

A Decade of Unfavorable Outcomes in Pulmonary Tuberculosis: Proportion and Factors Associated in Kelantan, Malaysia

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ABSTRACT

Objective: Unfavorable pulmonary tuberculosis (PTB) treatment outcomes remain a critical indicator of program performance because they are linked to preventable mortality, ongoing transmission, and potential amplification of drug resistance. This study aimed to determine the proportion of unfavorable treatment outcomes and identify factors associated with these outcomes among PTB patients in Kelantan, Malaysia.

Materials and Methods: A retrospective registry-based cohort study was conducted using data from the National Tuberculosis Registry in Kelantan covering the period from 2013 to 2022. A simple random sample of 1260 eligible PTB patients was selected. Unfavorable outcomes were defined as treatment failure, death, or loss to follow-up. Candidate predictors included sociodemographic characteristics, comorbidity indicators, clinical characteristics, and the type of directly observed treatment, short-course (DOTS) supervision. Univariable and multivariable logistic regression analyses were performed to identify factors associated with unfavorable outcomes.

Results: The proportion of unfavorable outcomes was 20.8% (262/1,260). In multivariable analysis, HIV-positive status was strongly associated with unfavorable outcomes (adjusted odds ratio [AOR], 5.69; 95% confidence interval [CI], 3.78–8.57; $p < 0.001$). Multidrug-resistant tuberculosis (MDR-TB) was also associated with increased odds of unfavorable outcomes (AOR, 5.69; 95% CI, 2.40–13.52; $p < 0.001$). Compared with DOTS supervised by healthcare workers, family-supervised DOTS was associated with higher odds of unfavorable outcomes (AOR 5.02; 95% CI, 1.73–14.59; $p = 0.003$).

Conclusion: Approximately one in five PTB patients experienced an unfavorable treatment outcome in Kelantan. Unfavorable outcomes were concentrated among patients with HIV infection and MDR-TB and were more frequent among those receiving family-supervised DOTS. These findings support risk-stratified care, strengthened TB-HIV integration, intensified MDR-TB case management, and improved support and accountability for family-based DOTS supervision.

Keywords: Pulmonary tuberculosis, unfavorable outcomes, associated factors, DOTS, Kelantan

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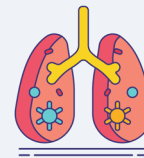
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Unfavorable Pulmonary Tuberculosis Outcomes: A 10-Year Malaysian Study



Background



- Pulmonary tuberculosis (PTB) is a leading infectious disease in Malaysia.
- Unfavorable outcomes include treatment failure, death, and loss to follow-up (LTFU).
- These outcomes are key indicators of TB program performance.

Methods



- **Design:** Retrospective cohort (2013–2022)
- **Study period:** 2013–2022 (10 years).
- **Sample size:** 1260 patients with pulmonary tuberculosis.
- **Statistical analysis:** Multivariable logistic regression.

Key Finding



20.8%
Unfavorable Outcomes

Approximately 1 in 5 patients (262 of 1260 PTB patients) experienced an unfavorable treatment outcome.

Risk Factors



- **HIV positive:** Adjusted odds ratio (AOR), 5.69 (AOR, 5.69 [95% CI, 2.40–13.52]).
- **Multidrug-resistant tuberculosis (MDR-TB):** AOR, 4.19 (95% CI, 1.80–9.77).
- **Family-supervised DOTS:** Higher odds of unfavorable outcomes compared with healthcare worker-supervised DOTS.

Conclusion

Approximately 20% of PTB patients in Kelantan experienced unfavorable outcomes over 10 years, with HIV co-infection and MDR-TB as key predictors. Results support risk-stratified care, stronger TB-HIV integration, and improved DOTS supervision.

