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Urgent Tsuro , Mojisola Clara Hosu , Ntandazo Dlatu , Lindiwe Modest Faye *

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Assessing Treatment Trajectories in Drug-Resistant TB Using Survival Analysis: Evidence from the Rural Eastern Cape

Urgent Tsuro [1], Mojisola Clara Hosu [1], Ntandazo Dlatu [2] and Lindiwe Modest Faye [1,*]

[1] WSU – TB Research Group, School of Pathology, Faculty of Medicine and Health Sciences, Walter Sisulu University, Private Bag X1, Mthatha 5100, South Africa

[2] Walter Sisulu Institute for Clinical Governance, Healthcare Administration, School of Public Health, Faculty of Medicine and Health Sciences, Walter Sisulu University, Mthatha 5099, South Africa

* Correspondence: author: lfaye@wsu.ac.za; Tel.: +27 (0) 47-502-2204

Abstract

Background: Drug-resistant tuberculosis (DR-TB) remains a critical public health challenge in South Africa, particularly in rural areas with high HIV prevalence. This study aimed to evaluate treatment outcomes and identify risk factors associated with unfavorable outcomes among DR-TB patients in the rural Eastern Cape using survival analysis. **Methods:** A retrospective cohort study was conducted using data from 323 patients diagnosed with DR-TB and treated between February 2018 and December 2021. Patient demographics, clinical characteristics, and treatment outcomes were extracted from medical records. Kaplan-Meier survival estimates were used to analyze time-to-event data, and Cox proportional hazards regression was used to identify predictors of treatment outcomes. Variables with $p < 0.1$ in univariate analysis were included in the multivariate model; statistical significance was set at $p < 0.05$. **Results:** The median treatment duration was 10 months (IQR: 9–11). The overall cure rate was 36.2% (n=117), treatment completion 26.0% (n=84), LTFU 9.0% (n=29), treatment failure 2.2% (n=7), death 9.3% (n=30), and transfer-out 9.3% (n=30); 8.1% (n=26) were still on treatment. HIV co-infection was present in 62% of patients and was associated with higher mortality (86% of deaths) and treatment failure (86%). In multivariate analysis, primary education (HR = 0.393, 95% CI: 0.23–0.68, p = 0.0017) and secondary education (HR = 0.504, 95% CI: 0.31–0.85, p = 0.0103) were protective. Pre-XDR (HR = 0.134, 95% CI: 0.03–0.81, p = 0.034) and XDR-TB (HR = 0.164, 95% CI: 0.03–0.94, p = 0.043) were unexpectedly associated with lower hazard, likely due to early mortality or transfer. HIV-negative status was linked with a higher hazard (HR = 1.735, 95% CI: 1.13–2.66, p = 0.010). **Conclusion:** Treatment success rates remain suboptimal among DR-TB patients in the rural Eastern Cape. HIV co-infection, prior treatment history, and low education levels were associated with unfavorable outcomes. Survival analysis highlighted critical timeframes for intervention and retention in care. Targeted support for younger patients, males, and HIV-positive individuals is essential to improve DR-TB treatment outcomes in high-burden rural settings.

Keywords: drug-resistant tuberculosis; treatment success; survival analysis; loss-to-follow-up; unfavorable outcomes

1. Introduction

Drug-resistant tuberculosis (DR-TB) remains a significant public health challenge globally, with South Africa among the countries bearing the highest burden [1,2]. The emergence and persistence of DR-TB, particularly in rural regions with limited healthcare infrastructure and high HIV co-infection rates, complicate efforts to control the disease and achieve favorable treatment outcomes [3]. In the Eastern Cape Province, one of the poorest and most underserved regions in South Africa,

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the burden of DR-TB is compounded by widespread poverty, malnutrition, and limited access to timely and effective care [4,5].

Treatment for DR-TB is complex, lengthy, and often associated with poor adherence, adverse drug reactions, and high rates of loss to follow-up (LTFU), failure leading to undesirable outcomes draining healthcare systems with accompanying detrimental effects on patients and their families [6,7]. These challenges are further exacerbated in populations with high HIV prevalence, where immunosuppression and drug interactions can compromise treatment efficacy [8]. Understanding the clinical and demographic factors influencing treatment trajectories is crucial to improving outcomes and guiding policy in resource-limited settings.

While national programs have made strides in scaling up diagnostic and treatment services, there remains a need for granular, context-specific data to inform targeted interventions. Survival analysis methods offer a powerful tool to assess time-dependent outcomes and identify predictors of treatment success or failure, particularly in complex diseases like DR-TB.

This study aims to evaluate treatment outcomes and identify factors associated with unfavorable outcomes among patients with laboratory-confirmed DR-TB in the rural Eastern Cape. By applying retrospective survival analysis, we provide insights into critical risk factors such as HIV status, previous treatment history, drug resistance patterns, and sociodemographic characteristics that can inform clinical decision-making and strengthen public health responses in high-burden rural settings.

