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Original Research Article

Factors Associated with Poor Treatment Outcomes in Newly Diagnosed Tuberculosis Patients in Sub-Sahara Africa: A Systematic Review

Muchenelah Chibasa[1*], Eustarckio Kazonga[1], Mwaka Chilinya[1], Wezi Chirambo[1], Sandra Matekenya[1], Sepiso Sikobela[1], Kennedy Banda[1]

[1]School of Postgraduate Studies, Department of Public Health, University of Lusaka, Zambia

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Abstract: ***Introduction*****:** The burden of Tuberculosis (TB) in Africa continues to rise despite numerous interventions to stop the spread. Addressing factors associated requires a robust model that addresses cross-cutting issues in the continuum of TB care and management. The objective of this systematic review is to determine factors associated with poor treatment outcomes in newly diagnosed TB patients in sub-Saharan Africa. ***Method*****:** The literature search identified 234 studies that were written in English. All the articles were identified via database search and imported into Mendeley for analysis. A total of 95 duplicates were removed and the abstracts of remaining studies were reviewed. A total of 139 abstracts were screened with misleading and non-open access journal articles removed. A full reading of the remaining 104 potentially relevant studies was done, in order to ascertain compliance with the inclusion/exclusion criteria and 24 studies were found to be eligible and were included in this review. ***Results*****:** HIV co-infection, type of TB infection and gender were observed as most common factors associated with poor treatment outcomes in newly diagnosed patients. Several studies emphasized the impact of male gender on poor treatment outcomes stating a higher likelihood to developing unfavorable outcomes. Other factors identified included social factors namely employment, location, nutrition, failure to gain weight, failure to present at facility, delay to be treated at the facility and the type of facilities where one was treated. ***Conclusion*****:** The common factors associated with poor treatment outcomes were HIV co-infection, type of TB infection and gender and these were notably underscored by social factors. Addressing these challenges will significantly improve the health outcomes of TB patients in the region.

Keywords: Newly Diagnosed Tuberculosis, Poor Treatment Outcomes, Sub-Saharan Africa.

INTRODUCTION

Tuberculosis (TB) remains a significant global health challenge, particularly in Sub-Saharan Africa, where its burden is most pronounced (WHO, 2021). Tuberculosis (TB) is an infectious disease that primarily affects adults in their most productive years. While commonly affecting the lungs, TB also affects the kidneys, brain, spine, and skin (WHO, 2023). Despite advancements in diagnosis and treatment, poor treatment outcomes persist in the region, posing a formidable barrier to TB control efforts (WHO, 2023). Understanding the factors contributing to these suboptimal outcomes is imperative for designing effective interventions and improving patient care. The WHO Global report 2023 on TB reported the global number of people newly diagnosed with TB was 7.5 million. This is the highest number since WHO began global TB monitoring in 1995, above the pre-COVID baseline (and previous historical peak) of 7.1 million in 2019, and up from 5.8 million in 2020 and 6.4 million in 2021 (WHO, 2023).

In sub-Saharan Africa, the epidemiological landscape of TB is complex, characterized by high prevalence rates, limited healthcare infrastructure, and various socioeconomic determinants that intersect to influence treatment outcomes (WHO, 2023). Most TB cases in 2021 were in the WHO regions of South, East Asia, Africa, and the Western Pacific, with smaller shares in the Eastern Mediterranean, the Americas, and Europe. Despite being preventable and curable, tuberculosis was the second leading infectious disease killer (after COVID-19) and the 13th leading cause of death worldwide during 2020–2021 (WHO, 2023). Previous research has identified several factors associated with

***Corresponding Author:** Muchenelah Chibasa
School of Postgraduate Studies, Department of Public Health, University of Lusaka, Zambia

poor treatment outcomes among newly diagnosed TB patients in this region. These factors encompass a broad spectrum ranging from individual patient characteristics to health system-related challenges (Ukwaja *et al.,* 2013).

Individual-level factors such as HIV co-infection, low socio-economic status, malnutrition, substance abuse, and medication non-adherence have been consistently implicated in suboptimal TB treatment outcomes (Ukwaji *et al.,* 2023). The synergy between TB and HIV poses a particularly daunting challenge, with HIV significantly increasing the risk of TB-related mortality and treatment failure (Odone, 2014). Malnutrition, prevalent in resource-constrained settings, compromises immune function and hampers treatment response, further exacerbating the TB burden (Gupta *et al.,* 2009). Substance abuse, including alcohol and illicit drug use, not only undermines treatment adherence but also contributes to treatment interruptions and adverse drug reactions (Pelissari & Diaz-Quijano, 2018).

Additionally, most transmissions occur between the onset of coughing and initiation of treatment. Health system-related factors such as inadequate healthcare access, diagnostic delays, substandard healthcare quality, inadequate number of reviews and medication stockouts significantly impede timely diagnosis and effective treatment initiation for TB patients, thus leading to poor prognostic outcomes in these patients (Segagni *et al.,* 2013). Treatment outcomes, as measured by a standardized method, are key indicators of national TB program (NTP) effectiveness (WHO, 2013). Factors affecting TB outcomes are crucial indicators of TB control program success. Prompt initiation and adherence to national TB treatment standards are essential for effective therapy (Kassim *et al.,*2021).