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Graphical Abstract

INTRODUCTION

Tuberculosis (TB) remains a major global infectious disease and an important cause of preventable mortality. According to the World Health Organization (WHO) Global Tuberculosis Report 2025, an estimated 10.7 million people fell ill with TB in 2024, with approximately 1.23 million deaths globally, including 150,000 deaths among people living with HIV (1). Despite decades of global control efforts, TB continues to disproportionately affect low- and middle-income countries, where structural inequalities, limited healthcare access, and comorbid conditions sustain transmission and compromise treatment outcomes. The global TB response is guided by the WHO End TB Strategy (2015–2035), which targets a 90% reduction in TB deaths and an 80% reduction in TB incidence by 2030 compared with 2015 levels (2). Achieving these targets

requires not only early case detection but also sustained treatment success rates exceeding 90% (3). However, treatment outcomes remain suboptimal in many settings, particularly among patients with HIV coinfection, multidrug-resistant TB (MDR-TB), and socioeconomic vulnerabilities (4).

Malaysia is classified as an intermediate-TB-burden country, with an estimated incidence of approximately 92–97 cases per 100,000 population in recent years and a treatment success rate of approximately 80–85%, slightly below the WHO target (5–7). Although Malaysia has a relatively strong healthcare infrastructure compared with many neighboring countries, TB control remains challenged by urban-rural disparities, migrant populations, and the growing prevalence of non-communicable comorbidities such as diabetes (8).

Unfavorable outcomes, comprising treatment failure, death, and loss to follow-up, are critical indicators of TB program performance because they prolong infectiousness, increase transmission, and drive the emergence of drug resistance, particularly through acquired resistance in patients lost to follow-up (9,10). Meta-analyses have identified HIV coinfection, advanced disease severity, drug resistance, older age, and socioeconomic disadvantage as predictors of poor outcomes (4,11). In particular, TB-HIV coinfection is associated with a three- to six-fold increased risk of mortality and treatment failure (12), while global MDR-TB treatment success rates remain around 60% (13).

Kelantan's TB burden is shaped by its predominantly rural population, socioeconomic disparities, and barriers to healthcare access that may delay diagnosis and treatment initiation (7). Although national registry-based studies have described determinants of unfavorable outcomes in Malaysia, state-level analyses remain limited, particularly for the East Coast region (14–16). Therefore, this study aimed to determine the proportion of unfavorable outcomes and identify factors associated with these outcomes among PTB patients in Kelantan between 2013 and 2022. We hypothesized that HIV coinfection, MDR-TB, and socioeconomic disadvantage would significantly increase the risk of unfavorable outcomes, with impacts expected to exceed national averages given the region's rural and economic conditions (17).

MATERIALS AND METHODS

This retrospective, registry-based cohort study was conducted using routinely collected data from the National Tuberculosis Registry (NTBR) in Kelantan, Malaysia, covering the period from 1 January 2013 to 31 December 2022.

The source population comprised all notified and registered pulmonary tuberculosis (PTB) cases in Kelantan during the study period. Eligible records were identified after excluding cases with a revised diagnosis, cases recorded as “not evaluated” (i.e., without an assignable treatment outcome), and records with more than 20% missing data across the predefined analytic variables, including

HIGHLIGHTS

- One in five PTB patients in Kelantan experienced an unfavorable treatment outcome.
- HIV coinfection and MDR-TB were independently associated with markedly higher odds of unfavorable treatment outcomes.
- Family-supervised DOTS was associated with higher odds of unfavorable outcomes than healthcare worker-supervised DOTS.
- The findings support risk-stratified TB care, stronger TB-HIV integration, and improved adherence supervision.
- Registry-based evidence from Kelantan provides valuable insight into programmatic TB control in routine practice.

sociodemographic characteristics, comorbidity indicators, clinical characteristics, directly observed treatment, short-course (DOTS) supervision, and outcome variables. Missingness was assessed at the record level by calculating the proportion of missing entries across all study variables for each patient. Records exceeding this threshold were excluded to reduce bias arising from incomplete registry records and to preserve interpretability of the regression estimates.