2. Materials and Methods

2.1. Study Design

This study employed a retrospective cohort design to evaluate treatment outcomes and associated risk factors in patients diagnosed with DR-TB in rural Eastern Cape, South Africa. The study used survival analysis to assess the cohort's duration and the probability of treatment success or failure.

2.2. Study Setting and Population

The study was conducted in rural healthcare facilities in the Eastern Cape province of South Africa, which serves a population with a high burden of DR-TB. The study population comprised all patients diagnosed with DR-TB and initiated treatment between 2018-02-10 and 2020-12-07.

2.3. Data Collection

Data were retrospectively extracted from patient medical records and electronic TB registers maintained at the participating healthcare facilities. Information collected included demographic details, clinical characteristics, and treatment outcomes. The duration of treatment and time-to-event data were also recorded for survival analysis.

2.4. Inclusion and Exclusion Criteria

The study included patients who met the following criteria: a laboratory-confirmed diagnosis of DR-TB, initiation of DR-TB treatment within the defined study period, and availability of complete medical records and follow-up data. Patients with incomplete or missing key clinical data were excluded.

2.5. Study Variables

The primary outcome variable in this study was the treatment outcome, classified according to World Health Organization (WHO) definitions. Outcomes included cured, defined as negative culture results in the final month of treatment and on at least one previous occasion; treatment completed, where patients finished treatment without signs of failure but lacked bacteriological confirmation of cure; and lost to follow-up, referring to patients who missed treatment for two

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consecutive months. Treatment failure was applied to cases in which treatment was terminated due to lack of clinical improvement or the development of further drug resistance. At the same time, death denoted patients who died during the treatment period. Transferred out refers to individuals who have been moved to another facility with unknown outcomes and are still on treatment, indicating patients who were undergoing treatment at the time of data collection. Explanatory variables included demographic and clinical characteristics such as age, sex, BMI category, TB type (pulmonary or extrapulmonary), drug resistance type (monoresistance, polyresistance, multidrug-resistant (MDR), extensively-drug resistant (XDR), previous TB treatment history, and comorbid conditions (HIV, hypertension, diabetes, epilepsy, mental illness, and hearing loss).

2.6. Statistical Analysis

Descriptive statistics were used to summarize baseline characteristics and treatment outcomes. Categorical variables were presented as frequencies and percentages, while continuous variables were summarized using medians and interquartile ranges. Kaplan-Meier survival analysis was used to estimate time-to-treatment outcomes, and log-rank tests were used to compare survival curves across patient groups. Cox proportional hazards regression models were employed to identify factors associated with treatment outcomes, adjusting for potential confounders. Univariate and multivariate analyses were performed using a Cox hazards model. For a variable to qualify for the multivariate model, at least one category must have a p-value < 0.1, and for a variable to be significant in the multivariate model, it must have a p-value < 0.05. Hazard ratios (HR) with 95% confidence intervals (CIs) were reported to assess the strength of associations.

2.7. Limitations

As a retrospective study, missing data and potential information bias were inherent limitations. Additionally, the study was limited to patients who had complete medical records, which may introduce selection bias. Despite these limitations, the findings provide valuable insights into DR-TB treatment outcomes in a high-burden rural setting.

3. Results

Among the 323 patients with DR-TB, the majority were aged 30–39 years, male, and had low income and education levels. Treatment outcomes varied notably across demographics: younger adults (20–29 years) and males had higher rates of loss to follow-up. At the same time, individuals with no formal education or income were more likely to experience treatment failure or death. Most participants were minors or unemployed, with minors showing particularly high rates of loss to follow-up. Overall, the findings point to poorer outcomes among socioeconomically disadvantaged groups, highlighting the influence of age, gender, education, and income on DR-TB treatment success.

Table 1. Demographic characteristics of study participants.

Characteristic	**N**	**Overall** N = 323[1]	**Cured** N = 117[1]	**Rx Completed** N = 84[1]	**LTFU** N = 29[1]	**Rx Failed** N = 7[1]	**Died** N = 30[1]	**Transferred Out** N = 30[1]	**Still on RX** N = 26[1]
Age group	323								