Limited access to healthcare facilities, especially in rural areas, often result in undiagnosed or missed cases and diagnostic delays, allowing TB to progress unchecked, increasing the infection rate and reducing treatment efficacy (Shah *et al.* 2022). Furthermore, healthcare quality issues, including diagnostic inaccuracies and treatment mismanagement, compromise patient outcomes and fuel drug resistance. Moreover, frequent medication stockouts and interruptions disrupt treatment continuity, leading to treatment failure and the emergence of drug-resistant TB strains (Tegegn *et al.,* 2020).

Despite the recognition of these factors, there remains a critical gap in understanding the nuanced interplay between them and their collective impact on TB treatment outcomes in Sub-Saharan Africa. This proposed study seeks to address this gap by comprehensively examining the multifactorial determinants of poor treatment outcomes among newly diagnosed TB patients in the region. By elucidating the complex interactions between individual-level and health system-related factors, this study aims to inform targeted interventions and policy reforms aimed at enhancing TB care delivery and optimizing treatment outcomes in Sub-Saharan Africa.

This systematic review aims to consolidate existing evidence on the factors associated with poor treatment outcomes among newly diagnosed TB patients in sub-Saharan Africa. By synthesizing findings from both quantitative and qualitative studies, this review aims to capture the complexity of factors influencing treatment outcomes and provide insights into the underlying mechanisms driving poor outcomes in this context.

METHODS AND MATERIALS

Search Strategies

A literature search was conducted on studies reporting on factors associated with poor treatment outcomes on newly diagnosed TB patients published from 2014 to 2024. Articles published in the English language and conducted in sub–Saharan Africa were considered eligible for this review. Original studies providing information on the outcome of interest were identified through a computerized systematic search using PubMed Central database.

Our focus of this study was newly diagnosed tuberculosis patients in sub-Saharan Africa who have been receiving treatment from 2014 to 2024. The intervention involves a multifaceted approach aimed at increasing awareness and education to reduce the stigma associated with tuberculosis, thereby improving access to healthcare services. Emphasis is placed on timely diagnosis and the early initiation of treatment. Community-based interventions are implemented to address poor compliance and high default rates, ensuring that patients remain engaged in their treatment regimen. Additionally, health promotion programs are designed to support both patients and healthcare providers in enhancing adherence to medication protocols. Special attention was given to encouraging men, who often delay seeking healthcare, to access timely health services.

The outcomes of interest include mortality, loss to follow-up, treatment failure, and cases that were not evaluated, as defined by the World Health Organization (WHO)

Inclusion and Exclusion

The inclusion criteria for this systematic review are specifically designed to collate relevant data concerning the factors associated with poor treatment outcomes among newly diagnosed tuberculosis (TB) patients in Sub-Saharan Africa. Eligible studies must be conducted within Sub-Saharan Africa, focusing on patients who have recently received a TB diagnosis. The study should have been original and conducted between 2009 and 2024. The research must concentrate specifically on poor treatment outcomes, offering

insights into the challenges and barriers faced during the treatment process. Furthermore, only those articles where patients have been on TB treatment for a minimum of two months will be considered, as this duration allows for an assessment of initial treatment response and adherence challenges.

Conversely, the exclusion criteria is set to ensure the specificity and relevance of the data analyzed. Articles that are not specific to the Sub-Saharan African context will be excluded to maintain the regional focus necessary for addressing localized public health strategies and outcomes. Additionally, the systematic review will only include articles published in English or those accompanied by an English translation to ensure clarity and consistency in data interpretation. Lastly, studies that have incomplete data on treatment outcomes will be omitted to uphold the quality and reliability of the systematic analysis. This rigorous selection process is essential to derive meaningful conclusions that can inform future TB treatment policies and interventions in the region.

Quality Assessment

The Joanna Briggs Institute's (JBI) appraisal criteria is used to assess the quality of systematic reviews, however due to limitation in time, the assessment was not used on this paper, however careful scrutiny and study of manuscripts was done to ensure that quality information was extracted in the development of this research paper.

Ethical Considerations

No ethical approval needed as data was extracted from previously published studies where consent was obtained

Data Extraction and Review Process

The search identified 234 studies via database search. All the articles identified were imported into Mendeley and duplicates were removed. A total of 95 duplicates were removed. Titles and abstracts of remaining studies were reviewed. A total of 139 abstracts were screened with 29 removed for being misleading and 6 for not being open access journal articles. A full reading of the text of the remaining 104 studies that were potentially relevant was done, in order to ascertain their compliance with the inclusion/exclusion criteria. After full text evaluation 24 studies were found to be eligible and were included in this review as shown in Figure 1.