From the eligible registry pool, a simple random sample was selected to achieve the planned analytic sample size. Sampling was performed by generating a random number for each eligible record, sorting the records in ascending order, and selecting the first record until the required sample size was reached.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Human Research Ethics Committee, Universiti Sains Malaysia (USM/JEPeM/KK/23110862), and the Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR ID-23-03575-SDH[IIR]). Access to the National Tuberculosis Registry (NTBR) data was granted by the Tuberculosis and Leprosy Unit, Kelantan State Health Department, under an institutional data access arrangement approved by the Ministry of Health Malaysia. Permission to access and publish findings derived from this registry

was granted by the Director General of Health Malaysia. The dataset used for analysis comprised deidentified records and did not contain any directly identifiable personal information.

Outcome and Variables

The primary outcome was an unfavorable treatment outcome, defined according to the WHO standard TB outcome definitions (18). Unfavorable outcomes comprised treatment failure, death, or loss to follow-up, whereas favorable outcomes comprised cure or treatment completion. According to the WHO, loss to follow-up is defined as a patient who does not start treatment or whose treatment is interrupted for at least two consecutive months. The WHO also provides standardized definitions for cure, treatment completion, and treatment failure, enabling comparability across settings and registry-based evaluations.

Predictors were specified a priori based on biological plausibility and prior registry-based evidence on determinants of TB treatment outcomes and were restricted to variables routinely and consistently captured in the NTBR to minimize measurement heterogeneity. The explanatory variables comprised sociodemographic characteristics (age [years], sex, nationality, district, place of residence [urban/rural], highest education level, and occupation), comorbidity indicators available in the registry (HIV status and smoking status), and baseline clinical characteristics (presence of a *Bacillus Calmette-Guérin* [BCG] scar, sputum smear result, sputum culture result, chest radiograph severity category, and drug resistance status, including multidrug-resistant/rifampicin-resistant tuberculosis [MDR/RR-TB], where available). In addition, DOTS supervision type (e.g., healthcare worker vs. family member) was included as a key programmatic variable because of its potential influence on treatment adherence and continuity of care. All variables were coded with clearly defined reference categories before modeling. Where categorical predictors had multiple levels, categories were retained only when clinically meaningful and sufficiently populated to minimize sparse-data bias and unstable estimates.

Prior to analysis, the dataset underwent structured data quality checks for continuous variables,

