

# Factors associated with tuberculosis treatment outcome under directly observed treatment short-course in Hulu Langat district, Selangor, Malaysia

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## ABSTRACT

**Introduction:** Tuberculosis (TB) is a significant public health concern despite being a preventable and treatable infectious disease, as indicated by the rising incidence and mortality rates. This study aims to compare treatment outcomes by different Directly Observed Treatment, Short-Course (DOTS) supervisors and to identify significant factors associated with Tuberculosis treatment outcomes under DOTS in the Hulu Langat district.

**Materials and Methods:** A retrospective cohort study was conducted using registry-based data from the National Tuberculosis Registry (NTBR) between 2019 and 2023. Smear-positive PTB patients' sociodemographic, clinical and DOTS supervisor factors were extracted and analysed. Logistic regression was used to determine the significant factors associated with unsuccessful treatment outcomes. The data were analysed using SPSS version 29.

**Results:** Out of 5225 cases of Tuberculosis during the five years (2019-2023), 2548 cases met the inclusion criteria and were added to the analysis. The treatment success rate among Tuberculosis patients who enrolled in DOTS in the Hulu Langat district was 74.5%, comprising 70.8% who were cured and 3.6% who completed treatment. In contrast, 25.5% had unsuccessful treatment outcomes; 12.7% of patients died, followed by defaulters (8%), not evaluated or transferred out (2.6%), and treatment failure (2.3%). Compared to patients supervised by other DOTS supervisors, those supervised by family members had a significantly lower risk of unsuccessful treatment outcomes (AOR 0.34, 95% CI: 0.177-0.660,  $p=0.001$ ). Besides that, significant factors associated with unsuccessful treatment outcomes include adult age (19-59 years) with an AOR of 3.60 (95% CI: 1.518-8.533,  $p=0.004$ ), elderly age ( $\geq 60$  years) with an AOR of 5.56 (95% CI 2.297-13.438,  $p<0.001$ ), male gender (AOR 1.48, 95% CI: 1.183-1.838,  $p<0.001$ ), foreigners (AOR 1.92, 95% CI: 2.366-3.687,  $p<0.001$ ), rural residence (AOR 1.6, 95% CI: 1.090-2.349,  $p=0.016$ ), HIV-positive (AOR 2.33, 95% CI: 1.508-3.586,  $p<0.001$ ), moderate changes CXR findings (AOR 2.72, 95% CI: 1.245-5.945,  $p=0.012$ ) and far-advanced CXR findings (AOR 5.30, 95% CI: 2.290-12.268,  $p<0.001$ ). In contrast, the study found a significant decrease in the risk of unsuccessful treatment outcomes among

Chinese ethnicity (AOR 0.74, 95% CI: 0.695-1.196,  $p=0.044$ ) and tertiary education (AOR 0.55, 95% CI: 0.334-0.914,  $p=0.021$ ).

**Conclusion:** This study challenges the traditional focus on healthcare worker DOTS by highlighting the effectiveness of family-supervised DOTS in improving TB treatment outcomes. The findings underscore the potential for family-DOTS to be scaled up as a complementary strategy within the national TB programme. Thus, the study recommends that the Ministry of Health adopt a risk-stratified framework based on sociodemographic and clinical factors to guide the assignment of DOTS supervisors, ensuring each patient receives the most suitable type of supervision throughout their TB treatment. Tailored TB control strategies should also expand risk stratification beyond existing MOH high-risk groups to include males, the elderly, foreign nationals, rural residents, and those with abnormal radiological findings, with strengthened screening and supervision to improve treatment outcomes.

## KEYWORDS:

Public Health, Tuberculosis, Directly Observed Therapy, Risk Factors, Treatment Outcome

## INTRODUCTION

Tuberculosis (TB) remains one of the deadliest infectious diseases globally.<sup>1</sup> Caused by *Mycobacterium tuberculosis*, it is primarily transmitted through airborne droplets and mainly affects the lungs. TB exists in two forms: latent TB infection (LTBI) and active TB disease, with approximately 5–10% of those with LTBI progressing to active disease.<sup>2</sup> Despite advances in medical treatment, TB continues to pose a significant global health challenge.