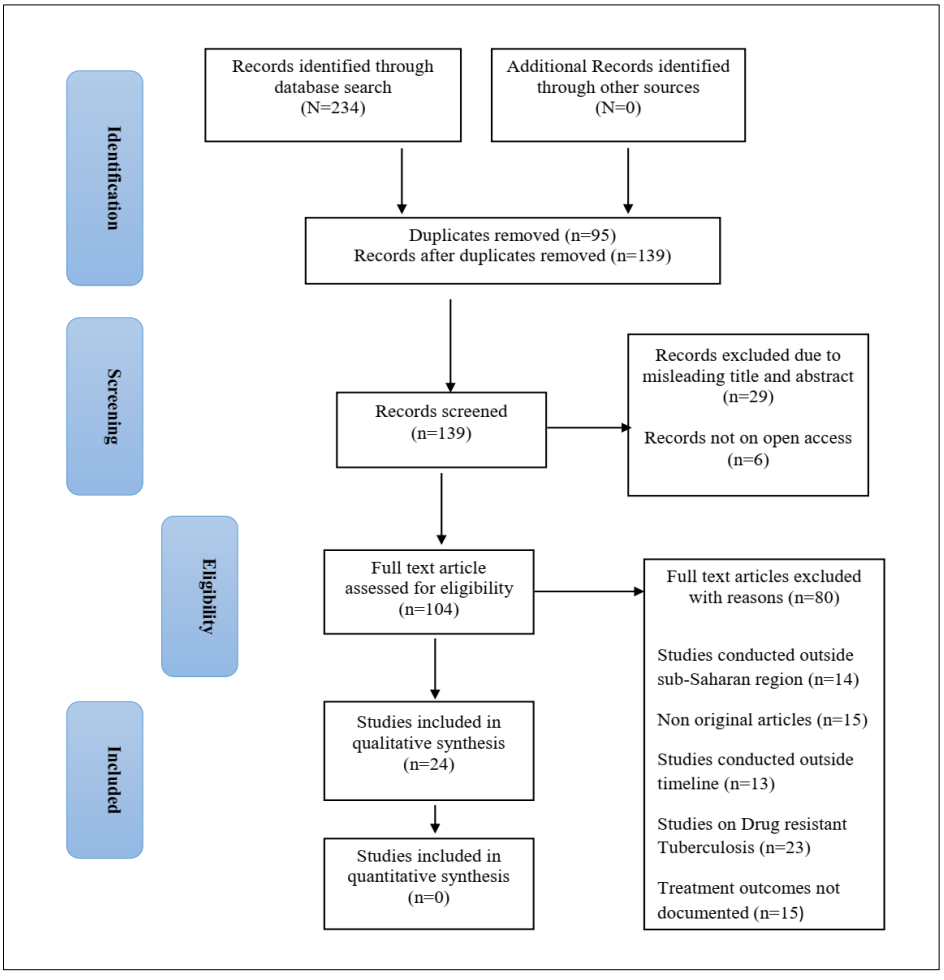

Figure 1: PRISMA Flow diagram for the selection of studies

Characteristics of Studies

The review included 24 studies made up of retrospective cross-sectional studies, mixed method and prospective cohort study. The studies included in the review were published between 2009 and March 2024. The characteristics of studies included in the review are shown in Table 1. The characteristics include the name of the author, the title of the study, duration, and sample size. Other considerations were region, population characteristics, and study design.

Table 1: Characteristics of studies included in the review

Author	Title	Duration	Sample size	Region	Population characteristics	Study design
Nanzaluka F. *et al.*, 2019 [1]	Factors associated with unfavorable tuberculosis treatment outcomes in Lusaka, Zambia, 2015: a secondary analysis of routine surveillance data	2015 to 2019	1,724	Lusaka, Zambia	People living with TB	Secondary analysis
Mirutse *et al.*, 2019 [2]	Epidemiology of childhood tuberculosis and factors associated with unsuccessful treatment outcomes	10 years	1,086	Ethiopia	Children with TB	Retrospective cross-sectional study
Ngah V.D *et al.*,, 2023 [3]	Evaluating determinants of treatment outcomes among tuberculosis patients in the mining district of Butha Buthe, Lesotho	2015-2022	1,792	Lesotho	TB patients between 20-59 years old	Retrospective cohort study
Nguna J. *et al.*,2022 [4]	Factors associated with poor treatment outcomes among tuberculosis patients in Kyangwali Refugee Settlement,	2016-2017	212	Uganda	TB patients in refugee settlement	Retrospective cohort study
Nidoi J. *et al.*, 2021 [5]	Impact of socio-economic factors on Tuberculosis treatment outcomes in north-eastern Uganda: a mixed methods study	2018-2019	313	Uganda	TB patients	Mixed methods
Oshi. C *et al.*, 2014 [6]	Profile and Treatment Outcomes of Tuberculosis in the Elderly in Southeastern Nigeria,	2011-2012	60	Nigeria	Adult TB patients	Retrospective cohort study
Adane. H *et al.*, 2023 [7]	Diabetes mellitus is associated with an increased risk of unsuccessful treatment outcomes among drug-susceptible tuberculosis	2020-2021	267	Ethiopia	Newly enrolled adult TB patients	Prospective Cohort study
Adisa. R *et al.*, 2021 [8]	Knowledge about tuberculosis, treatment adherence and outcome among ambulatory patients with drug-sensitive tuberculosis in two directly-observed treatment centers in Southwest Nigeria, 2019/2013-2017	2013-2017	2,262	Nigeria	Adult TB Patients Newly enrolled	Mixed Methods Design (Cross sectional study 2019/ retrospective review 2013-2017)
Amkongo. M *et al.*, 2023 [9]	Factors associated with the unsuccessful TB treatment outcomes in the northern regions of Namibia	2016-2020	4,447	Namibia	Adult TB patients newly enrolled	Mixed Methods Explanatory Sequential design

