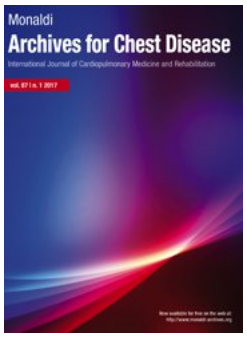

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Treatment outcomes and factors associated with unfavorable outcomes among drug-resistant tuberculosis patients treated with a bedaquiline-based oral regimen

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Abstract

The treatment success rate for drug-resistant tuberculosis (DR-TB) in Indonesia remains below the national target. Identifying factors associated with unfavorable treatment outcomes is essential to inform more targeted interventions. This retrospective study analyzed medical records of patients with DR-TB who received treatment at Surabaya Haji Hospital between 2020 and 2024. Demographic, clinical, behavioral, and treatment-related variables were evaluated in relation to unfavorable treatment outcomes, defined as a composite outcome of death, treatment failure, or loss to follow-up. Bivariate and binary logistic regression analyses were performed to estimate crude odds ratios and adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs). A total of 90 eligible patients were included in the analysis. Overall, 52 patients (57.8%) achieved a favorable treatment outcome (cure), whereas 38 (42.2%) experienced unfavorable treatment outcomes, including loss to follow-up (42.1%), death (34.2%), and treatment failure (23.7%). In the bivariable analysis, only a history of previous TB treatment was significantly associated with unfavorable treatment outcomes. After adjustment for diabetes mellitus and BCG vaccination history, previous TB treatment remained an independent predictor of unfavorable treatment outcomes (aOR = 11.47; 95% CI: 4.19–31.41; $p<0.001$). These findings indicate that patients with a history of previous TB treatment are at substantially greater risk of unfavorable treatment outcomes and underscore the need for closer monitoring and more comprehensive management strategies to improve treatment success.

Key words: drug-resistant tuberculosis, unfavorable treatment outcomes, multidrug-resistant tuberculosis, risk factors, Indonesia.

Introduction

Drug-resistant tuberculosis (DR-TB) remains a major challenge in global TB control. Indonesia ranks among the top three countries contributing to the global burden of multidrug-resistant/rifampicin-resistant TB (MDR/RR-TB), alongside India and China [1]. Indonesia represents a particularly important setting for evaluating DR-TB treatment outcomes. As one of the countries contributing the largest number of MDR/RR-TB cases globally, Indonesia continues to face substantial programmatic challenges despite recent advances in treatment. National treatment success rates remain considerably below the End TB targets, while loss to follow-up and mortality continue to impede program performance [2,3]. It indicates that the primary issue in DR-TB treatment is high unfavorable outcomes (treatment failure), due to high rates of loss to follow-up (LTFU). In addition, access to rapid and comprehensive drug susceptibility testing (DST) remains inequitable across healthcare facilities in Indonesia, contributing to delays in diagnosis and treatment initiation and further compromising the quality of DR-TB care [4].

The management of DR-TB has undergone a major paradigm shift over the past decade. Previous treatment strategies relied heavily on second-line injectable (SLID)-containing regimens, which were associated with prolonged treatment duration, poor tolerability, and frequent adverse events. In contrast, current WHO recommendations prioritize all-oral bedaquiline-based regimens and, more recently, shorter BPaLM regimens, which have demonstrated improved efficacy, better safety profiles, and higher treatment completion rates [2].

Although the implementation of all-oral bedaquiline-based regimens has improved treatment success [5], LTFU remains a persistent challenge and continues to undermine treatment outcomes, contributing to treatment failure, the emergence of additional drug resistance, and continued transmission of tuberculosis within the community [6,7]. Previous studies exhibit unfavorable outcomes, such as treatment failure, LTFU, and death among patients with DR-TB treated with bedaquiline-containing regimens [8-11]. Therefore, adequate treatment strategies and identification factors associated with unfavorable outcomes are imperative to improve treatment outcomes among DR-TB patients.

Variations in diagnostic capacity, referral systems, and healthcare resources may influence the timeliness of treatment initiation, the selection of appropriate treatment regimens, the quality of patient monitoring, and ultimately treatment outcomes. Consequently, evidence from other countries may not be directly generalizable to the Indonesian healthcare setting, underscoring

the need for context-specific real-world evidence to identify predictors of unfavorable treatment outcomes and inform national TB control strategies.

