THE PREVALENCE OF DRUG-RESISTANT TUBERCULOSIS (DR-TB) AND RISK FACTORS FOR UNFAVOURABLE TREATMENT OUTCOMES IN SELANGOR AND WILAYAH PERSEKUTUAN KUALA LUMPUR (WPKL), MALAYSIA

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by

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LIST OF SYMBOLS

<	Less than
>	More than
=	Equal to
≤	Less than and equal to
≥	More than and equal to
%	Percentage
α	Alpha
β	Beta
Δ	Precision

LIST OF ABBREVIATIONS

AdjOR	Adjusted odds ratio
AMR	Antimicrobial resistance
Crude OR	Crude odds ratio
DOSM	Department of Statistics Malaysia
DOTS	Directly observed therapy short course
DR-TB	Drug-resistant tuberculosis
DST	Drug sensitivity testing
HIV	Human Immunodeficiency Virus
HR-TB	Isoniazid resistant tuberculosis
MDR-TB	Multidrug-resistant tuberculosis
MOH	Ministry of Health Malaysia
Pre-XDR-TB	Pre-extensively drug-resistant tuberculosis
RR-TB	Rifampicin resistant tuberculosis
SPSS	Statistical Package for Social Sciences
TB	Tuberculosis
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis

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PREVALENS KES KERINTANGAN ANTI-TIBI DAN FAKTOR RISIKO TERHADAP KETIDAKSEMPURNAAN HASIL RAWATAN DI SELANGOR DAN WILAYAH PERSEKUTUAN KUALA LUMPUR (WPKL), MALAYSIA

ABSTRAK

Pendahuluan: Kes kerintangan anti-tibi merupakan beban kesihatan global yang memberikan impak besar terhadap kadar morbiditi dan mortaliti penduduk. Peningkatan kes dapat dilihat di Malaysia sejak beberapa tahun yang lalu. Rawatan yang efektif dan sistematik mampu menyelamatkan nyawa pesakit namun ketidaksempurnaan rawatan menjadi faktor penghalang. Kajian ini dijalankan bertujuan menentukan kadar prevalens dan faktor-faktor yang mempengaruhi ketidaksempurnaan hasil rawatan di kalangan pesakit kerintangan anti-tibi di Selangor dan WPKL dari tahun 2016 sehingga 2020. **Kaedah:** Kajian ini mempunyai dua komponen: kadar prevalens dan analisis berbentuk kes dan kawalan, menggunakan data sekunder yang diperolehi daripada pangkalan data tuberkulosis kebangsaan (MyTB). Semua kes kerintangan anti-tibi yang dilaporkan dalam MyTB antara tahun 2016 sehingga 2020 dan memenuhi kriteria kajian telah dianalisa. Sebanyak 181 kes dengan ketidaksempurnaan hasil rawatan diletakkan dalam kumpulan kes manakala kes yang dengan hasil rawatan sembuh dan sempurna rawatan diletakkan dalam kumpulan kawalan berjumlah 222 kes. Analisa regresi logistik berganda telah digunakan untuk menentukan faktor yang mempengaruhi ketidaksempurnaan hasil rawatan. **Keputusan:** Kadar prevalens kes kerintangan anti-tibi di Selangor dan WPKL menunjukkan aliran meningkat dari tahun 2016 sehingga 2020, dengan julat antara 0.31 dan 1.83 setiap 100,000 penduduk. Kes kerintangan anti-tibi dengan

ketidaksempurnaan rawatan menyumbang sebanyak 42%. Faktor-faktor signifikan yang mempengaruhi ketidaksempurnaan rawatan di kalangan kes kerintangan anti-tibi adalah jantina lelaki (AdjOR 2.38; 95% CI: 1.44, 3.94), bujang dan bercerai (AdjOR 1.61; 95% CI: 1.03, 2.49), tiada pendidikan formal (AdjOR 3.09; 95% CI: 1.49, 6.41), positif HIV (AdjOR 2.87; 95% CI: 1.40, 5.87), jenis kerintangan RR-TB (AdjOR 3.34; 95% CI: 1.90, 5.86) dan jenis kerintangan MDR/ Pre XDR/ XDR-TB (AdjOR 2.57; 95% CI: 1.52, 4.33). **Kesimpulan:** Justeru, ketidaksempurnaan rawatan di kalangan kes kerintangan anti-tibi ini perlu dititikberatkan melalui intervensi kesihatan awam yang menyeluruh dan melibatkan komitmen semua pemegang taruh. Kajian pada masa mendatang perlu meneliti parameter-parameter lain dan mendorong usaha untuk pengumpulan data pemboleh ubah penting tambahan dalam pangkalan data pemantauan bagi keseluruhan kes tuberkulosis.