Author	Title	Duration	Sample size	Region	Population characteristics	Study design
Asres *et al.*,2018 [10]	Delays to treatment initiation is associated with tuberculosis treatment outcomes among patients on directly observed treatment short course in Southwest Ethiopia: a follow-up study.	January 2015 to June 2016		South West Ethiopia	Adult newly diagnosed TB patients on treatment	Retrospective study
Belachew A. *et al.*, 2018 [11]	Poor treatment outcomes and its determinants among TB patients in selected health facilities in east wollegen, western Ethiopia	2018	435	Ethiopia	Adult new TB patients	retrospective cross-sectional study design
Berhan A. *et al.*, 2023 [12]	Tuberculosis treatment outcome and associated factors among TB patients linked to TB treatment clinics in Ethiopia, 2023, a multi-centre retrospective study.	2023		Ethiopia,	All newly diagnosed TB patients on treatment	Retrospective study
Chilyabanyama R. *et al.*, 2024 [13]	Factors associated with TB treatment outcomes among TB patients aged 15years and older at chawama level one hospital	2024	404	Zambia	Patients who were diagnosed and started treat at the said facility	Retrospective study
Tessema, B et al., 2009 [14]	Treatment outcome of tuberculosis patients at Gondar University Teaching Hospital, Northwest Ethiopia. A five - year retrospective study	September 2003 to May 2008	4000	North West Ethiopia	Population Characteristics: All TB patients who were registered at the facility	Retrospective study
Tola, A. M. M. *et al.*, 2019 [15]	Treatment outcome of tuberculosis patients at Gondar University Teaching Hospital, Northwest Ethiopia.	September 2003 to May 2008	4,000	Ethiopia	People Diagnosed with TB from age 0 to 65 and above in Gonder, Ethiopia	A five - Year retrospective study
Woldemichael *et al.*, 2021 [16]	Treatment Outcome of Tuberculosis and Associated Factors among TB-HIV Co-Infected Patients at Public Hospitals of Harar Town	April 1–10, 2018	349	Ethiopia	All TB/HIV co-infected patients who registered in the public hospitals in Harar town	Retrospective Study
Worku *et al.*, 2018 [17]	Treatment outcomes of tuberculosis patients and associated factors in Bale Zone, Southeast Ethiopia: a	1 September 2011 to 30 August 2016	7,205	Ethiopia	All registered TB Patients in Bale Zone	Retrospective Cohort Study
Zenbaba *et al.*, 2017 [18]	Treatment outcomes of tuberculosis patients under directly observed treatment short-course at Debre Tabor General Hospital, northwest Ethiopia: nine-years retrospective study	September 2008 to December 2016	985	Ethiopia	TB patients of all age groups under directly observed treatment short-course at Debre Tabor General Hospital	Retrospective Study

Author	Title	Duration	Sample size	Region	Population characteristics	Study design
Katana *et al.*, 2022 [19]	Trends of unsuccessful treatment outcomes and associated factors among tuberculosis patients in public hospitals of Bale Zone, Southeast Ethiopia	July 2013 to June 2018/19	1,257	Bale Zone, Southeast Ethiopia	Patients with TB	Retrospective study
Pizzol *et al.*, 2018 [20]	Predictors of therapy failure in newly diagnosed pulmonary tuberculosis cases			Mozambique	Adult TB patients (>18 years old)	Retrospective cohort study
Puplampu *et al.*, 2024 [21]	Evaluation of treatment outcomes among adult patients diagnosed with tuberculosis in Ghana	2012-2021	4,106	Ghana	Adult TB patients (>18 years old)	A 10-year retrospective review
Sahile Z. *et al.*, 2021 [22]	Nutritional status and TB treatment outcomes in Addis Ababa, Ethiopia:		456	Ethiopia	Adult TB patients (>18 years old)	Ambi-directional cohort study
Shin *et al.*, 2018 [23]	Tuberculosis treatment outcomes among prisoners and general population in Zomba, Malawi	2011-2016	1,652	Malawi	Prisoners & general population aged 15 & above	Retrospective Cohort Study
Singano *et al.*, 2020 [24]	Mixed Mycobacterium tuberculosis-Strain Infections Are Associated With Poor Treatment Outcomes Among Patients With Newly Diagnosed Tuberculosis, Independent of Pretreatment Hetero-resistance	2012-2016		Botswana	Undefined 173, 66, and 21 patients with single, possibly mixed, and mixed-strain infections, respectively	Mixed methods

RESULTS

Out of the twenty-four studies that were reviewed age, HIV co-infection, type of TB infection and gender were observed as most common factors associated with poor treatment outcomes in newly diagnosed patients. Specifically, Fifteen (15) studies specifically highlighted age as a significant factor influencing treatment outcomes [1,3,4,6,8-11,13,14,16,18,19,21,24], though the exact age ranges and implications may vary across studies. Eleven (11) studies emphasized the presence of HIV as a significant co-morbidity associated with poor TB treatment outcomes [1,5,8,10,11,13,15,17-19,24] with one study showing a higher likelihood of poor treatment outcomes in those that had a HIV positive status (aOR = 0.63: 95% C.I: 0.42–0.94) [24], whilst another showed that in the first three months of TB treatment, HIV infected not on ARVs (adjusted Hazard Ratio (aHR) 1.72 (95%CI 1.28–2.30)) and the year of starting treatment were significantly associated with higher hazard of poor outcomes [19]. Ten (10) studies pointed to Extrapulmonary Tuberculosis (EPTB) as a factor associated with poor outcomes, suggesting potential complexities or challenges in diagnosing and treating extrapulmonary manifestations of the disease [2-4,7,10-12,15,18,24]. Smear negative PTB and extra pulmonary cases were 2 times more likely to have a poor outcome compared to smear positive patients [11], as further evidenced by the four (04) studies which highlighted the detrimental effects of delayed diagnosis or sputum negativity on treatment outcomes [10,13,17,19]. However, one study noted mixed mycobacterium infection as a contributing factor as well [23]. Six (06) studies emphasized the impact of male gender on poor treatment outcomes [1,4,8,11,13,20]. One study specifically stated that Male TB patients were more likely (aOR = 1.24, 95% CI: 1.02-1.52, p = 0.03) to develop unfavorable outcomes compared to female TB patients [1]. Four studies (04) indicated variations in treatment outcomes based on the type of Directly Observed Therapy with Community-based DOTS (aOR = 0.356, 95% CI = 0.835 2.768, p = 0.006) being found to have a statistically significant association with TB treatment outcomes [8-10,13]. Five studies (05) examined the influence of urban, rural, or prison settings on treatment outcomes [8,11,14,16,18] wherein risk of unsuccessful TB treatment outcome was twice more likely in rural dwellers [11]. Additionally, Three (03) studies highlighted the impact of geographical distance and delayed presentation to healthcare facilities on treatment outcomes [8,14,18], whilst two studies (02) emphasized the influence of facility resources and