Consequently, the determinants of unfavorable treatment outcomes identified during the injectable era may no longer be directly applicable to patients receiving contemporary all-oral regimens. Changes in drug composition, toxicity profiles, treatment duration, and adherence patterns may have altered the relative importance of traditional risk factors. Therefore, updated evidence is needed to identify predictors of unfavorable outcomes among patients treated with current bedaquiline-based regimens in routine programmatic settings

Understanding TB treatment outcomes is essential, as the effectiveness of these treatment approaches is assessed using indicators such as cure, treatment completion, treatment failure, death, and loss to follow-up. Growing evidence indicates that treatment outcomes among patients with DR-TB are shaped by a complex interplay of clinical, psychosocial, and health system–related factors. Clinically, comorbidities and disease-related conditions, including HIV infection, diabetes mellitus, malnutrition, pulmonary cavitation, drug-related adverse events, and delayed sputum culture conversion, have been associated with an increased risk of unfavorable treatment outcomes. In addition, psychosocial factors such as stigma, depression, limited social support, and financial hardship may compromise treatment adherence and increase the likelihood of unfavorable outcomes among patients with DR-TB [12,13].

However, important knowledge gaps remain. Most available evidence regarding predictors of unfavorable outcomes has been derived from studies conducted before the widespread implementation of WHO-recommended all-oral bedaquiline-based regimens, or from cohorts in other countries with different epidemiological characteristics, healthcare systems, and treatment practices. In Indonesia, published studies have primarily evaluated the effectiveness of bedaquiline-containing regimens, while evidence identifying independent clinical predictors of treatment failure, death, and LTFU under routine programmatic conditions remains limited. Consequently, it is still unclear which patient characteristics are associated with unfavorable outcomes among Indonesian DR-TB patients receiving bedaquiline-based therapy in real-world clinical practice.

In the present study, we retrospectively evaluated treatment outcomes and identified clinical factors associated with unfavorable outcomes among DR-TB patients treated with bedaquiline-based all-oral regimens in Indonesia. This study addresses an important evidence gap by providing real-world data from the current treatment era, in which predictors identified during the injectable regimen era may no longer be directly applicable. Scientifically, the findings

will contribute updated evidence on determinants of treatment outcomes under contemporary DR-TB management. Programmatically, identifying patients at increased risk of treatment failure, death, or loss to follow-up may support risk stratification, strengthen patient monitoring, guide targeted interventions, and inform clinical decision-making and policy development within the Indonesian National Tuberculosis Program toward TB elimination.

Materials and Methods

Study design and setting

This is a retrospective cohort study conducted among DR-TB outpatients at Haji Hospital, Surabaya, East Java, covering the initial treatment period from January 2020 to December 2024. This study was approved by the Ethical Committee of Health Research of Haji Hospital (Approval Number: 445/014/KOM.ETIK/2025). The confidentiality of all participants' data was strictly maintained throughout the research process.

Study participants

The study included all DR-TB outpatients who received initial treatment between January 2020 and December 2024 and met the inclusion criteria. Patients with presumptive drug-resistant tuberculosis (DR-TB) were initially evaluated using the GeneXpert MTB/RIF assay to detect *Mycobacterium tuberculosis* and rifampicin resistance. Patients diagnosed with rifampicin-resistant tuberculosis (RR-TB) subsequently underwent additional drug susceptibility testing (DST), using phenotypic and/or molecular methods in accordance with the Indonesian National Tuberculosis Program guidelines, to assess resistance to other anti-tuberculosis drugs and to classify the type of DR-TB, such as multidrug-resistant tuberculosis (MDR-TB) or pre-extensively drug-resistant tuberculosis (pre-XDR-TB).

The inclusion criteria were patients aged ≥18 years with confirmed drug-resistant tuberculosis (DR-TB) who received an all-oral bedaquiline-based treatment regimen. Patients were excluded if they had incomplete medical records, lacked documented treatment outcomes, did not initiate treatment, were transferred to another healthcare facility, refused treatment, or had a change in their DR-TB treatment regimen during the study period. DR-TB treatment regimens were classified as shorter or longer regimens. The shorter regimen included the 6-month BPaL/BPaLM regimen and the standardized 9-month all-oral regimen, whereas the longer regimen comprised individualized all-oral regimens with a treatment duration of approximately 18 months.