KATA KUNCI: tuberkulosis, kerintangan anti-tibi, ketidaksempurnaan hasil rawatan, prevalen, faktor berkaitan

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ABSTRACT

Introduction: Drug-resistant TB (DR-TB) is a global public health burden that causes high morbidity and mortality among the population. The increase in DR-TB cases has become evident in Malaysia over the past few years. Effective and systematic treatment can save lives; however, unfavourable treatment outcomes are a barrier. This study aims to determine the prevalence rate and the associated factors with unfavourable treatment outcomes among DR-TB patients in Selangor and WPKL from 2016 to 2020. **Methods**: This study has two components: prevalence rate and case-control analysis, utilizing secondary data obtained from the National Tuberculosis Surveillance Database (MyTB). All reported DR-TB cases in MyTB between 2016 and 2020 that met the study criteria were analysed. The case group consists of 181 DR-TB cases with unfavourable treatment outcomes, whereas the control group consists of 222 DR-TB cases with favourable treatment outcomes. Multiple logistic regression was used for data analysis. **Results**: There was an increment in the prevalence rate of DR-TB cases in Selangor and WPKL from 2016 to 2020, from 0.31 to 1.83 per 100,000 population. DR-TB cases with unfavourable treatment outcomes accounted for 42%. The significant factors associated with unfavourable treatment outcomes among DR-TB cases were male (AdjOR 2.38; 95% CI: 1.44, 3.94), single and divorced (AdjOR 1.61; 95% CI: 1.03, 2.49), receive no formal education (AdjOR 3.09; 95% CI: 1.49, 6.41), HIV positive (AdjOR 2.87; 95% CI: 1.40, 5.87), DR-TB category for RR-

TB (AdjOR 3.34; 95% CI: 1.90, 5.86) and MDR/ Pre-XDR/ XDR-TB (AdjOR 2.57; 95% CI: 1.52, 4.33). **Conclusion**: Therefore, unfavourable treatment outcomes among DR-TB cases should be tackled through holistic public health interventions involving commitment from all stakeholders. Future studies need to explore other parameters as well as drive efforts to start capturing additional significant variables in the surveillance database for all TB cases.

KEYWORDS: tuberculosis, drug resistance, unfavourable treatment outcomes, prevalence, associated factors

CHAPTER 1

INTRODUCTION

1.1 Introduction of Tuberculosis

Tuberculosis (TB) is an endemic airborne infectious disease in Malaysia. It is caused by *Mycobacterium tuberculosis* and primarily affects the lungs, known as pulmonary TB, but also can affect other parts of the body, referred to as extrapulmonary TB. In order to boost TB management, the End TB strategy has been initiated to reduce TB incidence by 90% and reduce with TB death by 95% by 2035 compared to 2015 rates (WHO, 2020b). According to the WHO Tuberculosis Report 2020, around 10 million people worldwide were infected with TB in 2019, resulting in 1.2 million TB-related deaths. The bulk of TB cases in 2019 were concentrated in the WHO regions of Southeast Asia (44%), where Malaysia is located. Indonesia (8.5%) and the Philippines (6.0%) account for two-thirds of total global cases, with TB prevalence rates of 395/100,000 and 322/100,000 people, respectively (WHO, 2020a).

Malaysia is an intermediate TB burden country, with a TB notification rate ranging from 10 to 99 cases per 100,000 population (WHO, 2020b). Malaysia has a TB prevalence rate of 92 per 100,000 population (Bernama, 2019). Supplemented with the WHO End TB Strategy, the Ministry of Health Malaysia released the National Strategic Plan for Tuberculosis Control (2016–2020) to guarantee that eliminating TB by 2035 is met. Ending TB necessitates a significant shift in national TB control operations, emphasising on patient-centred TB care and universal access to high-quality diagnostic and treatment approaches.