patient transfers on treatment outcomes [16, 18]. One studies (01) identified low body mass index (BMI) as a factor associated with poor treatment outcomes whilst another [19], noted the association between overweight status and poor treatment outcomes. Also noted were two (02) studies that indicated unemployment as a socio-economic factor associated with poor treatment outcomes [5, 22], whilst another suggested that a lack of formal education could contribute to poor treatment outcomes [3]. Several categories of lack of family support were identified with one study indicating a lack of familial support as a contributing factor and another study suggesting that poor compliance within the family setting could negatively impact treatment adherence [3]. Yet another study noted the association between being bedridden and poor treatment outcomes [15]. One study (01) identified DM as a co-morbidity contributing to poor treatment outcomes [7], suggesting need for follow up research.

Table 2: Summary findings on the factors associated with poor treatment outcomes

Author	Factors associated with poor treatment outcomes based on review
Nanzaluka F. *et al.*, 2019	**Age:** Univariate logistic regression analysis revealed that TB patients above 59 years old had higher odds (unadjusted odds ratio (OR) = 1.65, 95% CI: 1.02, 2.68, p = 0.04) of having unfavourable outcomes compared to those aged 45-59 years **Gender:** Male TB patients were more likely (OR = 1.24, 95% CI: 1.02-1.52, p = 0.03) to develop unfavourable outcomes compared to female TB patients. **HIV co-infection:** HIV co-infected TB patients had a statistically significant increased chance of developing unfavourable outcomes compared to HIV negative TB patients (OR = 1.22, 95% CI: 1.00-1.51, p = 0.05).
Mirutse *et al.*, 2019	**Gender:** Holding other factors constant (sex, age, residence, HIV/AIDS type of TB pulmonary v. extra pulmonary). TB cases who are females were 1.79 times more likely to have unsuccessful treatment outcome (95% CI, 1.07–3.00) compared with males. **Type of TB:** pulmonary smear positive cases were 2.56 times (95% CI, 1.13–5.77), more likely to have unsuccessful treatment outcome compared with extra pulmonary cases.
Ngah V.D *et al.*, 2023	**Age:** Variables with increased hazards of unfavorable outcomes included being 60 years and older (HR=2.81, 95%CI 1.82 – 4.33), unemployment (HR=1.25, 95%CI 1.03 – 1.51) and susceptibility to TB treatment (HR=1.93, 95% CI 1.36 – 2.74). **Type of TB:** Patients who had pulmonary TB had increased favorable outcomes (79.8%) as compared to patients who had extrapulmonary (20.2%) (p<0.001). **Lack of family support:** noted among older persons living on their own and associated inability to access health services would enable treatment defaults and/or loss to follow-up.
Nguna J. *et al.*, 2022	**Age and Gender:** Most males affected across age groups. 66% completed treatment with none characterized as cured. A total of 71 (33.5%) had a poor outcome, including 53 (25%) lost to follow up, 13 (6.1%) died, whereas treatment failed in 5 (2.4%). We found that with increasing age, the more likely patients were to have unfavorable treatment outcomes to TB.
Nidoi J. *et al.*, 2021	**Unemployment:** 51.9% unsuccessful outcomes **Co-infection**: Regarding HIV, 4.5% of the TB patients were co-infected with HIV.
Oshi. C *et al.*, 2014	**Age:** Among all TB cases, elderly patients had lower rates of successful outcomes (68.9%% vs 77.1%; p=0.009). The proportion of death and loss to follow-up were higher among the elderly (12.3% vs 9.5% (p=0.1) and 12.3% vs 9% (p=0.07) respectively, But differences did not reach statistical significance
Adane. H *et al.*, 2023	**TBDM** comorbidity accounted for two of the seven (2/7) deaths, three of the four (3/4) transferred out, one of the four (1/4) lost to follow up and the only one failed treatment cases The adjusted odds of poor TB outcome among those with diabetes was 14.8 (95 %CI 3.5–62.7) times the odds of poor TB outcome observed among those without diabetes. Also noted history of other NCDs (aOR = 5.3; 95 %CI 1.0 – 28.0) **Type of TB:** smear positive pulmonary TB (adjusted odds ratio [aOR] = 16.4; 95 %CI 2.3 –119.3), extrapulmonary TB (aOR = 9.7; 95 %CI 1.3 – 73.1).
Adisa. R *et al.*, 2021	**Age:** 85(48.0%) of those that died and 26(48.1%) of those that failed treatment were aged between 35-54 years. 128(53.3%) of those that defaulted were aged 18-34 years (interestingly, 35-54 years had the highest cure and treatment completed rates) **Gender:** 111(62.7%) of those that died, 35(66.8%) of those that failed treatment and 160(66.7%) of those that defaulted were male. Overall, 306(65.0%) males had unsuccessful treatment **HIV co-morbidity:** 303(70.5%) HIV positive had unsuccessful treatment