Worldwide, TB remains a public health crisis, particularly in regions like Southeast Asia, Africa, and the Western Pacific, which together account for the majority of TB cases. In 2022, over 10 million people were infected, and TB caused more than 1.3 million deaths, making it deadlier than HIV and malaria combined.<sup>1</sup> High-burden countries such as India, China, and Indonesia contribute significantly to these figures, with men aged 15 years and above representing the

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majority of TB cases. While TB affects all age groups, children and people living with HIV (PLHIV) are particularly vulnerable.<sup>1</sup>

The World Health Organization (WHO) has spearheaded global TB control efforts with strategies like the End TB Strategy, introduced in 2014. This initiative, aligned with the Sustainable Development Goals (SDGs), aims to reduce TB incidence and mortality by 2030. Despite these global efforts, many countries, including Malaysia, have not met the initial milestones set for 2020.<sup>3</sup> Tuberculosis is endemic in Malaysia, with an intermediate TB burden of fewer than 100 cases per 100,000 people annually.<sup>1</sup> While TB notification rates have increased from 63.5 cases per 100,000 people in 2021 to 77.8 cases per 100,000 people in 2022, the success of the national TB control program has been variable.<sup>4</sup>

Malaysia's healthcare system, comprising a robust public sector and a thriving private sector, has made significant strides in controlling TB. The National TB Control Programme (NTP), established in 1961, introduced key strategies like the Bacillus Calmette-Guérin (BCG) vaccination, Tuberculosis Information System (TBIS) and Directly Observed Treatment Short Course (DOTS) to improve TB management.<sup>4</sup> However, the treatment success rate (TSR) under DOTS has yet to reach the Ministry of Health's Key Performance Indicator (KPI) target of 90%, with a reported TSR of 85% in 2022.<sup>4</sup> Treatment outcomes also vary depending on the type of DOTS supervisor, with healthcare workers achieving better outcomes than non-governmental organisation (NGO) volunteers or family members, as more cases of loss to follow-up are seen when patients are supervised by NGO volunteers, family members and healthcare workers (6.4%, 4.7%, and 3.5%), respectively.<sup>4</sup>

In 2022, the Hulu Langat district recorded a TB incidence rate of 79 cases per 100,000 population, which is higher than the national average and also reported rising trends in multidrug-resistant TB, treatment defaulters, and TB-related deaths.<sup>4,5</sup> Although DOTS is the cornerstone of TB control, the type of supervisor, whether a healthcare worker, family member, NGO volunteer, or others, can influence treatment adherence and outcomes. Healthcare workers, as trained professionals, are better equipped to provide consistent support, education, and early intervention when adherence issues arise, leading to improved outcomes.<sup>6</sup> Studies from Pakistan and India have reported higher treatment success rates under healthcare worker-supervised DOTS, while a study in Thailand shows family-supervised DOTS was not significantly associated with successful outcomes.<sup>6-8</sup> In contrast, Malaysian studies have not differentiated supervisor types and found no significant association between DOTS supervision and treatment outcomes.<sup>9-12</sup> This highlights a gap in local evidence, warranting district-level analysis that accounts for sociodemographic and clinical confounders to determine the comparative effectiveness of different DOTS supervisor categories.

This study aims to examine the relationship between DOTS supervision types and TB treatment outcomes in Hulu Langat, Selangor. It will also identify risk factors associated with TB treatment outcomes to inform future strategies for improving the management and control of TB in Malaysia.

## MATERIALS AND METHODS

This study employed a retrospective cohort design, which comprised all pulmonary TB (PTB) cases reported to the Hulu Langat District Health Office between January 1, 2019, and June 30, 2023. Data were sourced from the National Tuberculosis Registry (NTBR), which is the online platform of the Tuberculosis Information System (TBIS).

The study focused on Hulu Langat, the second most populated district in Selangor, with approximately 1.4 million residents, consisting primarily of Bumiputera (63%), Chinese (28.1%), Indian (8.2%), other ethnicities and foreigners (0.7%).<sup>13</sup> Hulu Langat is an urban district, with six subdistricts, of which Kajang, Ampang, and Cheras are the most densely populated and report the highest TB cases. The study population included all confirmed PTB smear-positive cases, new or relapsed, who enrolled in DOTS during the study period. Excluded were patients with extra-pulmonary TB (EPTB), multidrug-resistant TB (MDR-TB), and PTB category cases after default, failed treatment and changed diagnosis. These exclusion criteria followed the World Health Organization's (WHO) criteria for calculating Treatment Success Rate (TSR).<sup>14</sup>

The study employed universal sampling, including all PTB cases recorded in NTBR that met the inclusion criteria. The minimum sample size was calculated using the OpenEpi sample size calculator for cohort studies (Version 3.01), referencing treatment outcome differences reported by a previous study.<sup>9</sup> With 95% confidence, 80% power, and an odds ratio of 2.6, the required sample size to detect a difference in unsuccessful outcomes between males (28%) and females (13%) was 332 after an estimated 30% was added to the final sample size estimates to account for potential incomplete data.