1.2 The Emergence of Drug-Resistant Tuberculosis

Although tuberculosis is a treatable and preventable disease, the rise of drug-resistant tuberculosis (DR-TB) complicates matters. According to WHO Consolidated Guidelines on Tuberculosis, DR-TB is defined as TB disease caused by a strain of *Mycobacterium tuberculosis* (MTB) complex that is resistant to any TB medicines. Genetic mutations in MTB have led to the development of resistance, causing specific treatments or medications to lose their effectiveness against the pathogen (MOH, 2016a). Drug sensitivity testing (DST) in clinical isolates confirmed to be MTB defines monodrug-resistant TB, polydrug-resistant TB, isoniazid-resistant TB (HR-TB), multidrug-resistant TB (MDR-TB), extensively drug-resistant TB (XDR-TB), and rifampicin-resistant TB (RR-TB) (MOH, 2016b). WHO's Global TB Programme changed the definition of XDR-TB in October 2020, defining pre-XDR TB for the first time. The updated pre-XDR and XDR-TB classifications went into effect in January 2021 (WHO, 2021b).

Globally, 500,000 people developed RR-TB, with 78% developing MDR-TB (WHO, 2020a). Bangladesh, China, India, Indonesia, Myanmar, Nigeria, Pakistan, the Philippines, the Russian Federation, and South Africa are the top ten DR-TB high-burden countries (HBCs), accounting for 70% of the worldwide DR-TB burden. More than half of the worldwide burden is borne by India (27%, 130,000 cases), China (14%, 66,000 cases), and the Russian Federation (9%, 41,000 cases) (Monedero-Recuero *et al.*, 2021). In Malaysia, 192 DR-TB patients were reported in 2019, comprising 61 MDR-TB cases, 42 RR-TB cases, 62 HR-TB cases, 3 XDR-TB cases, and the remaining 25 cases resistant to various anti-TB medications (MOH, 2020). Therefore, appropriate preventive measures, adapted to the local context and incorporated into the National Tuberculosis Plan (NTP), are required to combat DR-TB.

1.3 Strengthening Strategy in Combating Drug-Resistant Tuberculosis

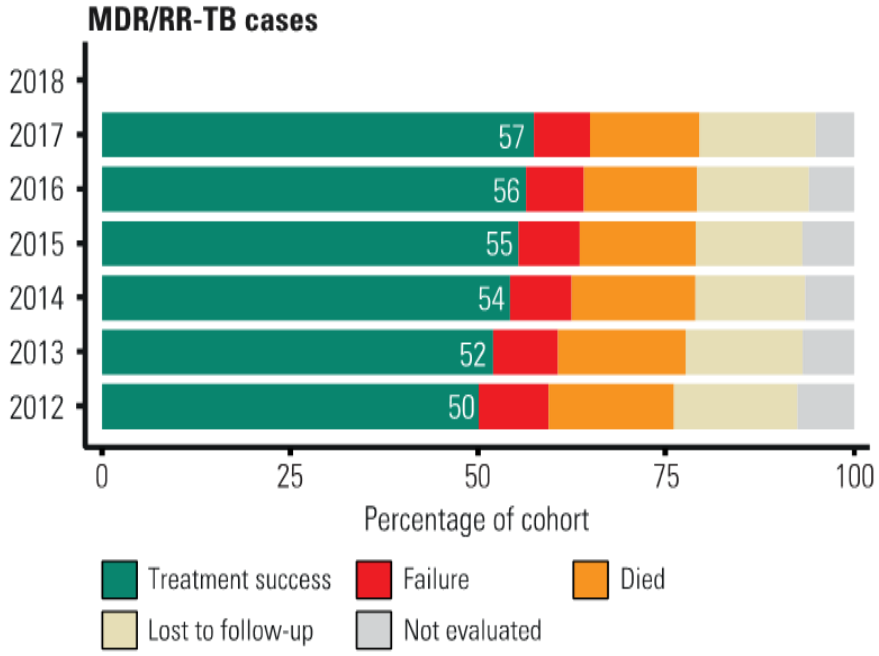
Malaysia is enhancing its programmatic management of DR-TB through the fourth strategy, which constitutes a crucial element of integrated, patient-centred treatment and prevention efforts. The main focal points of this strategy involve the early detection of DR-TB cases and the improvement of treatment for DR-TB patients (MOH, 2016b). Therefore, treatment failure and interruption cases, close contacts with DR-TB patients, and positive diagnoses with TB culture and DST should all be suspected of DR-TB.

Treating patients with DR-TB infections are more complex, costly, needs strict infection control measures, and involves a longer duration of treatment than treating patients with susceptible TB strains. Furthermore, it takes into consideration the potential toxicity and adverse effects of the anti-TB regimen instituted (MOH, 2016a). Management of DR-TB also incurs devastating economic impact, which involves high budget allocation. According to Atif *et al.* (2014), the overall average cost of TB treatment (from both the provider and patient perspectives) was MYR 2,218.14 (USD 727.24 per patient). In addition, government hospitals spend RM250 on the six-month treatment cost per patient. Meanwhile, for MDR-TB, the cost reaches RM8000 to RM 16000 and could be up to RM100,000 for XDR-TB per patient (Bernama, 2018).