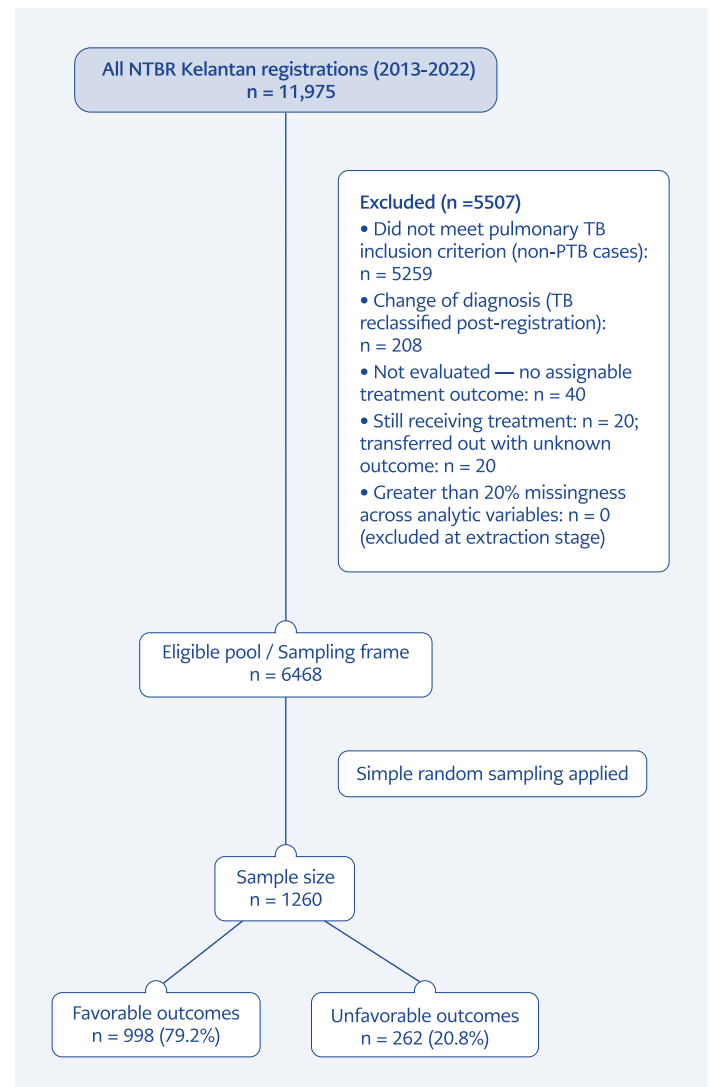


Figure 1. Flow diagram of patient selection from the National Tuberculosis Registry, Kelantan, Malaysia (2013–2022).

frequency checks for categorical variables, verification of implausible combinations (e.g., incompatible test results), and assessment of missingness patterns by key predictors and the outcome.

Statistical Analysis

The target sample size was determined to estimate the proportion of unfavorable outcomes with adequate precision using the standard single-proportion formula, where P represents the expected proportion of unfavorable outcomes, d is the absolute precision, and Z corresponds to the desired confidence level (19). The expected proportion was

informed by Malaysian registry-based evidence, and the calculated sample size was inflated to account for incomplete registry records, resulting in a final target of 1260 participants. Considerations for selecting P and d in prevalence-based sample size estimation have been described by Naing et al. (20). As the analysis also included multivariable logistic regression, the number of candidate predictors retained in the final model was guided by the events-per-variable principle to minimize overfitting and ensure stable coefficient estimates (21).

Continuous variables were summarized as mean (standard deviation [SD]) for normally distributed data and median (interquartile range [IQR]) for non-normally distributed data. Categorical variables were summarized as frequencies and percentages.

Associations between predictors and unfavorable outcomes were evaluated using univariable and multivariable logistic regression. Variables with p -values < 0.25 in the univariable analysis or with strong a priori clinical relevance were entered into the multivariable model using the purposeful selection approach recommended by Hosmer, Lemeshow, and Sturdivant (22,23), because using the conventional threshold of $p < 0.05$ during variable screening may prematurely exclude important predictors or confounders. The final multivariable model was constructed using the backward likelihood-ratio method under clinical oversight. Predictors that remained statistically significant ($p < 0.05$) or materially confounded key associations were retained. Adjusted odds ratios (AORs) with corresponding 95% confidence intervals (CIs) were reported for all variables included in the final model.

Table 1. Sociodemographic characteristics of pulmonary tuberculosis (PTB) patients in Kelantan, Malaysia ($n = 1260$).

Sociodemographic characteristics	n (%)	Sociodemographic characteristics	n (%)
Age, mean $\pm$ SD, years	48.7 $\pm$ 17.5	Pasir Puteh	114 (9.0)
Sex		Machang	111 (8.8)
Female	391 (31)	Tanah Merah	60 (4.8)
Male	869 (69)	Kuala Krai	51 (4.0)
Nationality		Jeli	25 (2.0)
Malaysian	1245 (98.8)	Gua Musang	21 (1.7)
Non-Malaysian	15 (1.2)	Place of residence	
Ethnicity		Rural	186 (14.8)
Malay	1216 (96.5)	Urban	1074 (85.2)
Non-Malay	44 (3.5)	Education level	
Case detection method		No formal education/Primary	366 (29.0)
Passive	1160 (92.1)	Secondary	705 (56.0)
Active	45 (3.6)	Tertiary	189 (15.0)
Screening	55 (4.4)	Occupation	
District		Government sector	101 (8.0)
Kota Bharu	333 (26.4)	Private sector	207 (16.4)
Pasir Mas	213 (16.9)	Self-employed	298 (23.7)
Tumpat	188 (14.9)	Not working	654 (51.9)
Bachok	144 (11.4)		

PTB: Pulmonary tuberculosis.