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0-9		1 (0.3%)	0 (0%)	1 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
10-19		24 (7.4%)	5 (4.3%)	9 (11%)	0 (0%)	1 (14%)	0 (0%)	7 (23%)	2 (7.7%)
20-29		71 (22%)	26 (22%)	12 (14%)	13 (45%)	1 (14%)	5 (17%)	8 (27%)	6 (23%)
30-39		102 (32%)	39 (33%)	25 (30%)	9 (31%)	4 (57%)	12 (40%)	4 (13%)	9 (35%)
40-49		55 (17%)	19 (16%)	19 (23%)	4 (14%)	1 (14%)	2 (6.7%)	6 (20%)	4 (15%)
50-59		45 (14%)	15 (13%)	13 (15%)	2 (6.9%)	0 (0%)	8 (27%)	3 (10%)	4 (15%)
60-69		17 (5.3%)	9 (7.7%)	2 (2.4%)	1 (3.4%)	0 (0%)	2 (6.7%)	2 (6.7%)	1 (3.8%)
>69		8 (2.5%)	4 (3.4%)	3 (3.6%)	0 (0%)	0 (0%)	1 (3.3%)	0 (0%)	0 (0%)
Gender	323								
Male		180 (56%)	59 (50%)	46 (55%)	19 (66%)	3 (43%)	22 (73%)	16 (53%)	15 (58%)
Female		143 (44%)	58 (50%)	38 (45%)	10 (34%)	4 (57%)	8 (27%)	14 (47%)	11 (42%)
Education	323								
No education		64 (20%)	29 (25%)	6 (7.1%)	7 (24%)	1 (14%)	8 (27%)	7 (23%)	6 (23%)
Primary		76 (24%)	24 (21%)	29 (35%)	3 (10%)	4 (57%)	10 (33%)	4 (13%)	2 (7.7%)
Secondary		150 (46%)	50 (43%)	35 (42%)	17 (59%)	2 (29%)	11 (37%)	17 (57%)	18 (69%)
Tertiary		33 (10%)	14 (12%)	14 (17%)	2 (6.9%)	0 (0%)	1 (3.3%)	2 (6.7%)	0 (0%)
Income	323								
No income		267 (83%)	99 (85%)	66 (79%)	24 (83%)	7 (100%)	21 (70%)	26 (87%)	24 (92%)

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Self-employed		4 (1.2%)	1 (0.9%)	2 (2.4%)	0 (0%)	0 (0%)	1 (3.3%)	0 (0%)	0 (0%)
Casual		1 (0.3%)	1 (0.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Salary		29 (9.0%)	9 (7.7%)	11 (13%)	2 (6.9%)	0 (0%)	2 (6.7%)	4 (13%)	1 (3.8%)
UIF		2 (0.6%)	0 (0%)	2 (2.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
DG		20 (6.2%)	7 (6.0%)	3 (3.6%)	3 (10%)	0 (0%)	6 (20%)	0 (0%)	1 (3.8%)
Occupation	323								
Minors		248 (77%)	91 (78%)	56 (67%)	26 (90%)	6 (86%)	25 (83%)	22 (73%)	22 (85%)
Student		30 (9.3%)	10 (8.5%)	11 (13%)	1 (3.4%)	1 (14%)	0 (0%)	4 (13%)	3 (12%)
Unemployed		15 (4.6%)	6 (5.1%)	5 (6.0%)	0 (0%)	0 (0%)	2 (6.7%)	1 (3.3%)	1 (3.8%)
Grant		5 (1.5%)	2 (1.7%)	2 (2.4%)	0 (0%)	0 (0%)	1 (3.3%)	0 (0%)	0 (0%)
Govt Department.		12 (3.7%)	5 (4.3%)	4 (4.8%)	1 (3.4%)	0 (0%)	1 (3.3%)	1 (3.3%)	0 (0%)
Private Sector		13 (4.0%)	3 (2.6%)	6 (7.1%)	1 (3.4%)	0 (0%)	1 (3.3%)	2 (6.7%)	0 (0%)
Social history	323								
None		209 (65%)	76 (65%)	55 (65%)	17 (59%)	6 (86%)	20 (67%)	21 (70%)	14 (54%)
Smoking		27 (8.4%)	11 (9.4%)	6 (7.1%)	3 (10%)	0 (0%)	1 (3.3%)	3 (10%)	3 (12%)
Drinking		27 (8.4%)	10 (8.5%)	6 (7.1%)	3 (10%)	1 (14%)	2 (6.7%)	1 (3.3%)	4 (15%)

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Smoking & Drinking	52 (16%)	18 (15%)	14 (17%)	5 (17%)	0 (0%)	7 (23%)	4 (13%)	4 (15%)
Smoking & Drugs	3 (0.9%)	2 (1.7%)	1 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Smoking &Drinking & Drugs	5 (1.5%)	0 (0%)	2 (2.4%)	1 (3.4%)	0 (0%)	0 (0%)	1 (3.3%)	1 (3.8%)

[1]n (%), LTFU-loss to follow-up, Rx-treatment; UIF-unemployment insurance fund; DG-disability grant

Figure 2 presents a stratified analysis of treatment outcomes across age groups, categorized by gender and HIV status, with four panels representing HIV-positive males, HIV-positive females, HIV-negative males, and HIV-negative females. Each bar illustrates the number of individuals per age group, with color-coded segments denoting various treatment outcomes. Among HIV-positive individuals, the highest concentration of cases occurs in the 30–39 age group, particularly among males, with most patients achieving cure or treatment completion. However, smaller proportions experienced LTFU, treatment failure, or death. HIV-positive females show a similar pattern, with peaks in the 30–39 and 40–49 age groups. In contrast, HIV-negative individuals demonstrate a more even age distribution and fewer overall cases, though treatment success remains the most common outcome. Mortality and LTFU persist across groups but are less frequent. Across all subgroups, older adults (>60 years) account for fewer cases, while the 20–49 age group accounts for most of the TB burden. A minority of individuals are still on RX or were transferred out. These results underscore disparities in treatment burden by age and HIV status, with younger, HIV-positive adults disproportionately affected and facing a broader range of outcomes, suggesting a need for targeted interventions in these high-risk groups.

