analyses were used to combine the results of included studies, and was measured as proportions of treatment outcomes with 95% CIs. The detailed description of the original studies was presented in a table and forest plot.

Table 2 Characteristics of included studies

Authors	Year of publication	Study design	Duration in years	Study area	Sample size	HIV (%)
Ali *et al*[22]	2016	Cross-sectional study	1	Addis Ababa	575	29.4
Amante *et al*[55]	2015	Case-control study	5	Oromia	976	18.3
Asebe *et al*[44]	2015	Retrospective cohort study	2.5	SNNPR	1156	24.2
Asres *et al*[23]	2016	Cross-sectional study	7	SNNPR	846	9.1
Balcha T *et al*[52]	2015	Cohort study	3	Oromia	439	100
Belayneh *et al*[45]	2016	Retrospective cohort	5	Amhara	403	38.5
Belayneh *et al*[24]	2015	Cross-sectional study	2.7	Tigray	342	100
Berhe *et al*[25]	2012	Cross-sectional study	3	Tigray	407	8.6
Birlie *et al*[46]	2015	Retrospective cohort study	5	North-East Ethiopia	810	17.4
Dangisso *et al*[26]	2014	Retrospective trend analysis	10	Southern Ethiopia	37070	–
Ejeta *et al*[47]	2015	Retrospective cohort study	5	Western Ethiopia	1175	17.1
Endris *et al*[27]	2014	Cross-sectional study	5	Amhara	417	5.8
Gebreegziabher S *et al*[43]	2016	Prospective cohort	1.7	Amhara	706	11.6
Gebremariam *et al*[48]	2016	Retrospective cohort study	6	Oromia	1649	9.5
Gebrezgabiher *et al*[28]	2016	Cross-sectional study	5.4	SNNPR	1537	–
Getahun *et al*[49]	2013	Retrospective cohort study	5	Addis Ababa	6450	–
Hailu *et al*[29]	2014	Cross-sectional study	5	Addis Ababa	2708	12.0
Hamusse *et al*[50]	2014	Retrospective cohort study	15	Central Ethiopia	14221	2.0
Ketema *et al*[51]	2014	Retrospective cohort study	3	Oromia	2226	9.7
Mekonnen *et al*[30]	2016	Cross-sectional study	4	Amhara	949	23.9
Melese *et al*[31]	2016	Cross-sectional study	5	Amhara	339	12.7
Moges *et al*[32]	2015	Cross-sectional study	5	Amhara	181	–
Mokenen D. *et al*[33]	2015	Cross-sectional study	4	Amhara	990	23.8
Munoz-Sellart *et al*[34]	2009	Cross-sectional study	5	SNNPR	851	–
Munoz-Sellart *et al*[35]	2010	Retrospective audit	5.8	SNNPR	6547	–
Shargie *et al*[36]	2005	Retrospective trend analysis	7	SNNPR	19971	–
Sinshaw *et al*[37]	2017	Cross-sectional study	5.5	Amhara	308	100
Tefera *et al*[38]	2016	Cross-sectional study	5	Amhara	1280	20.5
Tesfahuneygn *et al*[39]	2015	Cross-sectional study	5.5	North-East Ethiopia	4275	13.7
Tessema *et al*[40]	2009	Cross-sectional study	5	Amhara	4000	–
Tilahun *et al*[53]	2016	Retrospective cohort study	5	Addis Ababa	491	16.7
Workneh *et al*[54]	2016	Prospective cohort study	1.6	Amhara	1314	19.9
Zenebe T *et al*[42]	2016	Cross-sectional study	2	Afar	380	47.6
Zenebe Y *et al*[41]	2016	Cross-sectional study	5	Amhara	1761	3.5

SNNPR, Southern Nations, Nationalities, and Peoples' Region.

Patient and public involvement

This is a systematic review and meta-analysis,there were no direct involvement of patients and/or the public in this study.

Ethical consideration

This study was carried out in strict accordance with the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[21] Since it is a systematic review and meta-analysis, ethics committee or institutional review board permission was not sought.