The dependent variable was TB treatment outcomes, which were defined according to the World Health Organization (WHO) standard definitions:<sup>1</sup>

1. Cured: A bacteriologically confirmed pulmonary TB patient who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.
2. Completed treatment: A patient who finished the full course of TB treatment but lacks bacteriological confirmation of cure, although at least one earlier test was negative.
3. Treatment failure: A TB patient whose sputum smear or culture was positive at month five or later during treatment.
4. Died: A patient who died from any cause during TB treatment.
5. Treatment default: A patient who stopped TB treatment for at least two continuous months after being registered for treatment.
6. Transferred out / Not evaluated: A patient who was transferred to another facility or whose treatment outcome was unknown.

For analysis, both cured and completed treatment outcomes were categorised into successful treatment outcomes, while all other outcomes were categorised into unsuccessful treatment outcomes.

**Table I: Sociodemographic and Clinical Characteristics of Patients with Tuberculosis, and Their Treatment Outcomes**

Variables	n	%
Age	Mean 43.09	SD 16.5
Age group		
0-18	95	3.7
19-59	1987	78
≥60	462	18.1
Gender		
Male	1682	66
Female	866	34
Citizenship		
Citizen	2035	79.9
Non-citizen	513	20.1
Race		
Malay	1243	48.8
Chinese	453	17.8
Indian	215	8.4
Others	122	4.8
Foreigners	515	20.2
Residential Area		
Urban	2399	94.2
Rural	145	5.7
Educational Level		
No education	361	14.2
Primary	136	5.3
Secondary	1502	58.9
Tertiary	518	20.3
Monthly Income		
MYR ≤ 1500	1112	43.6
MYR 1501-3000	1392	54.6
MYR ≥3001	44	1.7
Employment status		
Employed	1868	73.3
Unemployed	680	26.7
Healthcare Worker		
Yes	23	0.9
No	2525	99.1
Smoking		
Yes	826	32.4
No	1722	67.6
Bcg scar		
Yes	2135	83.8
No	413	16.2
Diabetes		
Yes	725	28.5
No	1821	71.5
HIV status		
Yes	108	4.2
No	2431	95.4
CXR findings		
No changes	78	3.1
Minimal Changes	1244	48.8
Moderate Changes	1043	40.9
Far-Advanced Changes	167	6.6
DOTS supervisor		
Healthcare worker	1782	69.9
Family	712	27.9
NGO	6	0.2
Others	48	1.9
TB Treatment Outcomes		
Successful Treatment Outcome	1897	74.5
Cured	1804	70.8
Completed Treatment	93	3.6
Unsuccessful Treatment Outcome	651	25.5
Death	323	12.7
Treatment Failure	58	2.3
Treatment Default	205	8.0
Transferred Out/Not evaluated	65	2.6

Table II: Distribution and Simple Logistic Regression of Factors Associated With Tuberculosis Treatment Outcome