Data collection procedures

We retrieved the data sources from medical records and the National TB Information System (SITB). The first step was selecting patients with DR-TB diagnosed with initial treatment from January 2020 to December 2024 who met the criteria. A conceptual framework was developed based on a review of the literature on factors that may influence treatment outcomes among patients with drug-resistant tuberculosis (DR-TB). The independent variables were categorized into three domains: demographic characteristics, clinical characteristics, and behavioral and treatment characteristics.

Demographic characteristics included sex, age, and employment status. Clinical characteristics comprised body mass index (BMI), diabetes mellitus (DM), type of DR-TB, history of previous TB treatment, and baseline culture status. In this study, DM was the only comorbidity included in the analysis because it is the most prevalent comorbidity among patients with DR-TB. Furthermore, DM has been widely recognized as a clinically important factor that may affect immune function, treatment response, and treatment outcomes in patients with DR-TB. Behavioral and treatment characteristics included smoking history, BCG vaccination history, and TB treatment regimen. These variables were evaluated as potential predictors of unfavorable treatment outcomes, defined as a composite outcome of death, treatment failure, or loss to follow-up. The conceptual framework of factors associated with unfavorable treatment outcomes among patients with DR-TB is shown in Figure 1.

The operational definition for treatment outcome in this study was as follows [14]:

1. Cured: Pulmonary TB patients who are bacteriologically confirmed at the beginning of treatment, or confirmation as rifampicin resistant with molecular testing, who completed their treatment in accordance with program policy, with evidence of bacteriological response, and no evidence of treatment failure.
2. Treatment failure: Patients whose treatment regimen requires permanent discontinuation or switches to a new regimen due to poor clinical response or treatment, adverse drug reactions, and evidence of additional drug resistance in the regimen.
3. Loss to follow-up: Patients who have interrupted their treatment for two consecutive months or more
4. Death: Patients who died due to any cause during DR-TB treatment

No formal sample size calculation was performed because this retrospective cohort study employed a total sampling approach. All patients with DR-TB who initiated treatment at Haji General Hospital, Surabaya, between January 2020 and December 2024 and met the predefined inclusion and exclusion criteria were consecutively included in the study.

Data analysis

Descriptive statistics were used to summarize participants' demographic, clinical, and behavioral/treatment characteristics. Categorical variables are presented as frequencies and percentages. Bivariate logistic regression was performed to assess the association between each independent variable and unfavorable treatment outcomes. The results are presented as crude odds ratios (cORs) with 95% confidence intervals (95% CIs). Variables with a P-value < 0.25 in the bivariable analysis were considered candidates for inclusion in the multivariable logistic regression model, following the recommendations of Hosmer and Lemeshow. Multivariable logistic regression was then performed to identify independent predictors of unfavorable treatment outcomes after adjusting for potential confounders. The results are reported as adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs). A two-sided P-value < 0.05 was considered statistically significant. Data were analyzed using IBM SPSS Statistics version 23.0.

Results

Of the 158 patients with drug-resistant tuberculosis (DR-TB) identified between 2020 and 2024, 68 were excluded for the following reasons: transfer to another healthcare facility (n = 21), incomplete medical records (n = 11), failure to initiate treatment (n = 10), undocumented treatment outcomes (n = 11), refusal of treatment (n = 7), and changes to the DR-TB treatment regimen (n = 8). Consequently, 90 patients met the eligibility criteria. They were included in the final analysis, comprising 88 patients with multidrug-resistant tuberculosis (MDR-TB) and 2 with pre-extensively drug-resistant tuberculosis (pre-XDR TB). All enrolled patients had pulmonary DR-TB, and none were co-infected with human immunodeficiency virus (HIV). The flow chart of the study is shown in Figure 2.