1.4 Treatment Outcomes of Drug-Resistant Tuberculosis

As shown in Figure 1, data on treatment outcomes for MDR/RR-TB patients revealed an increment from 2012 to 2018, with an estimated global treatment success rate of 57% in 2017 (WHO, 2020a). The following are the main metrics for Strategy 4 National Strategic Plan for Tuberculosis Control (2016–2020): Notification of MDR-TB accounts for fewer than 3% of all TB cases, and the treatment success rate for DR-

TB is 90%. In 2019, Malaysia's treatment success rate for MDR/RR-TB was about 55% (MOH, 2020). Goroh *et al.* (2020) conducted research on DR-TB in Sabah and discovered that treatment effectiveness was 83% (range: 81–85%) in individuals with drug-sensitive TB and 36% (range: 25–45%) in MDR-TB patients. As a result, it signifies the need for more research to understand variables associated with poor treatment results among DR-TB patients in Malaysia.



(Source: WHO Global Tuberculosis Report 2020)

Figure 1.1 Global treatment outcomes for MDR/RR-TB cases, 2012-2018

The operational definitions of TB treatment outcomes were derived from the World Health Organisation's (WHO) "Definitions and Reporting Framework for Tuberculosis: 2013 Revision" (updated in December 2014 and January 2020). These definitions were adopted by the local Clinical Practice Guidelines on Tuberculosis in Malaysia (MOH, 2022).

The TB treatment outcomes were categorised into two primary groups: "successful outcomes", which encompassed "cured" and "completed treatment" and "unsuccessful outcomes", including "death", "treatment failure", and "loss to follow-up". However, in some studies, the terms "favourable treatment outcomes" and "unfavourable treatment outcomes" were preferred over "successful" and "unsuccessful" outcomes. This terminological preference can be observed in a few studies, such as Liew *et al*. (2015), Ma *et al*. (2022), and Bogale *et al*. (2021). Despite the variation in terminology, these terms essentially refer to the same outcome components.

1.5 Problem Statement

The escalating global and local burden of drug-resistant tuberculosis (DR-TB), including its impact on Malaysia, underscores the urgency of addressing this pressing issue. Moreover, the influence of globalisation and extensive migrations has contributed to the occurrence and spread of the disease. Therefore, it is essential for stakeholders and various agencies to engage in continuous efforts, including strengthening surveillance systems, developing strategies, guidelines, and enforcement measures.

It is worth emphasizing that the emergence and spread of DR-TB are fuelled by several key factors. Among these are inadequate or inconsistent treatment practises, direct transmission from infected individuals, and non-adherence to anti-TB medications, all of which play pivotal roles in driving the development of drug resistance (MOH, 2012). Importantly, DR-TB is marked by a distressingly high mortality rate and exerts devastating economic consequences on the nation, patients, and their families (MOH, 2016a). Consequently, the treatment strategy plays a critical role in determining treatment outcomes. Given the previously reported low success

rate of DR-TB treatment, further research becomes imperative. Regrettably, the dearth of local studies examining the factors associated with unfavourable treatment outcomes among DR-TB cases in Malaysia poses a significant gap in our understanding of the issue.

1.6 The Study Rationale

The findings from this study may help Ministry of Health and researchers better understand the burden of DR-TB and the factors that contribute to it. Selangor and WPKL were selected as the focus areas due to the substantial number of DR-TB patients in these states. Additionally, their high population density, particularly in urban areas inhabited by individuals from lower socioeconomic backgrounds and migrant workers, warrants the crucial need for research. Knowing the factors associated with unfavourable treatment outcomes, this research will contribute to the refinement of strategic planning for managing DR-TB cases. The ultimate objective is to decrease morbidity, mortality, and the economic burden linked to the disease.

1.7 Research Questions

1. What is the prevalence of DR-TB cases in Selangor and WPKL from 2016 to 2020?

2. What were the risk factors for unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL from 2016 to 2020?

1.8 Objectives

1.8.1 General Objective

To determine the prevalence and investigate the risk factors for unfavourable treatment outcomes among DR-TB patients in Selangor and WPKL from 2016 to 2020.