	Unsuccessful Treatment outcome n (%)	Successful Treatment Outcome n (%)	OR (95%CI)	p-value
Age group				
0-18	6 (6.3)	89 (93.7)	RC	
19-59	503 (25.3)	1484 (74.7)	5.03 (2.186, 11.563)	<0.001
≥60	141 (30.5)	321 (69.5)	6.52 (2.785, 15.245)	<0.001
Gender				
Female	163 (18.8)	703 (81.2)	RC	
Male	488 (29)	1194 (71)	1.76 (1.443, 2.154)	<0.001
Citizenship				
Citizen	427 (21)	1608 (79)	RC	
Non-citizen	224 (43.7)	289 (56.3)	2.92 (2.379, 3.581)	<0.001
Race				
Malay	257 (20.7)	986 (79.3)	RC	
Chinese	87 (19.2)	366 (80.8)	0.91 (0.695, 1.196)	0.505
Indian	56 (26)	159 (74)	1.35 (0.968, 1.887)	0.077
Others	27 (22.1)	95 (77.9)	1.09 (0.696, 1.708)	0.706
Foreigners	224 (43.5)	291 (56.5)	2.95 (2.366, 3.687)	<0.001
Residential Area				
Urban	595 (24.8)	1804 (75.2)	RC	
Rural	54 (37.2)	91 (62.8)	1.80 (1.269, 2.551)	<0.001
Educational Level				
Primary	43 (31.6)	93 (68.4)	RC	
Secondary	370 (24.6)	1132 (75.4)	0.71 (0.483, 1.034)	0.074
Tertiary	63 (12.2)	455 (87.8)	0.30 (0.191, 0.468)	<0.001
No education	166 (46)	195 (54)	1.84 (1.214, 2.792)	0.004
Monthly Income				
MYR ≥ 3001	4 (9.1)	40 (90.9)	RC	
MYR 1501-3000	263 (18.9)	1129 (81.1)	2.33 (0.826, 6.568)	0.110
MYR ≤ 1500	384 (34.5)	728 (65.5)	5.28 (1.873, 14.852)	0.002
Employment Status				
Employed	418 (22.4)	1450 (77.6)	RC	
Unemployed	233 (34.3)	447 (65.7)	1.81 (1.492, 2.191)	<0.001
Healthcare Worker				
Yes	2 (8.7)	21 (91.3)	RC	
No	649 (25.7)	1876 (74.3)	3.63 (0.849, 15.534)	0.082
Smoking				
No	408 (23.7)	1314 (76.3)	RC	
Yes	243 (29.4)	583 (70.6)	1.34 (1.114, 1.617)	0.002
BCG scar				
Yes	470 (22)	1665 (78)	RC	
No	181 (43.8)	232 (56.2)	2.76 (2.219, 3.443)	<0.001
Diabetes status				
No	464 (25.5)	1357 (74.5)	RC	
Yes	187 (25.8)	538 (74.2)	1.02 (0.835, 1.238)	0.870
HIV status				
No	600 (24.7)	1831 (75.3)	RC	
Yes	47 (43.5)	61 (56.5)	2.35 (1.590, 3.478)	<0.001
CXR Findings				
No lesion	8 (10.3)	70 (89.7)	RC	
Minimal changes	271 (21.8)	973 (78.2)	2.44 (1.158, 5.127)	0.019
Moderate changes	296 (28.4)	747 (71.6)	3.47 (1.648, 7.294)	0.001
Far-Advanced Changes	72 (43.1)	95 (56.9)	6.63 (3.001, 14.656)	<0.001
DOTS Supervisor				
Others	23 (47.9)	25 (52.1)	RC	
NGO	2 (33.3)	4 (66.7)	0.54 (0.091, 3.253)	0.504
Family	108 (15.2)	604 (84.8)	0.19 (0.106, 0.355)	<0.001
Healthcare Worker	518 (29.1)	1264 (70.9)	0.45 (0.251, 0.792)	0.006

Note: Variables with p-value < 0.25 in the simple logistic regression were selected for inclusion in the multivariable model  
RC: Reference Category

**Table III: Multiple Logistic Regression Analysis of Factors Associated With Unsuccessful TB Treatment Outcome**

Variables	AOR	95% CI	p-value
Age group			
0-18	RC		
19-59	3.60	(1.518, 8.533)	0.004
≥60	5.56	(2.297, 13.438)	<0.001
Gender			
Female	RC		
Male	1.48	(1.183, 1.838)	<0.001
Race			
Malay	RC		
Chinese	0.74	(0.550, 0.992)	0.044
Indian	1.21	(0.848, 1.728)	0.293
Others	1.11	(0.693, 1.783)	0.660
Foreigners	1.92	(1.374, 2.669)	<0.001
Residential Area			
Urban	RC		
Rural	1.60	(1.090, 2.349)	0.016
Educational Level			
Primary	RC		
Secondary	0.92	(0.604, 1.397)	0.690
Tertiary	0.55	(0.334, 0.914)	0.021
No education	1.26	(0.788, 2.015)	0.334
Monthly Income			
MYR ≥ 3001	RC		
MYR 1501-3000	1.05	(0.356, 3.065)	0.937
MYR ≤ 1500	1.72	(0.580, 5.075)	0.329
Employment Status			
Employed	RC		
Unemployed	0.92	(0.694, 1.211)	0.542
Healthcare Worker			
Yes	RC		
No	1.05	(0.233, 4.697)	0.954
Smoking			
No	RC		
Yes	1.07	(0.851, 1.338)	0.575
BCG scar			
Yes	RC		
No	1.10	(0.726, 1.660)	0.658
HIV status			
No	RC		
Yes	2.33	(1.508, 3.586)	<0.001
CXR Findings			
No changes	RC		
Minimal changes	2.03	(0.929, 4.430)	0.076
Moderate changes	2.72	(1.245, 5.945)	0.012
Far-Advanced Changes	5.30	(2.290, 12.268)	<0.001
DOTS Supervisor			
Others	RC		
NGO	0.33	(0.053, 2.122)	0.245
Family	0.34	(0.177, 0.660)	0.001
Healthcare Worker	0.67	(0.358, 1.256)	0.212