Characteristics of patients

A total of 90 patients with drug-resistant tuberculosis (DR-TB) were included in this study. In terms of demographic characteristics, most participants were male (56.6%), younger than 46

years (66.7%), and unemployed (55.5%). Clinically, the majority had a normal BMI; 18.5–24.9 kg/m² (61.2%), did not have diabetes mellitus (51.2%), were diagnosed with multidrug-resistant tuberculosis (MDR-TB) (97.7%), were newly diagnosed with DR-TB (60.0%), and had a positive baseline culture result (61.1%). Regarding behavioral and treatment characteristics, most patients had no history of smoking (96.6%), no history of Bacillus Calmette–Guérin (BCG) vaccination (80.0%), and were receiving the shorter treatment regimen (58.8%). The demographic, clinical, behavioral and treatment characteristics of DR-TB patients are shown in Table 1.

Treatment outcomes of DR-TB patients

Among the 90 patients included in the study, 52 (57.8%) achieved a favorable treatment outcome (cured), whereas 38 (42.2%) experienced unfavorable treatment outcomes. Among patients with unfavorable outcomes, 16 (42.1%) were lost to follow-up (LTFU), 13 (34.2%) died, and 9 (23.7%) experienced treatment failure.

Factors associated with treatment outcomes

Bivariate analysis showed that a history of previous TB treatment was the only factor significantly associated with unfavorable treatment outcomes. Patients who had previously received TB treatment had 2.50-fold higher odds of experiencing an unfavorable treatment outcome than those with newly diagnosed DR-TB (cOR = 2.50; 95% CI: 1.08–5.79; P-value = 0.031). In contrast, sex, age, employment status, body mass index (BMI), smoking history, diabetes mellitus, baseline culture status, BCG vaccination history, and treatment regimen were not significantly associated with unfavorable treatment outcomes (P-value $\geq$ 0.05). Although not statistically significant, patients with a history of BCG vaccination tended to have lower odds of an unfavorable treatment outcome than those without (cOR = 0.46; 95% CI: 0.15–1.47; P-value = 0.189). Bivariate analysis of factors associated with treatment outcomes is shown in Table 2.

Variables with a P-value < 0.25 in the bivariate analysis were considered candidates for inclusion in the multivariable logistic regression model. History of previous TB treatment (P-value = 0.031) and BCG vaccination history (P-value = 0.189) met the inclusion criterion. In addition, diabetes mellitus (p = 0.272) was retained in the multivariate model despite not meeting the predefined p-value criterion, given its well-established clinical importance and its consistent association with treatment outcomes in patients with drug-resistant tuberculosis

(DR-TB) reported in previous studies. Consequently, the final multivariate model comprised history of previous TB treatment, BCG vaccination history, and diabetes mellitus.

In the multivariate analysis, after adjustment for diabetes mellitus and BCG vaccination history, a history of previous TB treatment remained an independent predictor of unfavorable treatment outcomes. Patients who had previously received TB treatment had 11.47-fold higher odds of experiencing an unfavorable treatment outcome than those with newly diagnosed DR-TB (aOR = 11.47; 95% CI: 4.19–31.41; P-value < 0.001). In contrast, neither BCG vaccination history (aOR = 0.63; 95% CI: 0.18–2.23; P-value = 0.475) nor diabetes mellitus (aOR = 1.18; 95% CI: 0.43–3.21; P-value = 0.744) was independently associated with unfavorable treatment outcomes. Factors associated with unfavorable outcomes among DR-TB patients from multivariate analysis are shown in Table 3.

Discussion

To the best of our knowledge, this is the first study in Indonesia evaluating treatment outcomes and analyzing factors associated with unfavorable outcomes among DR-TB patients treated with an all-oral regimen containing bedaquiline. In our study, the prevalence of TB was higher in males than in females. It may be explained by the fact that estrogen in females enhances cell-mediated immunity, which is crucial in combating *Mycobacterium tuberculosis*. Conversely, testosterone in males tends to be immunosuppressive, reducing the activity of macrophages and T lymphocytes [15]. Previous studies demonstrated that males were more susceptible to TB infection compared to women. In addition, being male was associated with MDR-TB [16,17].