	Location of Health Facility where DOTs being done: Topmost of the reasons cited by patients for TB treatment non-adherence were inaccessibility to healthcare facility (55%), perhaps in terms of travel costs for daily DOT at the clinic, and the idea of taking many anti-TB medicines at once (16.7%) There were significant associations between sex ($\chi 2$=8.780, p=0.003), HIV status ($\chi 2$=29.110, p<0.001 DOT clinic attended ($\chi 2$ =18.215, p<0.001) and patients' with or without successful treatment outcome.
Amkongo. M *et al.,* 2023	**Region (rural/peri urban):**106(6.3%) died, 6(0.4%) failed and 31(2.9%) defaulted in Kunene while 157(9.8%) died, 32(2.0%) failed and 79(4.9%) defaulted in Oshana **Type of DOT used:** In Kunene region, only the Type of DOT used (Community-based DOTS) with adjusted odds ratio [aOR] = 0.356, 95% Confidence Interval [CI] = 0.835 2.768, p = 0.006) was found to have a statistically significant association with TB-TO. (as opposed to facility based, this could be due tied to location of facility). **Age:** In the Oshana region, only the Age Group variable had a significant effect on TB-TO. Specifically, age groups 21–30 years old (aOR = 1.643, 95% CI = 1.005–2.686, p = 0.048), 31–40 years old (aOR = 1.725, 95% CI = 11.026–2.9, p = 0.040), 41–50 years old (aOR = 2.003, 95% CI = 1.155 3.476, p = 0.013) and 51–60 years old (aOR = 2.106, 95% CI = 1.228–3.612, p = 0.007) had statistically significant associations with poor TB-TO.
Asres *et al.,* 2018	**Patient delays to present to the facility:** median 25days after onset of symptoms **Delays in diagnosis**: 84.7% on their 3rd visit and 15.3% on their 1st visit. This initiation of treatment took 22 days (provider delay) since first visit, bringing the total to approximately 55days after onset of symptoms. **TB/HIV co-infection**: (39.7%)- reported delays in initiation of anti-TB treatment **Age:** >65 years **Failure to gain weight**: within 2 months of initiating treatment increased the risk of poor outcomes **Type of DOTs:** hospital DOTs had poor outcomes compared to community DOTs. **Poor compliance:** treatment delays led to increase in direct and indirect costs on impoverished houses leading to poor compliance and outcomes. **Type of TB:** Pulmonary negative and extra pulmonary TB were predictors of poor outcome.
Belachew A. *et al.,* 2018	**Age:** Older patients had 4 times higher chances of a bad outcome than younger patients. **Gender:** males were 2 times more likely to have a poor outcome **Type of TB:** smear negative PTB and extra pulmonary cases were 2 times more likely to have a poor outcome compared to smear positive patients **Location:** rural dwellers were 2 times more likely to have a poor outcome **Co-infection:** those who were HIV positive were at higher risk of unsuccessful treatment.
Berhan A. *et al.,* 2023	**Co-infection:** HIV co-Infection was 3 times more likely to have an unsuccessful treatment outcome. **Type of TB:** patients with sputum negative PTB were more likely to have unsuccessful treatment than sputum positive TB patients
Chilyabanyama R. *et al.,* 2024	**Age:** those 55-64 were 44.9% less likely to have a good outcome compare to the those 15-24. **Gender:** Men were 8.5 time less likely to have a good outcome **Mode of Diagnosis:** clinically diagnosed TB patients were 30.5% less likely to have a good outcome compared to those that were bacteriologically confirmed TB. **Co-infection:** HIV positive were 5 times more likely to have a better outcome **Type of DOTs:** patients that were observed by a relative were 52.8 % more likely to have a success outcome compared to that that were observed by the clinic.
Tessema, *B et al.,* 2009	**Age:** As the age increase the death rate of patients was steadily increased from 4.6% in the age group of 0 - 14 years to 15.8% in the age group of 55 - 64 years. High age has been previously reported to be a risk factor for death, partly due to increasing comorbidities as well as the general physiological deterioration with age. **Location:** The default rate (18.3%) was higher than the average 6.2% among the 22 HBCs and 10% among the rural households
Tola, A. M. M. *et al.,* 2019	**Types of TB:** Smear-positive PTB patients had higher unsuccessful treatment outcomes (18.9%) than extrapulmonary TB (14.3%) and smear-negative PTB (6.7%) cases and this difference was statistically significant (p = 0.028). **Functional status:** More than half of the patients under the category of bedridden functional status had unsuccessful treatment outcome but only 11.5% of the patients with working functional status had unsuccessful treatment (p = 0.005). **WHO staging:** 30% of the TB/HIV co-infected patients with WHO stage 4 diseases had an unsuccessful treatment outcome whereas 8.9% of the patients with stage 1 disease had unsuccessful treatment. (p = 0.003).