RESULTS

Literature search results

An electronic search gave a total of 230 articles. Among these 70 were found to be duplicated. Then the titles of 160 articles were checked and 121 were found irrelevant. Five articles were excluded after checking their abstracts. Finally, 34 articles were selected for inclusion in the meta-analysis (figure 1).

Study characteristics

This analysis included studies conducted in different regions of the country published from 2005 to 2017. From a total of 230 articles obtained through electronic search, 34 were found to be eligible and were included in this review. Majority 21 (62%) of the included studies were cross-sectional in nature,[22–42] while 12 (35%) of the studies were cohort studies,[43–54] and 1 was a case-control study.[55] Most of the studies relied on 5 years data (range of 1–15 years) (table 2).

Table 3 Description of overall treatment outcome of included studies

Study Id	Authors	Successful treatment outcome	Unsuccessful treatment outcome	Successful treatment outcome (%)	Cured	Treatment completed	Defaulted	Treatment failure	Died	Transferred out
1.	Ali *et al*[22]	526	49	91.5	106	420	15	7	27	0
2.	Amante *et al*[55]	646	330	66.2	NR	NR	100	18	212	0
3.	Asebe *et al*[44]	814	144	85	262	552	97	4	43	198
4.	Asres *et al*[23]	695	88	88.8	162	533	41	1	46	0
5.	Balcha T *et al*[52]	349	59	85.5	NR	NR	32	0	27	31
6.	Belayneh *et al*[45]	318	29	91.6	76	242	7	2	20	56
7.	Belayneh *et al*[24]	242	100	70.7	43	199	7	5	88	0
8.	Berhe *et al*[25]	361	44	89.1	343	18	13	15	16	6
9.	Birlie *et al*[46]	685	68	91	103	582	2	6	60	57
10.	Dangisso *et al*[26]	30 300	4552	87	14 147	16 153	3263	92	1197	2087
11.	Ejeta *et al*[47]	832	181	82	170	662	84	2	95	162
12.	Endris *et al*[27]	379	21	94.8	77	302	5	2	14	17
13.	Gebregziabher S *et al*[43]	656	49	93	310	346	11	10	28	0
14.	Gebremariam *et al*[48]	1437	94	93.9	421	1016	28	7	59	115
15.	Gebrezgabher *et al*[28]	1310	227	85.2	181	1129	171	4	52	0
16.	Getahun *et al*[49]	5331	590	90	1167	4164	328	26	236	351
17.	Hailu *et al*[29]	2193	188	92.1	169	2024	99	6	83	184
18.	Hamusse *et al*[50]	11 888	2333	83.6	9608	2280	1215	70	1048	0
19.	Ketema *et al*[51]	2043	114	94.7	1906	137	27	24	63	69
20.	Mekonnen *et al*[30]	853	96	89.9	132	721	28	21	47	0
21.	Melese *et al*[31]	264	39	87.1	67	197	8	12	19	36
22.	Moges *et al*[32]	127	13	90.7	36	91	9	3	1	41
23.	Mokenen D *et al*[33]	853	107	88.9	NR	NR	NR	NR	NR	30
24.	Munoz-Sellart *et al*[34]	655	139	82.5	NR	NR	NR	NR	49	57
25.	Munoz-Sellart *et al*[35]	4900	1095	81.7	NR	NR	667	24	404	552
26.	Shargie *et al*[36]	8268	3708	69	NR	NR	3152	110	446	2000
27.	Sinshaw *et al*[37]	238	70	77.3	32	206	37	2	31	0
28.	Tefera *et al*[38]	1016	129	88.7	203	813	23	4	102	135
29.	Tesfahuneygn *et al*[39]	3853	215	94.7	491	3362	76	13	126	207
30.	Tessema *et al*[40]	1181	1139	50.9	NR	NR	730	6	403	1680
31.	Tilahun *et al*[53]	420	14	96.8	NR	NR	3	2	9	55

Continued

Table 3 Continued

Study Id	Authors	Successful treatment outcome	Unsuccessful treatment outcome	Successful treatment outcome (%)	Cured	Treatment completed	Defaulted	Treatment failure	Died	Transferred out
32.	Workneh *et al*[54]	1228	86	93.5	317	911	14	15	57	0
33.	Zenebe T *et al*[42]	320	52	86	128	192	34	1	17	8
34.	Zenebe Y *et al*[41]	542	129	80.8	NR	NR	30	1	98	1090

NR, not reported.