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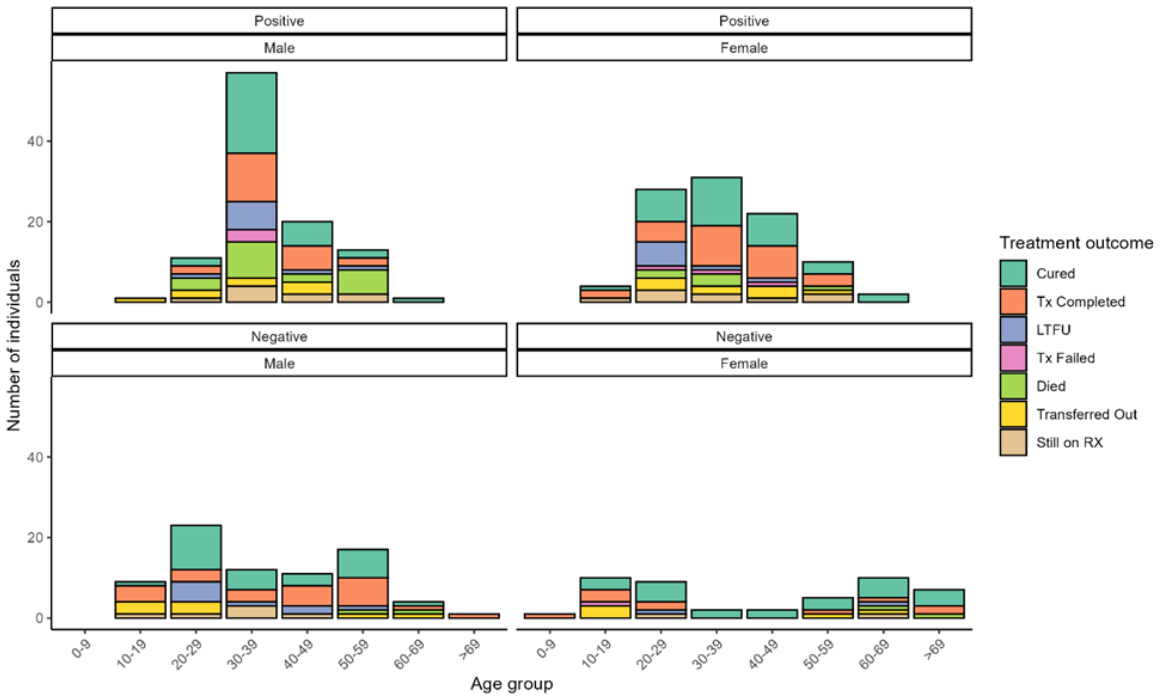

Figure 1. Stratified analysis of treatment outcomes.

Figure 3 presents the distribution of treatment duration and outcomes across patient subgroups stratified by sex, HIV status, DR type, and age group. The data reveal that patients with mono-DR-TB generally experienced shorter treatment durations and more favorable outcomes, including higher rates of cure and treatment completion, particularly among HIV-negative individuals. In contrast, poly-DR-TB was associated with longer treatment durations and poorer outcomes, especially in HIV-positive patients, who exhibited elevated rates of treatment failure and mortality. Age and sex also played significant roles: older patients (>60 years), particularly those who were HIV-positive, had shorter treatment durations but higher mortality and treatment failure rates. Younger patients (10–39 years), especially those who were HIV-negative, showed higher rates of cure and treatment completion. Female patients with mono-DR-TB demonstrated better outcomes, particularly in older age groups. In contrast, male patients with poly-DR-TB experienced longer treatment durations and higher rates of LTFU and mortality. Ongoing treatment and LTFU were most frequently observed in poly-DR-TB cases among younger individuals. In contrast, transferred-out cases were scattered across all subgroups but were more common in patients with extended treatment durations. Overall, these findings emphasize that treatment outcomes in DR-TB are strongly influenced by HIV status, resistance type, age, and sex. HIV-positive individuals with poly-DR-TB represent a particularly high-risk group, underscoring the need for tailored support strategies to enhance treatment adherence and reduce adverse outcomes.