	History of opportunistic infection: higher proportion of the TB/HIV co-infected patients with a history of opportunistic infection (18.9%) had unsuccessful TB treatment outcomes than those who had no history of opportunistic infection (6.3%)
Woldemichael *et al.*, 2021	**Type of Health facility:** TB patients who had continued their treatment at a hospital or health center showed a three-fold better treatment outcome and more than a two-fold improvement compared with patients who continued their treatment at a health post (adjusted odds ratio [AOR]: 2.96 [1.41–6.20] and 2.57 [1.44–4.57]), respectively. **Age:** those whose age was ≤14 years, 15 to 24 years, 25 to 34 years, and 35 to 44 years were more likely to show a successful treatment outcome, with the an AOR of 2.21 (1.53, 3.19), 1.61 (1.16, 2.22), 1.86 (1.34, 2.59), and 1.65 (1.16, 2.35), respectively
Worku *et al.*, 2018	**Low diagnostic capacity:** Due to limited resources, most of the health facilities in Ethiopia have been using AFB microscopy, which has low sensitivity (40–45%) and might contribute to lower notification rates of positive PTB. **Co-infection:** HIV-positive TB patients, the treatment success achieved was 88.1%, only about 2% lower than the success treatment rate of all subjects. The 2% unsuccessful treatment outcome among HIV co-infected TB patients might be attributed to factors such as underlying HIV and other undiagnosed opportunistic infections. **Gender: t**he proportion of patients who were successfully treated for TB/HIV co-infection was higher among female PTB positive patients.
Zenbaba *et al.*, 2017	**Type of Health facility:** Those being treated in the general hospital were nearly four times more likely to have treatment failure/loss to follow up than those treated in the referral hospital (AOR = 4.21 and 95% CI: 1.82, 9.75). **Type of TB:** Those with extrapulmonary TB were 52% less likely to have failure/loss to follow-up treatment outcomes in relation to patients with pulmonary TB (AOR = 0.48 and 95% CI: 0.25, 0.92) and had no relation to the death of patients with TB. **Hospital transfer:** Those who were transferred in from other health facilities had an almost four times higher risk of treatment failure/loss to follow up than newly registered patients with TB (AOR = 3.62 and 95% CI: 1.83, 7.16) but no association with death. **Age:** those with TB aged 45 years and above were four times at a higher risk of death than patients under 24 years of age (AOR = 4.20 and 95% CI: 2.03, 8.70). **Co-infection:** There were 68% lower odds of death among TB patients who had negative HIV test status compared to their counterparts (AOR = 0.32 and 95% CI: 0.19, 0.56) and no association with the TB patient's treatment failure
Katana *et al.*, 2022	**Co-morbidity:** In the first three months of TB treatment, HIV infected not on ARVs (adjusted Hazard Ratio (aHR) 1.72 (95%CI 1.28–2.30)) and the year of starting treatment were significantly associated with higher hazard of poor outcomes. **Overweight:** In the first three months of TB treatment, being overweight (aHR 0.85 (95%CI 0.73–0.98)) was negatively associated with hazard of poor outcome. **Age:** In the last three months of TB treatment, Elderly age (≥ 51years) (aHR 1.26 (95%CI 1.02–1.55)), were significantly associated with higher hazard of poor outcomes. **Gender:** Being female (aHR 0.83 (95%CI 0.70–0.97)) **Diagnostic Criteria:** those empirically treated without bacteriological confirmation (aHR 0.82 (95%CI 0.70–0.97)) were negatively associated with hazard of poor outcome.
Pizzol *et al.*, 2018	**Gender:** Patients who needed more medical attention were young males, malnourished, with low income and low educational degree and HIV positive. These subjects were more likely to fail therapy.
Puplampu *et al.*, 2024	**Age:** Those aged between 35-64 and 65 + were less likely to have successful treatment outcomes as compared to those between the ages of 18-34 years. **Co-morbidity:** It was found that HIV negative patients had increased odds of successful treatment outcomes as compared to TB patients who were HIV positive
Sahile Z. *et al.*, 2021	**Low BMI:** Under nutrition is associated with an increased risk of mortality and relapse in persons with TB disease. Being undernourished is also a risk factor for hepatotoxicity on TB treatment. **Nutritional support:** The death rate was higher in the Underweight patients (9.24%; 17/184) than in normal or overweight patients.
Shin *et al.*, 2018	**Strain of Mycobacterium:** Of the 260 patients with tuberculosis included in the study, 25 (9.6%) had mixed infections and 30 (11.5%) had poor treatment outcomes. Micro-heteroresistance, macro-heteroresistance, and fixed resistance were found among 11 (4.2%), 2 (0.8%), and 11 (4.2%), respectively, for isoniazid and 21 (8.1%), 0 (0%), and 10 (3.8%), respectively, for rifampicin.
Singano *et al.*, 2020	**Age:** Unsuccessful TB treatment outcomes were associated with age greater than 35 years (aOR = 0.68: 95% C.I: 0.58–0.80). **Type of TB**: Extra-Pulmonary TB (aOR = 1.69: 95% C.I:1.08–2.63).

	Co-morbidity: HIV positive status (aOR = 0.63: 95% C.I: 0.42–0.94).

DISCUSSION

The aim of this systematic review was to determine factors associated with poor outcome treatment outcome among newly diagnosed Tuberculosis patients in Sub-Sahara Africa, below is the discussion for the results presented in table 3.

Patient Delays to Present to the Facility

The analyzed articles underscored the critical role of patient delays in seeking healthcare as a major contributor to poor TB treatment outcomes (Asres *et al.,* 2018). These delays result in delayed diagnosis, which not only compromised patient health but also contributed to increased transmission within communities. Several factors are proposed to be among the reasons that exacerbated patient delays, and these include:

Firstly, lack of awareness and knowledge about TB symptoms and available healthcare services among rural populations hinder prompt healthcare-seeking behavior. Secondly, stigma associated with TB, especially among vulnerable populations such as prisoners, further deters individuals from seeking timely medical attention. Thirdly, socio-economic factors, including financial constraints and the inability to sustain hospital admission costs, contribute to high rates of defaulting and poor treatment outcomes. The observed higher pre- and post-diagnosis costs among delayed patients underscore the economic burden faced by affected households, (Asres *et al.,* 2018). Lastly, geographical barriers, such as distance to healthcare facilities, pose significant challenges, particularly for rural patients. Community-based interventions, such as community-directed directly observed treatment (community DOTs), have been shown to enhance patient convenience and compliance to treatment by bringing TB services closer to affected communities (Asres *et al.,*2018). Intensified case finding guideline such as those outlined in the WHO 2011 guidelines for intensified case finding could help in identifying TB patients in the community and refer for treatment without experiencing delays.