Figure 2 Funnel plot of SE by logit event rate.

Clinical characteristics of patients

A total of 117 750 patients with TB were included in the 34 studies. Of these, 51% (59916) patients with TB had PTB^{+}, 21% (24428) had PTB^{-} and 17.3% (20400) had EPTB. In this review around 5357 patients had TB-HIV co-infection which is reported by 26 studies. The remaining studies did not provide evidence for TB-HIV co-infection. The detailed description of individual study characteristics is mentioned in table 2.

TB treatment outcome in Ethiopia

This review showed that TB treatment success rate varies from 51% to 95%. Table 3 shows the detailed description of cure, treatment completed, defaulted, treatment failure, died and transferred out from individual included studies (table 3).

Meta-analysis

The Funnel plot depicted in figure 2 showed that there is symmetry between the studies and no significant publication bias was seen, or small study effect was insignificant. The sensitivity analysis also showed the absence of an excessive influence of individual studies. The point estimates calculated after omission of each study one by one lies within the CI of the 'combined' analysis (online supplementary file 3) (figure 2).

The overall estimate of TB treatment success

As indicated in the following forest plot the overall drug-susceptible TB treatment success rate in Ethiopia is 86% (95% CI 83% to 88%) (figure 3). Subgroup analysis based on the study area showed that Addis Ababa (93%), Oromia (84%), Amhara (86%), SNNPR (83%), Tigray (85%) and Afar (86%) had TB treatment success rate (figure 4). The finding of this study also showed that TB