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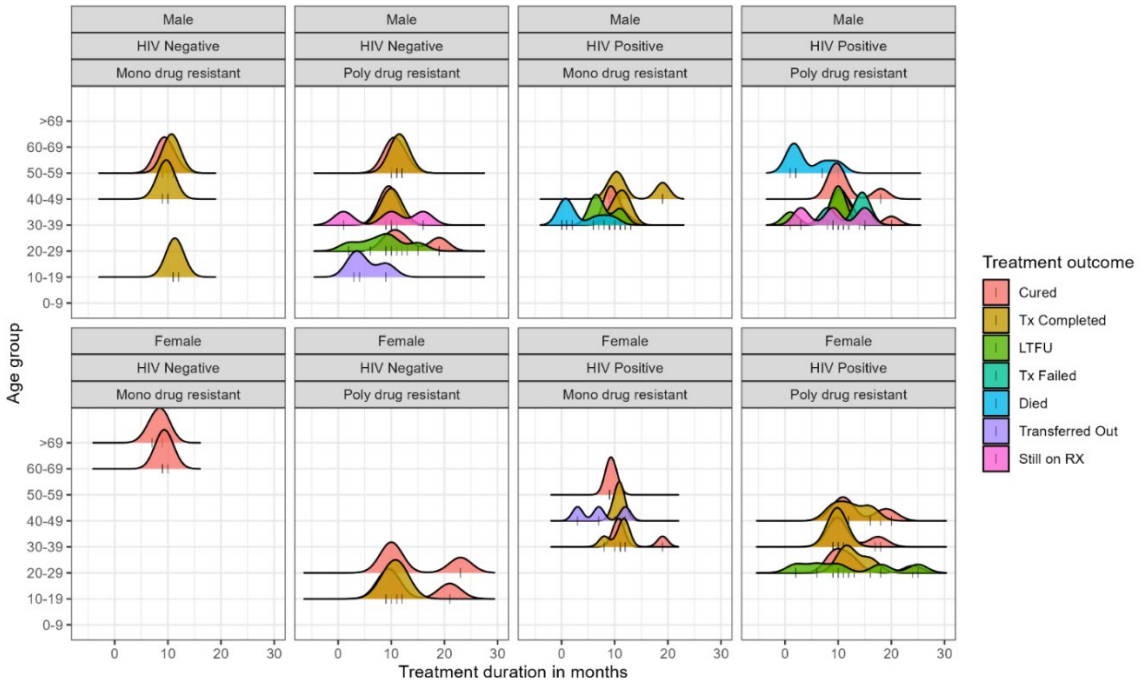

Figure 2. Treatment Duration and Outcomes.

Figure 4 illustrates how treatment duration and outcomes vary across patient subgroups stratified by HIV status, comorbidities, and age group. Overall, patients with at least one comorbidity tended to have shorter treatment durations, particularly in those over 40 years of age. Among HIV-negative patients with comorbidities, cure and treatment completion were common outcomes, while LTFU was rare. Interestingly, HIV-positive patients with comorbidities showed fewer treatment failures and deaths than their counterparts without comorbidities, although they still had lower cure rates. HIV-positive individuals without comorbidities experienced the most diverse and prolonged treatment courses, with higher rates of treatment failure, mortality, and ongoing treatment, particularly pronounced in the younger age group (10–39 years). Conversely, HIV-negative patients without comorbidities had the highest rates of cure and treatment completion, often completing treatment in shorter durations. Age-specific patterns further revealed that older patients (>50 years) with comorbidities had better outcomes and shorter treatment durations. In comparison, younger patients without comorbidities showed higher rates of LTFU and extended treatment periods. These findings underscore a complex interplay between HIV status, comorbidities, and age, with evidence suggesting that comorbidities may not necessarily predict worse outcomes—in fact, they may be associated with more structured treatment responses in older populations. Conversely, HIV-positive patients without comorbidities appear to face significant treatment challenges, highlighting the need for targeted interventions to support this high-risk group and improve their treatment adherence and outcomes.