More than half of the patients in our study were aged < 46 years old. A previous study suggests that the majority of TB cases occur between 15 and 50 years [18]. This finding may be explained by the fact that individuals in this age group are generally more socially active, leading to increased contact with infectious TB cases and a greater likelihood of exposure to *Mycobacterium tuberculosis* [19]. About one-third of patients had a BMI < 18.5 kg/m^2, and it was classified as underweight. The high prevalence of underweight among patients with MDR-TB is likely due to chronic inflammation caused by tuberculosis, which increases energy expenditure, suppresses appetite, and promotes muscle protein catabolism. These effects are exacerbated by prolonged illness, treatment-related adverse events, and inadequate nutritional intake [20]. Nearly all of the patients in this study were MDR-TB, characterized by resistance to rifampicin and isoniazid. We found that two patients were pre-XDR-TB, characterized by

resistance to levofloxacin. These patients had a history of treatment with first-line ATDs and discontinued their treatment. Patients with a history of TB treatment have a high risk of pre-XDR-TB [21].

Favorable outcomes (cured) in our study were 57.8%. Meanwhile, unfavorable outcomes, including LTFU, death, and treatment failure, were 17.8%, 14.4%, and 10.0%, respectively. Bedaquiline demonstrates strong antimycobacterial effectiveness by selectively inhibiting the mycobacterial ATP synthase, thereby disrupting ATP production and depleting cellular energy, which ultimately impairs bacterial survival and promotes mycobacterial killing [22]. The cure rate observed in this study was 57.8%, lower than the treatment success rates reported in several studies of patients with DR-TB receiving bedaquiline-based regimens, which ranged from 73% to 78%. A study conducted in Egypt reported a treatment success rate of 73.7% [23], while a multicenter cohort study in China reported treatment success rates at 92.9% [24]. The lower cure rate observed in our study is likely attributable to the relatively high proportion of unfavorable treatment outcomes, particularly LTFU, which was the most frequent adverse outcome and substantially reduced the overall treatment success rate.

The LTFU rate in our study was lower compared to the regimen using SLIDs for the management of DR-TB patients. It was supported by Soeroto *et al*., who suggested that the LTFU rate among DR-TB patients using SLIDs in West Java Province was 22.3% [25]. Ototoxicity and severe adverse effects from SLIDs are the primary issues contributing to LTFU. The percentage of LFTU cases in our study was similar to the study by Setyawan *et al*., who demonstrated that LTFU among Indonesian DR-TB patients undergoing treatment with bedaquiline-containing regimens was 19.0%.[8] It indicates that regimens containing bedaquiline effectively reduce the number of LTFU cases. The mortality rate in our study was lower than the findings by Wakjira *et al*., who indicated a mortality rate of 30% among MDR-TB patients. It was more likely that more than 60% of patients had a BMI < 18.5 kg/m^2, and more than 60% were HIV-positive [26].

In this study, most demographic, clinical, and behavioral characteristics were not significantly associated with unfavorable treatment outcomes. These findings are consistent with previous studies demonstrating that baseline patient characteristics, such as age, sex, BMI, and diabetes mellitus, are not consistently identified as independent predictors of treatment outcomes after adjustment for other clinical and programmatic factors. Instead, factors related to disease severity, treatment adherence, and the quality of healthcare delivery appear to have a greater influence on treatment outcomes among patients with DR-TB [27,28]. Differences in study

populations, sample size, access to healthcare services, and the implementation of bedaquiline-based regimens may also account for the variability in findings across studies.

In the multivariate analysis, a history of previous TB treatment was the only independent predictor of unfavorable treatment outcomes. Patients with a history of previous TB treatment had 11.47-fold higher odds of experiencing unfavorable treatment outcomes than those with newly diagnosed DR-TB (aOR = 11.47; 95% CI: 4.19–31.41; P-value < 0.001). These findings suggest that a history of TB treatment is a more significant predictor of unfavorable treatment outcomes than the demographic and clinical characteristics evaluated in this study.

Our findings are consistent with previous studies demonstrating that patients with a history of previous TB treatment are at a substantially higher risk of unfavorable treatment outcomes, including treatment failure, death, and loss to follow-up [27,29]. Previous TB treatment may reflect prolonged exposure to anti-tuberculosis drugs, more complex patterns of drug resistance, more extensive pulmonary damage, and a history of poor treatment adherence. Collectively, these factors can compromise treatment effectiveness and increase the likelihood of unfavorable outcomes. Furthermore, patients with prior TB treatment may be more susceptible to treatment fatigue, cumulative drug-related adverse events, and psychosocial challenges, all of which may negatively affect adherence to prolonged DR-TB therapy [30].