Delays in Making Diagnosis by Health Facility

The delay in diagnosing TB within healthcare facilities poses significant challenges, particularly for patients with smear-negative or extra-pulmonary TB presentations. These forms of TB often present atypical symptoms and lower bacillary loads, leading to a reduced index of suspicion among healthcare providers. As a result, patients may undergo multiple clinical visits and receive treatment for different ailments before TB is considered. As highlighted by Asres *et al.,* (2018), patients with delayed TB diagnosis of up to 55 days experienced prolonged infectiousness and were at greater risk of poor treatment outcomes (Asres *et al.,* 2018). The study found that these patients had more than twice the odds of unsuccessful treatment compared to those initiated on treatment within 30 days of symptom onset.

Co-Morbidities

Co-morbidities such as diabetes and HIV/TB co-infection present a significant challenge in TB management, with synergistic effects on disease progression, unpleasant side effects and treatment outcomes. Co-morbid individuals are at increased risk of mortality and treatment failure due to immunosuppression, high pill burden, TB immune reconstitution syndrome, drug interactions defaulting due to their inability to handle the side effects (Belachew *et al*., 2018).

Age

Most articles reported that, extremes of age (>5 and <60 years), was a predicator of poor outcome, compromised immune systems. Age as a factor contributing to treatment outcomes was consistent in the study by (Oshi *et al.,* and Chilyabanyma *et al*.,) where those patients who were 60 and above had poor outcomes as compared to those who age was lower.

Failure to Gain Weight

Failure to gain weight of more than 55kg during TB treatment was another indicator poor outcome. This underscored the poor nutritional status, treatment response, or disease progression mostly in rural patients (Pizzol *et al.,* 2018 & Sahile Z. *et al.,* 2021). Malnutrition can compromise micro nutrient absorption, immune function and impede treatment efficacy, leading to prolonged recovery and increased risk of complications.

Type of Treatment Centre

It was observed that patients receiving treatment from health centres had better outcomes than those from hospitals (Katana *et al.,* 2022). Several factors contributed to this disparity, including delays in diagnosis, patient follow-up, and the implementation of directly observed treatment (DOT) programs. Delays in Diagnosis could be due to various factors, including higher patient volumes, limited diagnostic capacity, and competing priorities. Additionally, reduced comprehensive Patient Follow-up is often due to the larger and more diverse patient population that hospitals have to serve while having inadequate stuffing (Asres *et al.,* 2018). Lastly the effective implementation of the DOT Program, where trained healthcare workers directly observe patients taking their medication, is a cornerstone of successful TB treatment. However, hospitals may face logistical challenges in implementing DOT due to staffing constraints, competing priorities, and resource limitations.

Poor Compliance and High Default Rates

Were observed to be among the factors contributing to poor outcomes. These factors contributed

to treatment failure, relapse, and drug resistance. Factors influencing adherence and compliance may include medication side effects, socio-economic factors, and lack of patient education and support (Asres *et al.,* 2018).

Gender

One of the factors that was also identified is gender and this was consistent with different authors, according to (Ngua J. *et al.*,) 33.5% in the study had a poor outcome, including 25% lost to follow up, 6.1% died and in (Adisa *et al.*,) 65.0% males had unsuccessful treatment. Generally, men have poor health seeking behaviors, in most cases they would not report to the facility until their health condition deteriorates, even when they do, adherence to medication is usually a challenge. Efforts need to be made to encourage men to seek health services early. The Zambian Ministry of Health introduced triaging of men when they visit health facilities because it was identified that one of the factors that led to men not visiting the facility was the long hours spent in the line before being attended to.

Limitations

This review has certain limitations, including geographical constraints that may limit the generalizability of the findings to all of sub-Saharan Africa due to the diverse healthcare systems, TB prevalence, and socio-economic conditions across different countries. Additionally, publication bias is a concern, as there may be an overrepresentation of studies with positive results, while studies with negative or inconclusive results are less likely to be published. Furthermore, the variability in data sources poses a limitation, as the included studies used different methodologies, definitions of treatment outcomes, and data collection processes, potentially impacting the comparability of results.

CONCLUSIONS

The systematic review of TB treatment outcomes for newly diagnosed patients in Sub-Saharan Africa has highlighted several significant challenges. Addressing these challenges will significantly improve the health outcomes of TB patients in the region. Factors such as patient delays, health facility delays, comorbidities, poor nutritional status, and gender disparities have all contributed to poor TB treatment outcomes in the region. Increasing awareness and education to reduce stigma and improve access to healthcare services will ensure timely diagnosis and treatment initiation, with a focus on reducing patient and health facility delays. There is need to Implement community-based interventions and adherence to WHO guidelines for intensified case finding to enhance the overall success of TB treatment programs in the region. To address poor compliance and high default rates, programs should be designed to focus on health promotion, support to patients and healthcare providers to improve adherence to medication and encouraging men to seek timely health services.

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