Note: Level of significance p < 0.05  
RC: Reference Category

Independent variables included a range of sociodemographic, clinical and DOTS supervision factors. Sociodemographic factors included age, gender, citizenship, race, residential area, education level, monthly income, employment status and healthcare worker status. Clinical factors comprised smoking status, presence of a Bacillus Calmette-Guérin (BCG) scar, diabetes status, HIV status, and chest X-ray (CXR) findings. The DOTS supervisor categories included healthcare workers, family members, NGOs or others.

The study relied on secondary data from NTBR. After obtaining approval from the Medical Research and Ethics Committee (MREC) and the Selangor State Health Department, data were downloaded from NTBR and transferred into Microsoft Excel format. A structured data collection form was used to extract relevant variables. Data were thoroughly cleaned, including identifying and correcting errors or inconsistencies. As the proportion of missing data was less than 1% across four variables, age, HIV, diabetes and CXR findings, listwise deletion was applied. Given the minimal extent of missingness, the impact on statistical power and validity of estimates was considered negligible, and advanced methods such as multiple imputation were not deemed necessary.

Data were analysed using IBM SPSS Statistics for Windows, version 29 (IBM Corp., Armonk, NY, USA). Descriptive statistics summarised continuous variables like age as means and standard deviations, while the rest of the categorical variables were presented as frequencies and percentages. For inferential statistics, bivariate analysis uses simple logistic regression to examine associations between independent variables and treatment outcomes. Variables with a  $p$ -value  $< 0.25$  were considered for multivariate analysis to prevent premature exclusion of potential predictors.<sup>9</sup>

Multivariate analysis was then employed using multiple logistic regression with stepwise backwards selection to identify significant predictors of unsuccessful treatment outcomes. Variables with a  $p$ -value  $< 0.05$  in the final model were deemed statistically significant. Model fitness was assessed using the Hosmer–Lemeshow goodness of fit test, classification tables, and the area under the ROC curve. A non-significant Hosmer–Lemeshow test ( $p > 0.05$ ), a classification accuracy exceeding 70%, and an area under the ROC curve  $> 0.5$  indicated a well-fitted model.<sup>9</sup>

## RESULTS

Table I presents the sociodemographic and clinical characteristics of 2,548 tuberculosis (TB) patients in Hulu Langat. The mean age was 43.1 years (SD: 16.5), with the majority aged 19–59 years (78.0%). Males made up 66.0% of the cases. Most patients were Malaysian citizens (79.9%) and of Malay ethnicity (48.8%). A large proportion resided in urban areas (94.2%). Regarding education, 58.9% had secondary-level education, and 54.6% had a monthly income between MYR 1,501 and MYR 3,000. The majority (73.3%) were employed. In terms of clinical characteristics, 28.5% had diabetes mellitus and 4.2% were HIV positive. Chest X-ray abnormalities were reported in 96.3% of patients, and 32.4%

were smokers. Most patients (69.9%) received directly observed treatment (DOTS) supervised by healthcare workers, while others were supervised by family members (27.9%), NGOs (0.2%) or others (1.9%). Overall, the treatment success rate was 74.5%, while 25.5% experienced unsuccessful treatment outcomes, including death, default, treatment failure, or not evaluated.

Table II presents the distribution of tuberculosis (TB) treatment outcomes by sociodemographic, clinical, and DOTS supervisor factors, with  $p$ -values from simple logistic regression. Regarding DOTS supervision, patients monitored by family members (15.2%,  $p < 0.001$ ) had lower proportions of unsuccessful treatment outcomes compared to those supervised by healthcare workers (29.1%,  $p = 0.006$ ). Unsuccessful treatment outcomes were more frequent among patients aged  $\geq 60$  years (30.5%,  $p < 0.001$ ), males (29%,  $p < 0.001$ ), non-citizen (43.7%,  $p < 0.001$ ), the unemployed (34.3%,  $p < 0.001$ ), those with monthly income  $\leq$  MYR 1500 (34.5%,  $p = 0.002$ ), rural residence (37.2%,  $p < 0.001$ ) and individuals with no formal education (46%,  $p = 0.004$ ). Clinically, higher proportions of unsuccessful outcomes were seen among smokers (29.4%,  $p = 0.002$ ), patients with no BCG scar (43.8%,  $p < 0.001$ ), HIV-positive individuals (43.5%,  $p < 0.001$ ) and far-advanced CXR changes (43.1%,  $p < 0.001$ ).