Table 2. Comorbidity characteristics of patients with pulmonary tuberculosis (PTB) in Kelantan, Malaysia (n = 1260).

Comorbidities	n (%)
Smoking status	
No	780 (61.9)
Yes	480 (38.1)
HIV status	
Negative	1105 (87.7)
Positive	114 (9.0)
Unknown	41 (3.3)

HIV: Human immunodeficiency virus, **PTB:** Pulmonary tuberculosis.

RESULTS

A total of 11,975 patients were reported and registered in the NTBR for Kelantan from 1 January 2013 to 31 December 2022. Of these, 5507 records were excluded: patients with a subsequent change of diagnosis were removed, those recorded as “not evaluated” were excluded, and records with more than 20% missingness across the predefined analytic variables were excluded to reduce bias. This yielded an eligible pool of 6468 PTB patients that served as the sampling frame. In a simple random sampling, 1260 patients diagnosed with PTB were included in the final analysis, representing a sampling fraction of 19.5% of the eligible population.

Sociodemographic and Clinical Characteristics

The mean age of the 1260 patients was 48.71 years (SD $\pm$ 17.46; median, 49.0; range, 1–93 years). The majority were male (n = 869, 69.0%), Malaysian (n = 1245, 98.8%), and Malay (n = 1216, 96.5%). The highest proportions of patients were from Kota Bharu (26.4%), Pasir Mas (16.9%), and Tumpat (14.9%). Most resided in urban areas (n = 1074, 85.2%), had secondary-level education (n = 705, 56.0%), and were self-employed (n = 298, 23.7%). Full sociodemographic characteristics are presented in Table 1.

Regarding comorbidities, 480 patients (38.1%) were smokers, whereas 780 (61.9%) were non-smokers. Regarding HIV status, 1105 patients (87.7%) were HIV-negative, 114 (9.0%) were HIV-positive, and 41

Table 3. Clinical characteristics of patients with PTB in Kelantan, Malaysia (n = 1260).

Clinical characteristics	n (%)
BCG scar	
Present	1119 (88.8)
Absent	141 (11.2)
Sputum smear result	
Positive	897 (71.2)
Negative	363 (28.8)
Sputum culture result	
Negative	662 (52.5)
Positive	546 (43.3)
Not performed	52 (4.1)
Chest radiograph findings	
No lesion	45 (3.6)
Minimal	753 (59.8)
Moderately advanced	426 (33.8)
Far advanced	36 (2.9)
MDR-TB status	
No	1236 (98.1)
Yes	24 (1.9)
DOTS supervision type	
Healthcare worker	1245 (98.8)
Family member	15 (1.2)

BCG: Bacillus Calmette–Guérin, **DOTS:** Directly observed treatment, short-course, **MDR-TB:** Multidrug-resistant tuberculosis, **PTB:** Pulmonary tuberculosis.

(3.3%) had unknown HIV status. Comorbidity characteristics are presented in Table 2.

Smear positivity was recorded in 71.2% of patients, sputum culture was positive in 43.3%, and a BCG scar was present in 88.8%. Chest radiograph findings were predominantly minimal (59.8%), followed by moderately advanced (33.8%), no lesion (3.6%), and far advanced (2.9%). MDR-TB was identified in 1.9% of patients, and 98.8% received DOTS supervision from healthcare workers. Clinical characteristics are detailed in Table 3.

Table 4. Treatment outcomes among patients with PTB in Kelantan, Malaysia (n = 1260).

Outcome	n (%)
Favorable outcome	998 (79.2)
Unfavorable outcome	262 (20.8)
Death	201 (16.0)
Loss to follow-up	48 (3.8)
Treatment failure	13 (1.0)

PTB: Pulmonary tuberculosis.