1.8.2 Specific Objective

1. To determine the prevalence of drug-resistant tuberculosis (DR-TB) cases in Selangor and WPKL from 2016 to 2020.
2. To describe the sociodemographic characteristics and clinical characteristics of drug-resistant tuberculosis (DR-TB) cases in Selangor and WPKL from 2016 to 2020.
3. To investigate the risk factors for unfavourable treatment outcomes among drug-resistant tuberculosis (DR-TB) cases in Selangor and WPKL from 2016 to 2020.

1.9 Research Hypothesis

There are associations between sociodemographic (age, gender, ethnicity, nationality, level of education, marital status, employment status) and clinical characteristics (diabetes mellitus, HIV status, type of drug-resistant, smear positivity, chest x-ray status, DOTS supervision, treatment category, smoking history) with unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL.

2

LITERATURE REVIEW

Several literatures from various countries, including Malaysia, were studied to explore the epidemiology of DR-TB and factors associated with unfavourable treatment outcomes. Bibliographic databases, including PubMed, Scopus, and Google Scholar, were used to search for literature. Keywords such as prevalence, incidence, drug resistance, TB, Malaysia, factors associated, and treatment outcomes were used to filter recent literature aged less than ten years. As a search method, Boolean operators such as "AND", "OR", and "NOT" were used.

Therefore, the aim of the literature review in the first place is to search recent and relevant data pertaining to DR-TB at the global, regional, and country levels. Several studies and publications from the World Health Organization (WHO) website were reviewed, including blueprints such as the End TB Strategy and the Sustainable Development Goals (SDGs). In addition, national TB guidelines and circulars from the Ministry of Health (MOH) Malaysia have been reviewed to understand the theoretical aspect, operational definitions, current practices, and recommendations. Good social support, financial capability, empowerment of patient education and accessibility to health care determine the favourable outcome of treatment (MOH, 2016).

2.1 The Burden of Drug-Resistant Tuberculosis

Tuberculosis (TB) remains a global public health concern. However, despite enormous efforts, the emergence of drug-resistant TB (DR-TB) further complicates TB prevention and control programs. In 2019, MDR/RR-TB was reported in 3.3% of new TB patients and 18% of previously treated cases. In addition, TB is often associated with disease of poverty, vulnerability, stigmatisation in the community and discrimination (WHO

2020a). There were 465,000 incident cases of RR-TB (range: 400,000–535,000), with 78% having MDR-TB. India (27%), China (14%), and the Russian Federation (8%) contributed the most to the world load. During the same year, HR-TB was found in an estimated 13.1% of new cases and 17.4% of previously treated patients (WHO, 2020a).

Increasing number of DR-TB cases can be attributed to several factors such as insufficient treatment, poor adherence to medication regimens, and the spread of drug-resistant strains within communities. Antibiotic misuse, both in the healthcare system and in the private sector, has also contributed to the rise of drug resistance (WHO, 2020).

Addressing the emergence of DR-TB necessitates a multifaceted and comprehensive strategy. The WHO emphasises the significance of expanding access to quality diagnostic tools, guaranteeing correct treatment regimens, and improving surveillance and monitoring systems. Collaboration is vital for developing and implementing successful policies among healthcare professionals, policymakers, and international organisations. Furthermore, efforts should be directed towards promoting awareness among healthcare professionals, communities, and those at risk in order to encourage early identification, prompt treatment, and drug adherence (WHO, 2021).

2.2 Prevalence of Drug Resistance Tuberculosis

MDR-TB is defined as resistance to two of the most effective anti-TB medications, isoniazid, and rifampicin, which initially emerged as a threat to global TB control in the 1990s (WHO, 2021b). The DR-TB burden generally poses an intense challenge to the prospect of TB control. DR-TB detection rate in Malaysia is lower than global estimates, and many are still undetected or notified (MOH, 2016). The prevalence of DR-TB varies among countries. One study carried out in Sabah, Malaysia by Goroh *et*

al. (2020) revealed that MDR-TB prevalence was 0.3% of TB cases. The research was based on an assessment of 33,193 TB cases recorded in Sabah between 2012 and 2018 from the MyTB database. In the Western Pacific Region (WPR), the notification rate for MDR/RR-TB in 2020 was approximately 2.32%, slightly higher than the global rate of 2.15% (WHO, 2021a). The Western Pacific Regional Framework to End TB (2021–2030) reported around 101,000 people with MDR/RR-TB in 2019, representing a rate of 5.2 per 100,000 population. In Malaysia, the overall incidence of MDR/RR-TB in 2021 was 1.6 per 100,000 population, with 0.94% among new cases and 19.0% among retreatment cases (WHO, 2022b). MDR/RR-TB rates in Indonesia were reported as 2.8% among new cases and 16.0% among retreatment cases (Chadha, 2018). Thailand, on the other hand, had an estimated 2.2% of new TB cases and 24.0% of MDR/RR-TB retreatment patients (Bhatia, 2018).