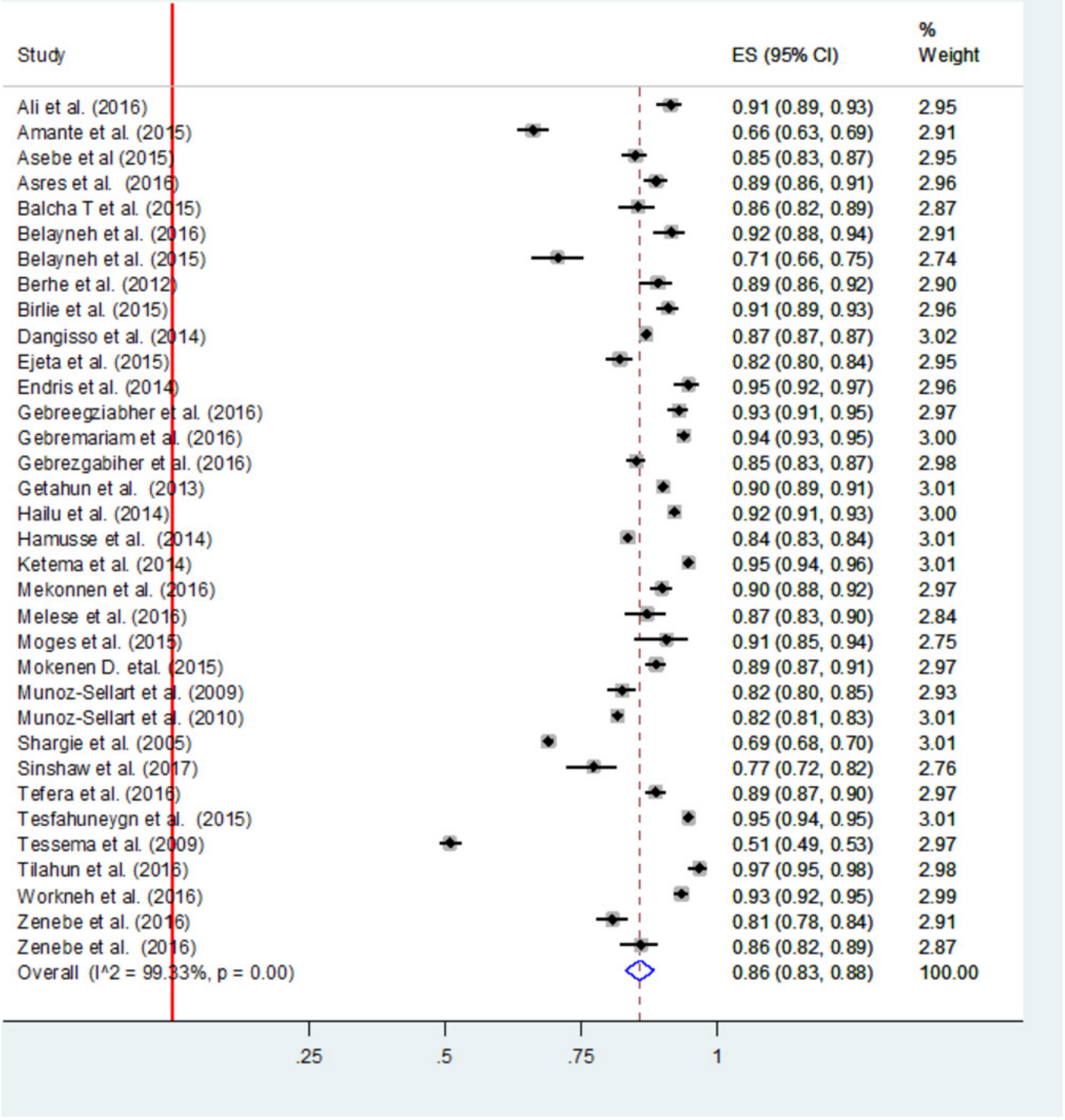

Figure 3 Main meta-analysis of success of tuberculosis treatment in Ethiopia.

treatment outcome in Ethiopia was improving over time. The subgroup analysis showed that TB treatment success from 2005 to 2010 was 71%, from 2011 to 2015 it was 87% and from 2016 to 2017 it was 89% (figure 5).

Factors significantly associated with poor treatment outcome

As indicated in table 4, different demographic and clinical characteristics were reported by the reviewed studies as having a significant association with poor TB treatment outcome ($p < 0.05$). Among these the most frequently mentioned were old age, HIV co-infection, retreatment case and rural residence.

DISCUSSION

TB treatment outcome is one of the performance indicators of the effectiveness of TB control programmes.[40]

Study	ES	[95% Conf.	Interval]	% Weight
Addis Ababa				
Ali et al.	0.91	0.89	0.93	2.95
Getahun et al.	0.90	0.89	0.91	3.01
Hailu et al.	0.92	0.91	0.93	3.00
Tilahun et al.	0.97	0.95	0.98	2.98
Sub-total				
Random pooled ES	0.93	0.90	0.95	11.95
Oromiya				
Amante et al.	0.66	0.63	0.69	2.91
Balcha T et al.	0.86	0.82	0.89	2.87
Ejeta et al.	0.82	0.80	0.84	2.95
Gebremariam et al.	0.94	0.93	0.95	3.00
Hamusse et al.	0.84	0.83	0.84	3.01
Ketema et al.	0.95	0.94	0.96	3.01
Sub-total				
Random pooled ES	0.84	0.78	0.91	17.75
SNNPR				
Asebe et al	0.85	0.83	0.87	2.95
Asres et al.	0.89	0.86	0.91	2.96
Dangisso et al.	0.87	0.87	0.87	3.02
Gebrezgabiher et al.	0.85	0.83	0.87	2.98
Munoz-Sellart et al.	0.82	0.80	0.85	2.93
Munoz-Sellart et al.	0.82	0.81	0.83	3.01
Shargie et al.	0.69	0.68	0.70	3.01
Sub-total				
Random pooled ES	0.83	0.76	0.89	20.85
Amhara				
Belayneh et al.	0.92	0.88	0.94	2.91
Birlie et al.	0.91	0.89	0.93	2.96
Endris et al.	0.95	0.92	0.97	2.96
Gebreegziabher et al	0.93	0.91	0.95	2.97
Mekonnen et al.	0.90	0.88	0.92	2.97
Melese et al.	0.87	0.83	0.90	2.84
Moges et al.	0.91	0.85	0.94	2.75
Mokenen D. etal.	0.89	0.87	0.91	2.97
Sinshaw et al.	0.77	0.72	0.82	2.76
Tefera et al.	0.89	0.87	0.90	2.97
Tessema et al.	0.51	0.49	0.53	2.97
Workneh et al.	0.93	0.92	0.95	2.99
Zenebe et al.	0.81	0.78	0.84	2.91
Sub-total				
Random pooled ES	0.86	0.79	0.93	37.94
Tigray				
Belayneh et al.	0.71	0.66	0.75	2.74
Berhe et al.	0.89	0.86	0.92	2.90
Tesfahuneygn et al.	0.95	0.94	0.95	3.01
Sub-total				
Random pooled ES	0.85	0.74	0.96	8.66
Afar				
Zenebe et al.	0.86	0.82	0.89	2.87
Overall				
Random pooled ES	0.86	0.83	0.88	100.00