Our previous study indicated that a history of previous TB treatment was significantly associated with depressive symptoms among patients with DR-TB [31]. Depression has been shown to adversely affect treatment adherence and increase the risk of loss to follow-up and other unfavorable treatment outcomes. A systematic review and meta-analysis by Ruiz-Grosso et al. demonstrated that depressive symptoms were strongly associated with poor tuberculosis treatment outcomes, including a markedly increased risk of loss to follow-up (OR = 8.70; 95% CI: 6.50–11.64) and death (OR = 2.85; 95% CI: 1.52–5.36) [32]. Therefore, depression may represent an important pathway through which a history of previous TB treatment contributes to unfavorable treatment outcomes. Although depression was not evaluated in the present study because of the retrospective design and the absence of routinely collected mental health data, it may represent an important mechanism underlying the observed association between previous TB treatment and unfavorable treatment outcomes. Further prospective studies are needed to clarify this relationship.

Among patients with DR-TB, the relationship between a history of previous TB treatment and psychosocial distress is particularly important because the prolonged duration of therapy, high pill burden, and frequent drug-related adverse events increase the risk of treatment fatigue.

These factors may contribute to the development of depressive symptoms, which have been consistently associated with poor treatment adherence and loss to follow-up [33]. These findings are consistent with the World Health Organization (WHO) recommendations, which emphasize that patients with a history of previous TB treatment require closer clinical monitoring, enhanced adherence support, and individualized patient-centered management to optimize treatment outcomes [2].

In contrast, a history of BCG vaccination was not independently associated with unfavorable treatment outcomes after adjustment for potential confounders. This finding is biologically plausible, as the primary protective effect of the BCG vaccine is against severe forms of tuberculosis in childhood, such as miliary TB and tuberculous meningitis. Its protective efficacy against adult pulmonary TB is variable, and there is limited evidence to suggest that prior BCG vaccination influences treatment outcomes once active DR-TB has developed [34].

Similarly, diabetes mellitus was not independently associated with unfavorable treatment outcomes in the present study. Although diabetes is a well-established risk factor for impaired immune function, delayed sputum culture conversion, and poor TB treatment outcomes, its effect may be attenuated after adjustment for other clinical and treatment-related factors [35]. The absence of a significant association in this study may be attributable to the relatively small sample size, the lack of information on glycemic control (e.g., HbA1c levels), and the inability to distinguish between well-controlled and poorly controlled diabetes. In addition, patients with diabetes who received appropriate management during TB treatment may have achieved outcomes comparable to those without diabetes. Nevertheless, diabetes remains an important comorbidity in clinical practice and should continue to be routinely screened for and optimally managed, given its potential impact on disease progression, treatment response, and long-term prognosis.

Strengths and limitations

This study has several strengths. First, it comprehensively evaluated demographic, clinical, behavioral, and treatment-related factors that may influence unfavorable treatment outcomes among patients with drug-resistant tuberculosis (DR-TB). Second, all patients received all-oral bedaquiline-based regimens, allowing the findings to reflect treatment outcomes under the current WHO-recommended standard of care for DR-TB. Finally, this study provides real-world evidence from Indonesia, one of the countries with the highest DR-TB burdens globally,

where data on predictors of treatment outcomes among patients receiving bedaquiline-based regimens remain limited.

This study has several limitations that should be acknowledged. First, its retrospective design relied on the completeness and accuracy of routinely collected medical records, preventing the assessment of several potentially important variables, including treatment adherence, depression and other mental health conditions, social support, socioeconomic status, alcohol use, and glycemic control (e.g., HbA1c levels). Second, the study was conducted at a single referral hospital with a relatively small sample size, which may limit the generalizability of the findings to the broader DR-TB population. Finally, the use of secondary retrospective data precludes causal relationships between the identified predictors and treatment outcomes. Therefore, larger prospective multicenter studies incorporating comprehensive clinical, psychosocial, and adherence-related assessments are warranted to validate these findings and provide a more complete understanding of the determinants of unfavorable treatment outcomes among patients with DR-TB.