Table III presents the results of multiple logistic regression analysis conducted to adjust for potential confounding factors. Several variables were independently associated with unsuccessful treatment outcomes. Family-supervised DOTS remained significantly associated with a lower likelihood of unsuccessful outcomes ( $p = 0.001$ ). Furthermore, independent risk factors for unsuccessful treatment outcome included adults aged 19–59 years ( $p = 0.004$ ), elderly individuals aged  $\geq 60$  years ( $p < 0.001$ ), male gender ( $p < 0.001$ ), non-Malaysian nationality ( $p < 0.001$ ), and residence in rural areas ( $p = 0.016$ ). Clinical factors significantly associated with unsuccessful treatment outcomes included HIV positivity ( $p < 0.001$ ), as well as moderate ( $p = 0.012$ ) and far-advanced ( $p < 0.001$ ) chest X-ray findings. Conversely, a significantly lower likelihood of unsuccessful treatment outcome was observed among individuals of Chinese ethnicity ( $p = 0.044$ ) and those with tertiary education ( $p = 0.021$ ).

The model demonstrated a good fit, as indicated by a non-significant Hosmer–Lemeshow goodness-of-fit test ( $p = 0.175$ ). It correctly classified 75.6% of the cases, with an area under the ROC curve (AUC) of 0.734, reflecting acceptable discriminatory power.

## DISCUSSION

The treatment success rate among TB patients who enrolled on DOTS in the Hulu Langat district was 74.5%. The success rate fell below the WHO target of more than 90%.<sup>1</sup> The results were comparable to prior local research, with success rates of 77.2% and 76% respectively.<sup>9,12</sup> However, a local study and another study in Indonesia revealed a better success rate and achieved the WHO's aim.<sup>15,16</sup> The comparisons revealed inadequate TB control in the Hulu Langat district, highlighting the need for improvement.

The leading cause of unsuccessful treatment outcomes in our study was death (12.7%), which is higher than the 10% reported in the national studies.<sup>10,11</sup> This growing trend contradicts the World Health Organization's End TB plan milestone, which seeks to reduce mortality by 90% by 2030.<sup>3</sup> The rest of the unsuccessful outcomes are treatment default (8%), not evaluated or transferred out (2.6%), and treatment failure (2.3%). Previous research in Ethiopia and Morocco found that the defaulter group had the largest rate of unsuccessful treatment outcomes.<sup>17,18</sup> Previous literature consistently demonstrates that gaps in the TB care cascade, especially at diagnosis and treatment, high rates of treatment interruption and loss to follow-up, persistent barriers among high-risk groups (such as prisoners, migrants, and people living with HIV), and the growing threat of drug-resistant TB.<sup>10,11,19,20</sup> Socioeconomic factors, health system limitations, knowledge gaps, and stigma further hinder program effectiveness.<sup>21-23</sup> Interventions that are patient-centred, community-based, and leverage technology have shown the most significant promise in improving outcomes, particularly when tailored to local contexts and vulnerable populations.<sup>24</sup>

Given the unachievable success and mortality rates from 2019 to 2023, it is crucial to investigate the evidence on the most effective DOTS supervisors and the significant factors leading to unsuccessful treatment outcomes. This will help develop effective interventions and strategies to reduce TB morbidity and mortality. Based on the final model of the multiple logistic regression, this study found that a significant decrease in the risk of unsuccessful treatment outcomes among family-DOTS supervisors as compared with other DOTS supervisors. Besides that, unsuccessful treatment outcomes were significantly associated with the adult and elderly age group, male gender, foreigners, rural residential area, HIV-positive, moderate and far-advanced changes in CXR findings. In contrast, the study also found a significant decrease in the risk of unsuccessful treatment outcomes among individuals of Chinese ethnicity and those with tertiary education.