Figure 4 Subgroup analysis of success of tuberculosis treatment in the different regions of Ethiopia.

Study	ES	[95% Conf.	Interval]	%Weight
2016 and 2017				
Ali et al.	0.92	0.90	0.94	2.96
Asres et al.	0.89	0.86	0.91	2.96
Belayneh et al.	0.92	0.88	0.94	2.91
Gebregziabher S et al	0.93	0.91	0.95	2.97
Gebremariam et al.	0.94	0.93	0.95	3.00
Gebrezgabiher et al.	0.85	0.83	0.87	2.98
Mekonnen et al.	0.90	0.88	0.92	2.97
Melese et al.	0.87	0.83	0.90	2.84
Sinshaw et al.	0.77	0.72	0.82	2.76
Tefera et al.	0.89	0.87	0.90	2.97
Tilahun et al.	0.97	0.95	0.98	2.98
Workneh et al.	0.93	0.92	0.95	2.99
Zenebe T et al.	0.86	0.82	0.89	2.86
Zenebe Y et al.	0.81	0.78	0.84	2.91
Sub-total random pooled ES	**0.89**	0.87	0.91	41.07
2011-2015				
Amante et al.	0.66	0.63	0.69	2.91
Asebe et al	0.85	0.83	0.87	2.95
Balcha T et al.	0.86	0.82	0.89	2.87
Belayneh et al.	0.71	0.66	0.75	2.74
Berhe et al.	0.89	0.86	0.92	2.90
Birlie et al.	0.91	0.89	0.93	2.96
Dangisso et al.	0.87	0.87	0.87	3.02
Ejeta et al.	0.82	0.80	0.84	2.95
Endris et al.	0.95	0.92	0.97	2.96
Getahun et al.	0.90	0.89	0.91	3.01
Hailu et al.	0.92	0.91	0.93	3.00
Hamusse et al.	0.84	0.83	0.84	3.01
Ketema et al.	0.95	0.94	0.96	3.01
Moges et al.	0.91	0.85	0.94	2.75
Mokenen D. etal.	0.89	0.87	0.91	2.97
Tesfahuneygn et al.	0.95	0.94	0.95	3.01
Sub-total random pooled ES	**0.87**	0.84	0.89	47.02
2005-2010				
Munoz-Sellart(2009)	0.82	0.80	0.85	2.93
Munoz-Sellart(2010)	0.82	0.81	0.83	3.01
Shargie et al.	0.69	0.68	0.70	3.01
Tessema et al.	0.51	0.49	0.53	2.97
Sub-total Random pooled ES	**0.71**	0.60	0.82	11.91
Overall Random pooled ES	0.86	0.83	0.88	100.00

Figure 5 Subgroup analysis of success of tuberculosis treatment based on year of publication.