Based on the findings of this study, patients with DR-TB who have a history of previous TB treatment should be identified as a high-risk group at the initiation of therapy and receive closer clinical monitoring, continuous adherence support, and patient-centered care in accordance with WHO recommendations. In addition, routine screening for mental health conditions, particularly depression, together with the provision of psychosocial support, should be considered, as these factors may substantially influence treatment adherence and outcomes, although they were not evaluated in the present study. Furthermore, large-scale prospective multicenter studies are warranted to investigate the mediating roles of psychosocial factors, treatment adherence, glycemic control, and other programmatic factors in the relationship between previous TB treatment and unfavorable treatment outcomes. Such evidence would provide a stronger foundation for developing more effective, targeted interventions to improve DR-TB treatment outcomes in Indonesia.

Conclusions

In this study, more than two-fifths of patients with drug-resistant tuberculosis (DR-TB) experienced unfavorable treatment outcomes, underscoring the ongoing challenges in DR-TB management. Although most demographic, clinical, behavioral, and treatment-related characteristics were not significantly associated with treatment outcomes, a history of previous TB treatment emerged as the only independent predictor of unfavorable outcomes after

adjustment for diabetes mellitus and BCG vaccination history. These findings highlight the importance of early identification of patients with a history of TB treatment and the implementation of targeted, patient-centered interventions to improve treatment adherence and optimize treatment outcomes.

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Table 1. Characteristics of DR-patients.

Variables	n = 90
Demographic characteristics	
Sex	
Male	51 (56.6)
Female	39 (43.4)
Age (years)	
>46	30 (33.3)
<46	60 (66.7)
Occupational status	
Unemployed	50 (55.5)
Employed	40 (44.5)
Clinical characteristics	
BMI (kg/m²)	
<18.5	35 (38.8)
18.5–24.9	55 (61.2)
Diabetes mellitus	
Yes	44 (48.8)
No	46 (51.2)
Type of DR-TB	
pre-XDR TB	2 (2.3)
MDR-TB	88 (97.7)
History of TB treatment	
Previously treated	36 (40.0)
New DR-TB	54 (60.0)
Baseline culture status	
Positive	55 (61.1)
Negative	35 (38.9)
Behavioral and treatment characteristics	
History of smoking	
Smoking	3 (3.4)
Non-smoking	87 (96.6)
History of BCG vaccination	
No	72 (80.0)
Yes	18 (20.0)
TB treatment regimen	
Shorter	53 (58.8)
Longer	37 (41.2)

Data are presented as n (%). BMI, body mass index; BCG, *Bacillus Calmette–Guérin*; DR-TB, drug-resistant tuberculosis; MDR-TB, multidrug-resistant tuberculosis; pre-XDR TB, pre-extensively drug-resistant tuberculosis.

Table 2. Bivariate analysis of factors associated with unfavorable outcomes.

Variables	Favorable n (%)	Unfavorable n (%)	cOR (95% CI)	p
Sex				
Male (Ref)	30 (57.7)	21 (55.2)	1.00	
Female	22 (42.3)	17 (44.8)	1.10 (0.48–2.54)	0.819
Age (years)				
>46 (Ref)	18 (34.6)	12 (31.5)	1.00	
<46	34 (65.4)	26 (68.5)	1.15 (0.47–2.79)	0.761
Occupational status				
Unemployed (Ref)	27 (52.0)	23 (60.6)	1.00	
Employed	25 (48.0)	15 (39.4)	0.70 (0.30–1.62)	0.404
BMI (kg/m²)				
<18.5 (Ref)	21 (40.3)	14 (36.8)	1.00	
18.5–24.9	31 (59.7)	24 (63.2)	1.16 (0.49–2.72)	0.741
History of smoking				
Smoking (Ref)	2 (3.9)	1 (2.7)	1.00	
Non-smoking	50 (96.1)	37 (97.3)	1.48 (0.13–17.16)	1.000
Diabetes mellitus				
No (Ref)	24 (46.2)	22 (57.9)	1.00	
Yes	28 (53.8)	16 (42.1)	0.62 (0.27–1.45)	0.272
Type of DR-TB				
pre-XDR TB (Ref)	2 (3.9)	0 (0.0)	1.00	
MDR-TB	50 (96.1)	38 (100.0)	NA	NA
History of TB treatment				
New DR-TB (Ref)	36 (69.3)	18 (47.3)	1.00	
Previously treated	16 (30.7)	20 (52.7)	2.50 (1.08–5.79)	0.031*
Baseline culture status				
Positive (Ref)	33 (63.4)	22 (57.8)	1.00	
Negative	19 (36.6)	16 (42.2)	1.26 (0.54–2.94)	0.593
History of BCG vaccination				
No (Ref)	39 (75.0)	33 (86.9)	1.00	
Yes	13 (25.0)	5 (13.1)	0.46 (0.15–1.47)	0.189
TB treatment regimen				
Shorter (Ref)	30 (57.6)	23 (60.5)	1.00	
Longer	22 (42.4)	15 (39.5)	0.89 (0.38–2.08)	0.793