Proportion of Unfavorable Outcomes among PTB Patients

The study found that 20.8% (n = 262) of PTB patients experienced unfavorable treatment outcomes, while 79.2% (n = 998) achieved favorable outcomes. Of the 262 unfavorable outcomes, death was the predominant subtype, accounting for 201 cases (76.7% of all unfavorable outcomes; 16.0% of the total sample). Loss to follow-up accounted for 48 cases (18.3% of unfavorable outcomes; 3.8% of the total sample), while treatment failure accounted for the remaining 13 cases (5.0% of unfavorable outcomes; 1.0% of the total sample). Detailed figures are presented in Table 4.

Factors Associated with Unfavorable Outcomes among PTB Patients

Univariable logistic regression identified variables with $p < 0.25$, including age, nationality, case detection method, education level, occupation, chest radiograph findings, MDR status, DOTS supervision, and HIV status, for inclusion in the multivariable modeling. Notably, HIV-positive patients experienced unfavorable outcomes at more than three times the rate of HIV-negative patients (54.4% vs. 17.8%; crude OR 5.49; $p < 0.001$).

The final multivariable model identified three independent predictors of unfavorable outcomes. HIV-positive patients had significantly higher odds compared to HIV-negative patients (AOR 5.69; 95% CI 3.78–8.57; $p < 0.001$), while unknown HIV status showed no significant association (AOR 0.36; 95% CI 0.11–1.17; $p = 0.090$). MDR-TB was also independently associated with markedly higher odds (AOR

5.69; 95% CI 2.40–13.52; $p < 0.001$). Compared with healthcare worker-supervised DOTS, family-supervised DOTS was associated with significantly higher odds of unfavorable outcomes (AOR 5.02; 95% CI 1.73–14.59; $p = 0.003$). The model showed no evidence of multicollinearity or significant interactions, demonstrated acceptable calibration (Hosmer-Lemeshow goodness-of-fit test, $p = 0.208$), correctly classified 79.2% of cases, and achieved an area under the receiver operating characteristic curve (AUC) of 68.6%. Full results are presented in Tables 5 and 6.

DISCUSSION

Main Findings

The proportion of unfavorable outcomes was 20.8%, broadly comparable to other Malaysian registry-based studies reporting 19% to 22% (14–16), likely reflecting standardized TB management protocols and harmonized outcome definitions across Malaysia (5,18). Nevertheless, a one-in-five unfavorable rate represents a persistent gap in the TB care cascade, with implications for continued transmission, avoidable mortality, and the emergence of drug resistance (2,3). Descriptive findings from the present study suggest that additional clinical factors may have contributed to these outcomes. Patients with far-advanced chest radiograph findings had an unfavorable outcome rate of 39.8%, consistent with delayed diagnosis and advanced disease at presentation. Death occurred in 32.5% of HIV-positive cases, which may be partly attributable to immune reconstitution inflammatory syndrome (IRIS) and drug-drug interactions between rifampicin-based regimens and antiretroviral therapy. Among MDR-TB patients, high pill burden and drug toxicity may have further compromised adherence, as reflected by the 58.3% unfavorable outcome rate observed in this subgroup.

After adjustment, three factors remained independently associated with unfavorable outcomes: HIV positivity, MDR-TB status, and family-supervised DOTS, consistent with prior evidence that poor outcomes cluster among patients with immunosuppression, drug resistance, and adherence-related vulnerabilities (4,24,25). The AUC of 0.686 indicates modest discrimination, suggesting that additional unmeasured factors, including household

Table 5. Factors associated with unfavorable treatment outcomes among patients with PTB in Kelantan, Malaysia: univariable and multivariable logistic regression analyses (n = 1260).