This systematic review and meta-analysis was conducted mainly to estimate the pooled treatment success rate of patients with drug-susceptible TB in Ethiopia. This review identified 34 studies (from 2005 to 2017) that assessed the treatment outcomes of drug-susceptible TB. All the studies included were observational studies which were conducted in different regions of Ethiopia; Amhara, Addis Ababa, Tigray, Oromia, Afar and Southern Nations, Nationalities and Peoples' Region (SNNPR). The inclusion of studies conducted in various parts of Ethiopia makes this review representative to figure out the overall TB treatment success rate in the country. We analysed data from these studies which reported on treatment outcomes for a total of 117 750 patients with TB. All the included studies used NTLCP guidelines to define TB treatment outcomes which were adopted from WHO.[15 16]

The result of this study showed that the pooled estimate of TB treatment success rate of drug-susceptible TB in Ethiopia is 86% (95% CI 83% to 88%). This pooled TB treatment success rate was lower than the Ethiopian National Strategic Plan (2010–2015) treatment success target of 90%[56] and WHO 2030 international target of ≥90%.[3] This study result is relatively higher compared with a recent review done in Ethiopia which was 83.7%.[14] According to the 2017 WHO global TB report, Ethiopia achieved a TB treatment success rate of only 84% for new TB cases when compared with the

Table 4 Factors which had a significant association with poor tuberculosis treatment outcome

Authors	Reported factors
Ali *et al*[22]	Age >65 years, PTB$^+$
Amante *et al*[55]	Lack of person to be contacted at a time of treatment interruption, sputum smear-negative diagnosis, HIV-positive status
Asebe *et al*[44]	The age group 45–64 years had significantly lower treatment success rate
Asres *et al*[23]	Older, rural dwellers and HIV-positive
Balcha T *et al*[52]	Low mean upper arm circumference (MUAC)
Belayneh *et al*[45]	NR
Belayneh *et al*[24]	Having low baseline CD4 count (less than 200 cells/L), to be at WHO stage IV
Berhe *et al*[25]	Older age, family sizes greater than five persons, unemployed and retreatment cases
Birlie *et al*[46]	Old age, of low baseline body weight and in TB/HIV co-infected patients
Dangisso *et al*[26]	PTB$^-$ cases, older than 65 years, retreatment cases
Ejeta *et al*[47]	HIV serostatus, smear result follow-up at the second, fifth and seventh months
Endris *et al*[27]	No significantly associated factors
Gebreegziabher *et al*[43]	HIV-positive
Gebremariam *et al*[48]	Patients without known HIV status, HIV-positive patients with TB
Gebrezgabiher *et al*[28]	PTB$^-$, rural residence, EPTB, 55–64 years old
Getahun *et al*[49]	NR
Hailu *et al*[29]	PTB$^+$, HIV co-infection and unknown HIV serostatus
Hamusse *et al*[50]	Patients aged 25–49 years, ≥50 years, retreatment cases and TB/HIV co-infection
Ketema *et al*[51]	HIV-positive patients who remained sputum smear-positive at the end of month 2 and patients who reported missed doses
Mekonnen *et al*[30]	PTB$^+$, HIV-positive
Melese *et al*[31]	Female, rural resident, negative smear result at the second month of treatment
Moges *et al*[32]	NR
Mokenen D. *et al*[33]	NR
Munoz-Sellart *et al*[34]	Age <5 years, living in a rural area, lack of smear conversion in the second month
Munoz-Sellart *et al*[35]	Having a positive smear at the second month of follow-up, PTB$^-$, age >55 years, and being male
Shargie *et al*[36]	Patients on LCC (long-course chemotherapy)
Sinshaw *et al*[37]	Rural residence, baseline weight<43.7 kg, bedridden functional status, treatment side effect.
Tefera *et al*[38]	NR
Tesfahuneygn *et al*[39]	Non-adherence to anti-TB drugs
Tessema *et al*[40]	Rural areas, age group 25–34 years, PTB$^-$
Tilahun *et al*[53]	TB/HIV co-infected patients, age less than 1 years
Workneh *et al*[54]	HIV-positive, diabetes
Zenebe T *et al*[42]	Age, sex, HIV status, associated with treatment outcome
Zenebe Y *et al*[41]	HIV-TB co-infection, young age (15–24 years), rural residence and retreatment of patients