*significant: p<0.05

Table 3. Multivariate analysis of factors associated with unfavorable outcomes.

Variables	aOR (95% CI)	p
History of TB treatment		
New DR-TB (Ref)	1.00	
Previously treated	11.47 (4.19–31.41)	<0.001*
History of BCG vaccination		
No (Ref)	1.00	
Yes	0.63 (0.18–2.23)	0.475
Diabetes mellitus		
No (Ref)	1.00	
Yes	1.18 (0.43–3.21)	0.744

*significant: p<0.05

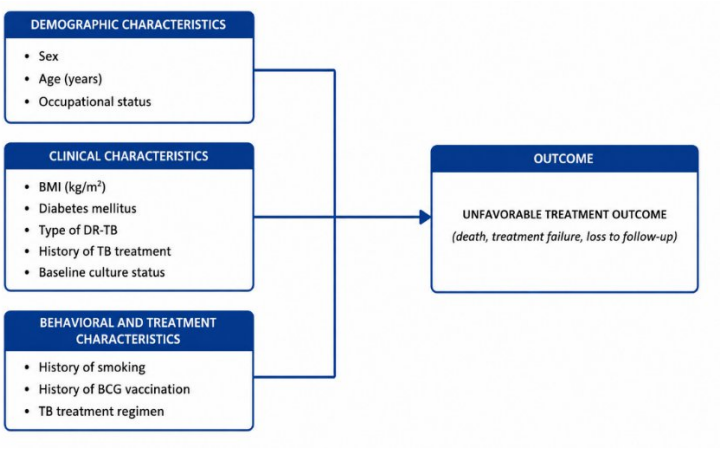

Figure 1. Conceptual framework of factors associated with unfavorable treatment outcomes.

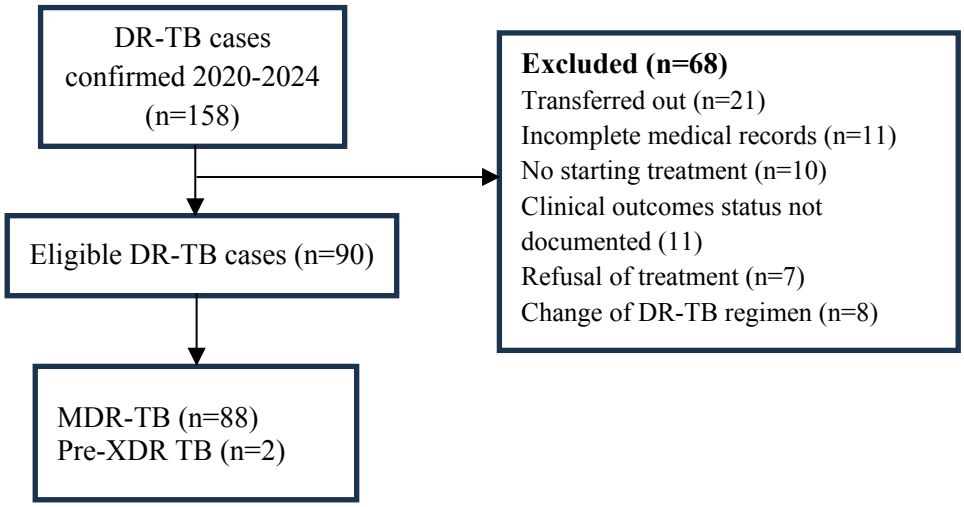

Figure 2. Flow diagram of the included DR-TB patients.