Variables	Crude OR (95% CI) *	p	AOR (95% CI) **	p
Age (years)	1.01 (0.99–1.01)	0.238	-	-
Nationality				
Malaysian	1	-	-	-
Non-Malaysian	1.92 (0.65–5.67)	0.237	-	-
Case detection method				
Passive	1	-	-	-
Active	1.59 (0.82–3.08)	0.168	-	-
Screening	1.21 (0.64–2.29)	0.555	-	-
Education level				
No education / Primary	1	-	-	-
Secondary	1.02 (0.75–1.38)	0.925	-	-
Tertiary	0.75 (0.48–1.19)	0.221	-	-
Occupation				
Government sector	1	-	-	-
Private sector	1.19 (0.63–2.27)	0.586	-	-
Self-employed	1.57 (0.86–2.86)	0.139	-	-
Not working	1.45 (0.82–2.55)	0.201	-	-
Chest radiograph findings				
No lesion	1	-	-	-
Minimal	0.71 (0.34–1.47)	0.357	-	-
Moderately advanced	1.28 (0.61–2.67)	0.512	-	-
Far advanced	1.54 (0.57–4.18)	0.397	-	-
HIV status				
Negative	1	-	1	-
Positive	5.49 (3.69–8.19)	< 0.001	5.69 (3.78–8.57)	< 0.001
Unknown	0.36 (0.11–1.19)	0.095	0.36 (0.11–1.17)	0.090
MDR-TB status				
No	1	-	1	-
Yes	5.58 (2.45–12.71)	< 0.001	5.69 (2.40–13.52)	< 0.001
DOTS supervision type				
Healthcare worker	1	-	1	-
Family member	3.39 (1.22–9.46)	0.019	5.02 (1.73–14.59)	0.003

AOR: Adjusted odds ratio, **CI:** Confidence interval, **DOTS:** Directly observed treatment, short-course, **HIV:** Human immunodeficiency virus, **MDR-TB:** Multidrug-resistant tuberculosis, **OR:** Odds ratio, **PTB:** Pulmonary tuberculosis.

*Univariable logistic regression.

** Multivariable logistic regression adjusted for variables selected using the purposeful selection approach. Only variables retained in the final model are shown.

Note: Reference categories are indicated by OR = 1.00.

Table 6. Final multivariable logistic regression model of factors associated with unfavorable treatment outcomes among patients with PTB in Kelantan, Malaysia (n = 1260).

Variables	Adjusted regression coefficient (b)	Wald statistic (df)	AOR (95% CI)	p
HIV status				
Negative	-	-	1	-
Positive	1.74	69.27 (1)	5.69 (3.78–8.57)	< 0.001
Unknown	-1.04	2.88 (1)	0.36 (0.11–1.17)	0.090
MDR-TB status				
No	-	-	1	-
Yes	1.74	15.57 (1)	5.69 (2.40–13.52)	< 0.001
DOTS supervision type				
Healthcare worker	-	-	1	-
Family member	1.61	5.02 (1)	5.02 (1.73–14.59)	0.003

Model diagnostics: Backward likelihood ratio method; no evidence of multicollinearity or significant interaction effects; Hosmer-Lemeshow goodness-of-fit test, $p = 0.208$; overall classification accuracy, 79.2%; area under the receiver operating characteristic curve (AUC = 0.686).

AOR: Adjusted odds ratio, **CI:** Confidence interval, **DOTS:** Directly observed treatment, short-course, **HIV:** Human immunodeficiency virus, **MDR-TB:** Multidrug-resistant tuberculosis, **PTB:** Pulmonary tuberculosis.

income, nutritional status, comorbid diabetes mellitus, alcohol use, and detailed adherence patterns, may have contributed to the observed variation in treatment outcomes. Diabetes mellitus, in particular, impairs cellular immunity and delays sputum conversion (26), but these variables were not available in the NTBR and therefore could not be included in the model.