All the factors included in this table had a p value <0.05 in each study report.
EPTB, extrapulmonary tuberculosis; NR, not reported; PTB, pulmonary tuberculosis; PTB$^+$, smear-positive PTB; PTB$^-$, smear-negative PTB.

high TB burden countries reached or exceeded a 90% treatment success rate such as; Cambodia (94%), China (94%), Pakistan (93%), Bangladesh (93%), Vietnam (92%), Philippines (91%) and Korea (90%).[3] Even though the treatment success rate was below the target, this systematic review and meta-analysis result was good compared with the WHO report. This might be a clue indicating that Ethiopia is within the track of WHO treatment success target currently. However, a collaborative effort among healthcare providers and policy makers is crucial for achieving both national and international treatment targets.

The success rate of TB treatment in the different regions of Ethiopia was also evaluated in this study. Pooled estimate results showed that the lowest treatment success rate of 83% (95% CI 76% to 89%) was in the SNNPR region of Ethiopia[23 26 28 34–36 44] and the highest success rate was in Addis Ababa (capital city of Ethiopia), that is, 93% (95% CI 90% to 95%).[22 29 49 53] This might be due to the differences in the quality of healthcare facilities, the health-seeking behaviour/awareness/of the population towards TB in each region, the emphasis given by regional governments and policy makers towards TB control programmes, and so on.[57 58] Therefore, close supervision of each TB control programme is required to achieve effective nationwide TB control.

There are so many challenges stated as factors that affect TB treatment outcomes.[57–59] The results of this review showed that different demographic and clinical characteristics were reported to have significant association with poor TB treatment outcome in

Ethiopia.[22–31 34–37 39–44 46 47 50–55] Mainly old age, HIV co-infection, retreatment cases and rural residence were most frequently identified factors associated with poor outcome of TB treatment. In the current study around 5357 patients with TB were HIV-positive. Being HIV-positive lowered the chances of successful treatment outcome. Globally, the treatment success rate of HIV-positive new and relapse TB cases was 78%[3] and HIV significantly affects the overall TB treatment success rate which is reported by other similar studies done in Ethiopia, Somalia, Uzbekistan and Turkey.[14 60–62] Furthermore similar studies done in Ethiopia, Finland and South Korea also reported that older age and retreatment[14] were significantly associated with poor TB treatment outcome.[57 63]

In spite of such imperative 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, SNNPR, Tigray and Afar. Therefore, interpretation of the results of this review should take into consideration of these limitations.

CONCLUSION

This systematic review and meta-analysis revealed that the success rate of drug-susceptible TB treatment in Ethiopia is below the WHO global target (90%) and there is also a discrepancy in TB treatment success rate among different regions of Ethiopia. In addition to these, HIV co-infection, older age, retreatment cases and rural residence were factors reported most frequently that had a significant association with poor outcome of TB treatment. The overall TB treatment success rate obtained in this study, which is closer to the WHO target, is an indicator of the good efforts in the country initiated against TB. In order to further improve the success rate of TB treatment, it is necessary to make a strategic plan for improving the treatment outcome in patients with TB with HIV co-infection, older patients, patients residing in rural areas and retreatment cases. Special consideration should also be given to regions that had a lower TB treatment success rate.

Contributors MAS and MBA conceptualised the research, developed the protocol, conducted the literature search, assessed potentially relevant studies for inclusion into the review, assessed the methodological quality of the included studies, independently extracted the data, performed the statistical analysis, and drafted the manuscript, critically reviewed the manuscript, and wrote the final manuscript. EAM extracted the data, EAM, EAG and TMA assessed the methodological quality of the included studies, and critically reviewed the manuscript. All authors reviewed the final manuscript.

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