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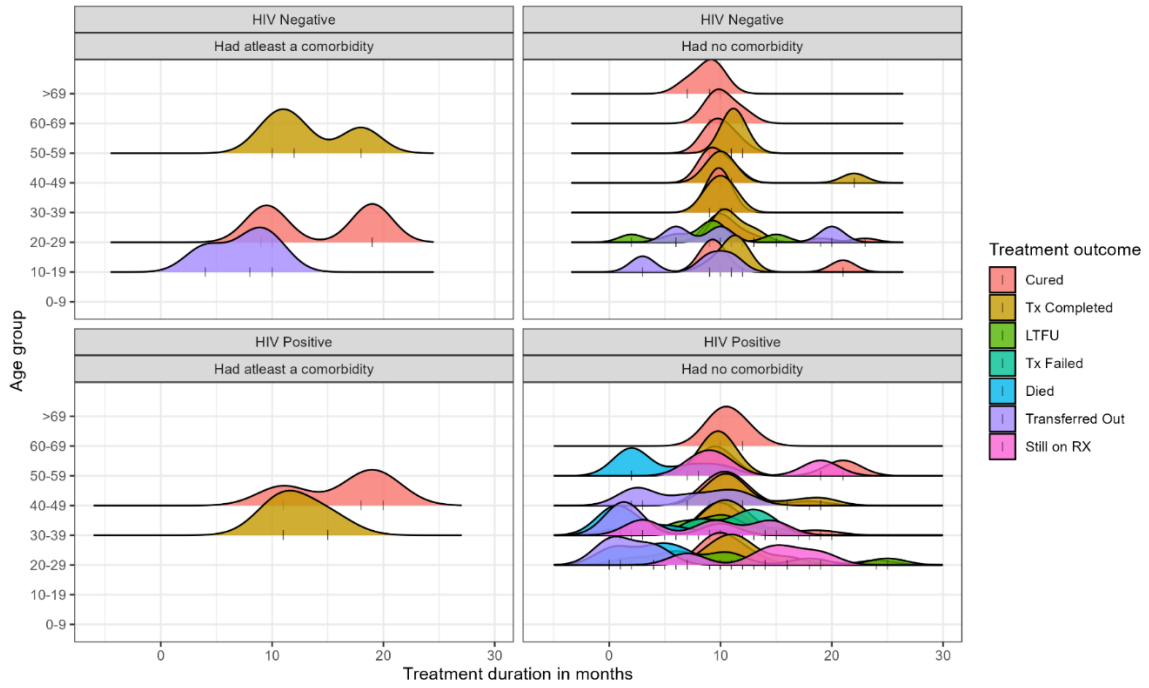

Figure 3. Impact of Comorbidities and HIV Status on Treatment Duration and Outcomes.

The cumulative incidence graph illustrates various treatment outcomes for patients with DR-TB over 25 months. The highest proportion of patients achieved a cure (red line), with a notable increase between 8 and 15 months, followed by those who completed treatment (blue dashed line). However, adverse outcomes were also observed. A significant number of patients were lost to follow-up (green dotted line), suggesting adherence challenges. Treatment failure (purple dashed-dotted line) remained relatively low, suggesting that most patients responded to therapy, though some did not achieve successful outcomes. Mortality (yellow dashed line) showed a gradual increase, with most deaths occurring within the first 10 months, highlighting the critical period for intervention. Additionally, some patients were transferred out (black solid line), which may have impacted the overall success rate of the treatment program. A portion of patients remained on treatment (gray line) by the end of follow-up, indicating ongoing management. These findings underscore the need for improved patient retention, early intervention strategies, and enhanced treatment monitoring to optimize DR-TB outcomes in rural settings.

The hazard ratios and p-values from both univariate and multivariate Cox proportional hazards models. In the univariate model, each variable is analyzed independently to assess its association with the hazard, while the multivariate model accounts for multiple variables simultaneously, adjusting for potential confounders. Comparing the two models reveals how the strength and significance of the associations change when other factors are adjusted for. In terms of education, both primary and secondary levels remain significantly protective across both models. Still, their hazard ratios decrease in the multivariate model (e.g., primary education HR drops from 0.4976 to 0.393), suggesting that other covariates partially explain the effect. In contrast, tertiary education remains non-significant across both models. Regarding income sources, no category shows a significant effect in either model, though casual workers have higher hazard ratios in both models, indicating increased risk but without statistical significance.

In the previous drug history category, PT2 (previous treatment 2) shows a highly significant protective effect in the univariate model (HR = 0.0511, p = 0.00319), but loses significance in the multivariate model. This suggests that other covariates may be driving the observed association. Similarly, in the patient category, the TAL (treatment after loss to follow-up) group has a significantly lower hazard in the univariate model (HR = 0.1665, p = 0.00248). Still, this difference loses significance

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after adjustment for other factors. Regarding resistance type, pre-XDR TB remains significantly protective in both models, though the hazard ratio decreases when adjusting for other variables (HR = 0.2278-0.134). A similar pattern is observed for XDR TB, where the protective effect is more pronounced in the multivariate model (HR = 0.164, p = 0.04264), indicating that additional factors strengthen its association with lower hazard. Lastly, HIV-negative status, which is non-significant in the univariate model, becomes significantly associated with increased hazard in the multivariate model (HR = 1.735, p = 0.01038). This suggests that when controlling for other covariates, being HIV-negative is linked to a higher risk, possibly due to differences in treatment protocols or comorbidities. Overall, these comparisons highlight how univariate models can detect significant associations that may weaken or disappear when confounders are adjusted for in a multivariate model. The multivariate approach provides a more accurate estimate of each variable's independent effect while controlling for confounding influences.