Regarding the comparison of DOTS supervisors, DOTS by healthcare workers reduced the odds of unsuccessful outcomes by 55% (OR: 0.45), while family-supervised DOTS showed an 81% reduction (OR: 0.19). NGO-supervised DOTS (OR: 0.54) was not statistically significant. However, multivariate analysis confirmed that only family-supervised DOTS remained significant, with an AOR of 0.34, reducing the risk of unsuccessful outcomes by 66%. Most of the study's findings, locally and abroad, show that DOTS supervisors were not significantly associated with treatment outcomes.<sup>6,7,9-11</sup> Our study suggests that family-supervised DOTS is more effective in Hulu Langat or other similar settings in Malaysia, as family members provide consistent support to enhance adherence and outcomes. The reduced significance of DOTS by healthcare workers in the multivariate analysis implies that other factors, such as patient-provider relationships and socioeconomic status, play a more crucial role in determining treatment success.

Culturally, strong family ties in Malaysia provide emotional support, reminders, and encouragement that help patients adhere to and complete their TB treatment.<sup>25</sup> Structurally,

family involvement serves as a vital link between patients and healthcare providers, assisting with overcoming stigma, financial difficulties, and ensuring timely access to care for better treatment outcomes.<sup>25</sup> While family-supervised DOTS shows better outcomes, healthcare worker-supervised DOTS remains crucial, particularly for non-compliant patients. In contrast, family DOTS may benefit well-educated patients with work commitments. Enhancing both supervision types to complement each other and incorporating family-centred approaches into TB programs through routine counselling sessions, training family members, and recognising their role can further strengthen treatment success in Malaysia's culturally diverse settings.<sup>25</sup>

Prior research has indicated that older individuals diagnosed with TB exhibited a significant mortality rate.<sup>9,10,17,26</sup> Older age was found to be a significant factor associated with unsuccessful treatment outcomes in this study. Adult patients aged 19-59 had 3.6 times higher odds for unsuccessful treatment outcomes compared to those aged 0-18. For elderly patients aged over 60 years, the odds increase to 5.6 times, indicating a higher likelihood of unsuccessful outcomes as age increases. The elderly's susceptibility to TB treatment failure is driven by immune system decline due to ageing and is powerfully compounded by comorbidities like malnutrition, diabetes, and cancer. These factors increase the risk of initial infection, progression to active disease, and failure to respond effectively to standard TB therapies.<sup>27</sup> To reduce unsuccessful TB outcomes in the elderly, need to focus on infection control to stop the transmission, systematic screening and preventive therapy for high-risk groups, rapid diagnosis with effective treatment and close monitoring, and tailored programmatic management addressing their specific needs and comorbidities.<sup>28</sup>

Besides that, the adult group also show a significant association with unsuccessful outcomes, and these findings are similar to a study done in Brazil that shows young adults are associated with unsuccessful treatment outcomes.<sup>29</sup> A possible explanation is that the young adult group are more likely to be non-compliant and may miss follow-up appointments due to work or other commitments.<sup>9,11</sup> Public health strategies should support older adults by improving healthcare access, managing comorbidities, and providing nutritional aid. For young adults, efforts should focus on enhancing treatment adherence through flexible scheduling, workplace or family support, and technology-based tools like reminders or telemedicine.<sup>24</sup>

The male predominance in the unsuccessful treatment outcomes in our study concurs with the TB burden and mortality trend observed nationally and worldwide.<sup>1,9-11</sup> Men were found to be a significant factor associated with unsuccessful treatment outcomes in this study, with 1.5 times higher odds as compared to women. Men face a higher TB burden and unsuccessful outcomes due to risk behaviours and barriers like stigma and financial constraints.<sup>30</sup> To address these disparities, gender-sensitive interventions such as risk reduction campaigns and strategies to improve healthcare access are essential and recommended by frameworks advocating for gender-responsive TB programs.<sup>30</sup>

This study also found that non-citizens were significantly associated with unsuccessful TB treatment outcomes, with a 1.9 times higher risk as compared to the local citizens, aligning with multiple studies from Malaysia and Busan.<sup>9-11,31</sup> Malaysia's industrialisation has attracted many job-seeking immigrants, increasing TB transmission risks. These individuals often face barriers like low income, limited healthcare access, and poor education, leading to inadequate treatment adherence.<sup>9</sup> Public health policies must ensure inclusive TB services, offering culturally appropriate education, legal protections, and social support for migrants to improve outcomes and reduce transmission.<sup>32</sup>

Our findings of ethnicity show that Chinese ethnicity had significantly lower odds (26.2%) of experiencing unsuccessful treatment outcomes for TB compared to other ethnic groups, such as Malays and Indians, who did not show significant differences in treatment outcomes. Another study conducted in Malaysia and the neighbouring country that shares the same ethnicities as Singapore indicates that non-Malay patients, including Chinese, had lower odds of recurrent TB and better treatment outcomes, possibly due to factors such as healthcare access and cultural attitudes towards treatment adherence.<sup>10,32-34</sup>