HIV Coinfection

HIV positivity was strongly associated with unfavorable outcomes in the present study. This is consistent with existing literature showing higher risks of mortality and treatment failure among TB-HIV coinfecting patients due to impaired cellular immunity, greater frequency of disseminated disease, atypical presentation, and competing risks from opportunistic infections (4,27). The overall proportion of unfavorable outcomes in the present study was lower than that reported in a Kuala Lumpur cohort restricted to TB-HIV-coinfecting patients, as expected, because the present sample represented the general PTB population rather than a high-risk coinfecting subgroup (28). From a programmatic perspective, this finding supports closer integration of TB and HIV services, including timely HIV

testing, early linkage to antiretroviral therapy, and active monitoring of treatment complexity in coinfecting patients (29).

MDR-TB

MDR-TB was associated with markedly increased odds of unfavorable outcomes. MDR-TB requires prolonged treatment with multiple second-line drugs, which are associated with greater toxicity and require more intensive monitoring, thereby increasing the risk of treatment interruption, adverse events, and poor adherence (24,25). Global and regional analyses have consistently highlighted the persistent burden and inequities of MDR-TB, including elevated mortality and substantial disability (30). Although MDR-TB affected only 1.9% of the study population, the large effect size underscores its disproportionate clinical importance, despite the limited precision associated with the small subgroup. These findings support prioritized management, including rapid drug-resistance detection, early initiation of effective treatment, and closer follow-up throughout treatment (29).

DOTS Supervision

Family-supervised DOTS was independently

associated with higher odds of unfavorable outcomes compared with healthcare worker supervision. This association should be interpreted cautiously, as it may reflect selection bias whereby patients at higher risk of non-adherence or with access barriers are preferentially assigned family supervision, rather than a direct effect of supervision quality. While family-based DOTS reduces travel burden and improves flexibility, it may introduce variability in dose observation, documentation, and recognition of adverse effects (5). Evidence syntheses suggest that DOTS does not uniformly outperform self-administered therapy and that its effectiveness depends heavily on implementation quality and patient-centered support (25,31). These findings should therefore be interpreted as a signal to strengthen competency, accountability, and support systems for non-professional supervisors through structured training, periodic verification by healthcare staff, and clear escalation pathways for missed doses or adverse effects.

This study has several strengths. The analytic sample of 1260 patients drawn from 6468 eligible registry records provides substantial statistical power and broad representativeness across all districts of Kelantan under routine programmatic conditions. The decade-long period (2013–2022) supports stable multivariable estimates and captures contemporary programmatic practice, while the statewide registry design enhances external validity, and standardized WHO-aligned outcome definitions ensure comparability with other registry-based studies (5,18). However, several limitations should be acknowledged. The reliance on secondary registry

data may have introduced misclassification, and important confounders, including diabetes, undernutrition, and socioeconomic indicators, were unavailable. Using a random sample rather than the full eligible cohort may have reduced precision, and the logistic regression analysis did not account for time-to-event or competing-risk dynamics, which future survival analyses could address.

Despite these limitations, the findings have direct implications for TB control in Kelantan. Patients with HIV infection and MDR-TB warrant closer monitoring and differentiated support. For DOTS, the emphasis should extend beyond supervisor type to supervisor capacity, including structured training, verification, and practical support for family supervisors. These targeted approaches are consistent with patient-centered TB care and may help improve treatment success in Kelantan and similar settings (2,17).

CONCLUSION

To improve treatment outcomes among PTB patients in Kelantan, public health interventions should prioritize support for patients with HIV infection and MDR-TB, while strengthening the training, support, and monitoring of DOTS supervision. Targeted efforts focused on these high-risk groups may help reduce the incidence of unfavorable outcomes and strengthen TB control efforts in the state. Overall, the study's findings provide evidence to support refining TB treatment strategies in Kelantan, particularly through risk-targeted interventions.

Ethical Approval: Ethical approval was obtained from the Human Research Ethics Committee, Universiti Sains Malaysia (USM/JEPeM/KK/23110862) on December 3, 2023, and the Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR ID-23-03575-SDH[IIR]) on 15 January 2024.

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