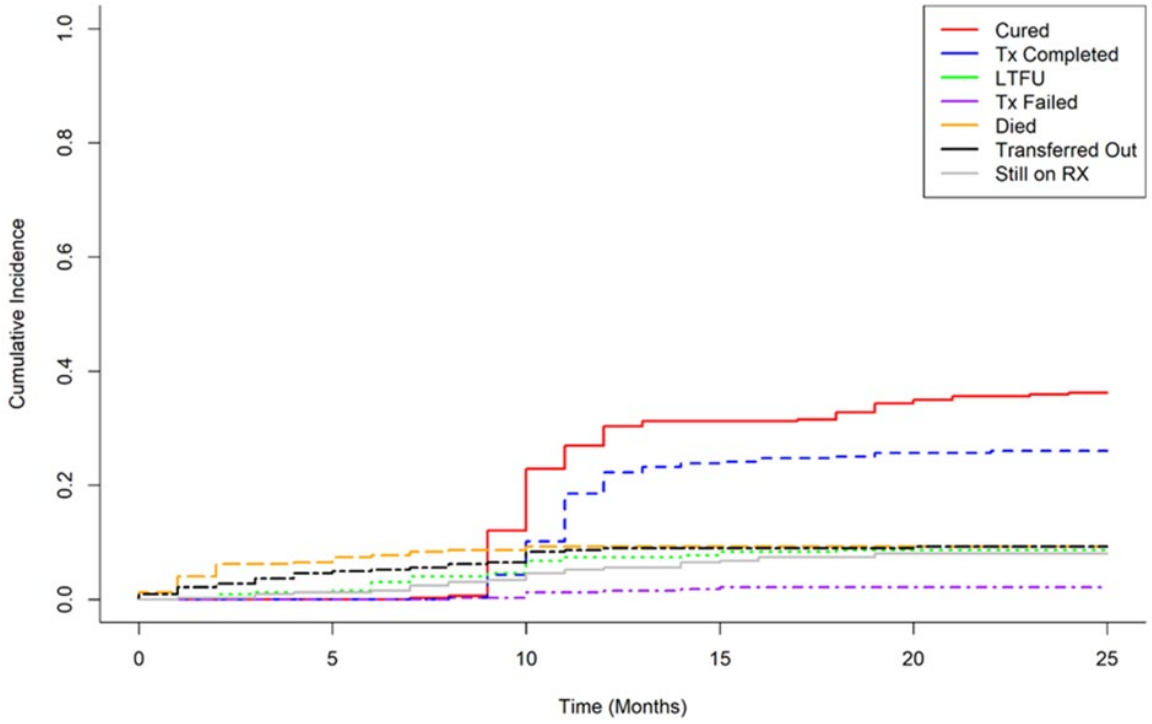

Figure 4. The cumulative incidence graph.

4. Discussion

This study provides important insights into the treatment outcomes and associated risk factors among patients with DR-TB in a rural, high-burden setting in the Eastern Cape, South Africa. Despite the availability of DR-TB treatment services, outcomes remain suboptimal, with cure and treatment completion rates at 36.2% and 26.0%, respectively, and considerable proportions of patients experiencing loss to follow-up (9.0%), death (9.3%), or remaining on treatment beyond the study period (8.1%). Several clinical and demographic variables were found to influence treatment trajectories. Notably, education level emerged as a significant protective factor, with both primary and secondary education associated with reduced hazard for delayed sputum conversion. Health literacy and the kind of health-seeking behaviour necessary to achieve favourable treatment outcomes are influenced by educational level [9]. Contradictory evidence abounds in the literature: some studies report an association between educational level and treatment outcomes [10,11], while others conclude otherwise [12]. The study conducted among Indonesian TB patients found that low education directly correlated with delayed conversion due to difficulties understanding treatment protocols and lower health literacy [13]. This underscores the importance of health literacy and patient understanding in adopting healthier behavior and enhancing successful TB treatment

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adherence. Conversely, individuals with no formal education experienced higher rates of treatment failure and mortality. Several other studies have reported an association between lower educational levels and unfavorable treatment outcomes [14–16], reinforcing the need for targeted support and communication strategies tailored to patients with limited literacy. In contrast, a South African study in KwaZulu-Natal found no association between educational attainment and clinical outcomes, including loss to follow-up, mortality, virologic response, or immunologic response [9].

HIV co-infection, which affected 62% of the cohort, was strongly associated with adverse outcomes, including higher rates of mortality and treatment failure. This aligns with previous local and global studies. TB-HIV co-infected patients have a higher risk of an unsuccessful treatment outcome. [16–22]. Malnutrition, diarrhoea, which prevents nutrient absorption, loss of appetite, immunosuppression, pharmacological interactions between anti-TB medications and antiretroviral agents, poor anti-TB medication concentrations, and anti-TB medication malabsorption could all contribute to the unfavorable treatment outcome [22–24]. A significant challenge to the control of the TB epidemic, which alters the progression of latent TB to active TB, is the HIV pandemic, which in turn affects its clinical outcomes. Due to the joint burden of HIV and TB, the WHO advocated the necessity of the provision of integrated HIV and TB services and drug toxicity control [16,22]. Surprisingly, HIV-negative status was associated with a significantly higher hazard of delayed sputum conversion in the multivariate analysis, potentially reflecting complex interactions with comorbidities, immune response, or differential treatment protocols. Consistent with this finding, HIV-negative status was a predictor of prolonged time to sputum culture conversion (aHR = 0.24; 95% CI: 0.1–0.4; $p < 0.001$) in Abebe et al [25]. This counterintuitive finding warrants further investigation into the quality of care and monitoring strategies for both HIV-positive and HIV-negative patients.