Besides that, our study indicates that patients living in rural areas had 1.6 times higher odds of experiencing unsuccessful treatment outcomes for tuberculosis compared to those in urban areas. The national study and other countries in India, England and Africa also showed that rural populations often face greater challenges in TB management that can lead to unsuccessful outcomes compared to their urban counterparts.<sup>11,22,35,36</sup> Public health strategies should focus on improving healthcare infrastructure in rural areas, training healthcare workers to manage TB more effectively, and implementing community-based TB programs that can reach remote populations.<sup>11,22,35,36</sup>

Educational attainment is also a significant factor associated with TB treatment outcomes in Hulu Langat District, Selangor. Patients with tertiary education had 44.8% lower odds of unsuccessful treatment outcomes compared to those with primary education. This finding is similar to the national study that shows a higher risk of unsuccessful outcomes among low-education patients.<sup>10,11</sup> Higher education's link to better TB outcomes highlights the importance of health literacy. Public health efforts should focus on educating patients and the public about treatment adherence, early symptom recognition, and the risks of non-compliance, especially for those with lower education levels.<sup>19,21</sup>

TB-HIV co-infection also had significant impacts on TB treatment outcomes, as the findings of our study indicate that HIV-positive patients had 2.3 times higher odds of experiencing unsuccessful TB treatment outcomes compared to HIV-negative patients. Previous studies in Malaysia, South Korea and Africa also show similar significant findings of association between HIV-positive patients and unsuccessful treatment outcomes.<sup>9-11,22,37-39</sup> HIV co-infection significantly worsens TB treatment outcomes due to impaired immunity, higher drug resistance, and reduced adherence.<sup>40</sup> This

underscores the need for integrated TB-HIV care, early HIV diagnosis, and continuous monitoring of collaborative efforts to improve outcomes.<sup>22</sup>

CXR findings were significantly associated with TB outcomes, with moderate changes increasing odds by 2.7 times and far-advanced changes by 5.3 times. Consistent with previous studies, these findings highlight that extensive lung damage and higher bacterial loads complicate treatment.<sup>9,11,37</sup> Early diagnosis, close monitoring of significant CXR abnormalities, and routine use of radiological assessments to guide treatment decisions are crucial for improving outcomes.<sup>37</sup>

This study had certain limitations. Since this is a retrospective cohort study using secondary data from a surveillance database, some variables, such as underlying chronic illness like malnutrition, and some behavioural traits like alcohol or drug intake, were not easily accessible for examination. Apart from that, the study included only PTB Smear Positive cases; therefore, the outcome cannot be applied to other types of TB. Furthermore, using secondary data limits the ability to establish causality, as it only allows for analysis of associations without confirming cause-and-effect relationships; thus, recommendations for future studies are to consider a longitudinal design to assess causality better.

## CONCLUSION

This study challenges the traditional focus on healthcare worker DOTS by highlighting the effectiveness of family-supervised DOTS in improving TB treatment outcomes. The findings underscore the potential for family-DOTS to be scaled up as a complementary strategy within the national TB programme. Thus, this study proposes that the Ministry of Health adopt a risk-stratification framework based on sociodemographic and clinical factors to guide the assignment of DOTS supervisors, ensuring each patient receives the most suitable type of supervision throughout their TB treatment. This study also showed that unsuccessful treatment outcomes were significantly associated with the adult and elderly age group, male gender, foreigners, rural residential area, HIV-positive, moderate and far-advanced changes in CXR findings, but a significant decrease in the risk of unsuccessful treatment outcomes among the Chinese ethnicity and tertiary education. Tailored TB control strategies should expand risk stratification beyond existing MOH high-risk groups to include males, the elderly, foreign nationals, rural residents, and those with abnormal radiological findings, with strengthened screening and supervision to improve treatment outcomes.<sup>4</sup>

## ETHICS APPROVAL

Ethics approval was obtained from Medical Research & Ethics Committee Ministry of Health, Malaysia (NMRR ID-24-00625-IVT(IIR)).

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**AUTHOR CONTRIBUTIONS**

MHSAJ and RAZ conceptualized and designed the study. ZS, NAH, and MKHZ were responsible for data acquisition. MHSAJ conducted the data analysis and prepared the initial draft of the manuscript. All authors critically revised the manuscript and approved the final version for submission.

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