Previous TB treatment history, particularly among patients classified as PT2, was associated with unfavorable outcomes, including higher rates of treatment failure and ongoing treatment. This aligns with global evidence that repeated TB exposure and prior incomplete treatment increase the risk of resistance amplification and poorer prognosis [26,27]. It is important to provide extra support to previously treated patients to emphasise the importance of treatment adherence and completion [27]. However, Seloma et al. found no significant association between previous DR-TB episodes and treatment outcomes ($p > 0.05$) in a study conducted in Limpopo, South Africa [28]. Similarly, relapse cases and those treated after loss to follow-up showed a higher risk for poor outcomes. This is supported by the findings of Kim et al., where relapse rates were highest among patients with prior treatment failure (21.55%) or treatment cessation (25.08%), and another study conducted in Malaysia, which found 32.25% of relapse TB patients had unsuccessful outcomes [29,30]. Relapse and post-LTFU patients usually face worse outcomes due to drug resistance and comorbidities such as HIV [30,31]. This highlights the critical need for continuity of care and robust patient tracing systems. The type of drug resistance also significantly influenced outcomes. While MDR-TB and rifampicin-resistant TB (RR-TB) were the most common forms, patients with pre-XDR and XDR-TB exhibited unexpectedly lower hazards in the multivariate model, likely due to early mortality or referral, as reflected by shorter treatment durations. In contrast to our findings, global reports indicate that MDR/RR-TB treatment success rates are around 63%, with pre-XDR and XDR-TB generally having lower success rates due to increased resistance complexity. [32,33]. Furthermore, another study found higher mortality rates in XDR and pre-XDR-TB patients (45.8%) compared to MDR-TB (25.3%), reflecting the challenges of managing highly resistant strains [34]. This suggests that crude hazard ratios should be interpreted cautiously in the context of competing risks and that survival analysis should be complemented by more complex models in future research. In terms of nutritional status, underweight patients had worse outcomes, including higher mortality and LTFU rates, while those with normal BMI showed the best treatment success. Our result aligns with findings reported in the literature. In a study in Chennai, India, BMI <18.5 kg/m² was linked to higher odds of treatment failure or death [35]. This reinforces the role of nutritional support in DR-TB care and the need for integrated TB HIV nutrition programs, especially in rural, resource-constrained settings.

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5. Conclusions

LTFU was particularly common among younger adults, males, and those with low or no income, suggesting socioeconomic and behavioral barriers to sustained care. Social history factors such as smoking and alcohol use were also more common among patients who transferred out or failed treatment, indicating potential targets for behavioral intervention and psychosocial support.

The findings from this study emphasize the need for patient-centered, differentiated care strategies that address both clinical and socioeconomic risk factors. Interventions such as enhanced adherence counseling, nutritional supplementation, integration of TB and HIV services, and active follow-up systems for at-risk groups (e.g., previously treated, underweight, low-education patients) could significantly improve DR-TB outcomes in rural areas.

6. Limitations

Limitations of this study include its retrospective design, reliance on existing medical records, and potential underreporting of comorbidities or social risk factors. Additionally, the relatively small numbers in some subgroups (e.g., XDR-TB, PT2) may limit the generalizability of some findings. Nonetheless, this study contributes valuable evidence on the real-world challenges and determinants of DR-TB treatment in high-burden rural settings.

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Institutional Review Board Statement: The study was conducted in accordance with the principles of the Declaration of Helsinki and received ethical approval from the Research Ethics and Biosafety Committee of the Faculty of Medicine and Health Sciences, Walter Sisulu University (Ref. No. 026/2019; approved on 2 November 2022). Permission to conduct the study was also obtained from the Eastern Cape Department of Health (Ref. No. EC_201904_011; approved on 10 April 2019).

Informed Consent Statement: Not applicable.

Data Availability Statement: The raw genetic sequences and phenotypic datasets generated and analysed during this study are openly available in the published *Infectious Disease* or *Microorganisms* via MDPI at https://doi.org/10.3390/xxxxx.

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Abbreviations

The following abbreviations are used in this manuscript:

DR-TB	Drug-resistant TB
HIV	Human immunodeficiency virus
LFTU	Loss to follow up
WHO	World Health Organization

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