Meanwhile, of 188 cases of DR-TB in one hospital in Bangkok, Thailand, from 2010 to 2012, the prevalence was 2.6% (Jitmuang *et al*., 2015). Several other studies have documented DR-TB prevalence rates ranging from 3.0% to 5.0%. Amin *et al.* (2021) conducted a study in Ethiopia and reported a prevalence rate of 3.8%. Similarly, Al Ammari *et al*. (2018) and Sambas *et al*. (2020) conducted studies in Saudi Arabia and found prevalence rates of 4.4% and 5.0%, respectively.

2.3 Diagnosis and Management of Drug Resistance Tuberculosis Cases

The five categories used by WHO to classify DR-TB cases are isoniazid-resistant TB (HR-TB), rifampicin-resistant TB (RR-TB), multidrug-resistant TB (MDR-TB), pre-extensively drug-resistant TB (pre-XDR-TB), and extensively drug-resistant TB (XDR-TB). In addition to bacteriological confirmation of TB, drug-resistance must be assessed using rapid molecular testing, culture methods, or sequencing technologies. The WHO

recommends a course of second-line medicine for at least nine months and up to 20 months, together with counselling and side effect monitoring (WHO, 2021). WHO anticipated in 2019 that 17.4% (95% CI: 0.5–54) of previously treated patients and 13.1% (95% CI: 9.9–16.9) of new cases worldwide would acquire HR-TB (WHO, 2020a). A similar trend is observed globally, in which HR-TB is the commonest DR-TB in Malaysia, followed by RR-TB and MDR-TB, which contribute 45% of total cases. However, drug-resistance diagnostic algorithms are prone to rifampicin-resistant cases and have inadequate testing coverage for isoniazid-resistant cases. As a result of this condition, HR-TB patients may not be treated with the WHO-recommended modified regimen, risking poor treatment results and the development of further resistance (WHO, 2020a).

2.4 The Treatment Success Rate of Drug Resistance Tuberculosis Cases

The global surveillance and treatment of DR-TB are based on three primary categories: RR-TB, MDR-TB, and MDR-TB with added fluoroquinolone resistance. Treatment for all types of DR-TB requires a second-line regimen, which typically lasts between nine and 20 months, and it must be accompanied by counselling and monitoring for adverse effects (WHO, 2016; WHO, 2021). The duration of treatment can be adjusted based on the patient's response, with the shorter MDR-TB regimen typically lasting 9–12 months (MOH, 2016a). In Malaysia, the enrollment rate of DR-TB cases in second-line treatment was 84.4% overall, with Selangor and WPKL achieving rates of 86.0% and 79.3%, respectively, in 2020 (Halim, 2022).

In 2018, the global treatment success rate for MDR/RR-TB was 59% (WHO, 2021). Several studies from various countries found a higher treatment success rate compared to global data, such as 63.9% in Pakistan (Khan *et al*., 2022), 65.5% in

Vietnam (Wrohan *et al.*, 2022), and 77.12% in Ethiopia (Belachew *et al.*, 2022). However, studies conducted in our countries showed different results. For example, Goroh *et al.* (2020) showed the rate was 36% (range: 25–45%) in Sabah, and Elmi *et al.* (2015) reported 17.1% in a study represented by five referral TB hospitals in Peninsular Malaysia based on the highest prevalence of MDR-TB in each centre.

2.5 Factors Associated with Unfavourable Treatment Outcomes among Drug-Resistance Tuberculosis

Unfavourable treatment outcomes in the context of TB refer to patients who experience treatment failure, death, or loss of follow-up. According to the World Tuberculosis Report 2020, the 2017 cohort of DR-TB cases had a 43.0% proportion of unfavourable outcomes, consisting of loss to follow-up (16.0%), death (15.0%), and treatment failure (7.0%). The report did not provide outcome information for the remaining 5.0% of cases. In Thailand, our neighbouring country, higher rates of loss to follow-up (28.0%), followed by death (18.0%) and treatment failure (2.6%) were reported (Bhatia, 2018).

In contrast, according to MOH Malaysia, a significant number of DR-TB cases in the country had unfavourable treatment outcomes, with death being the most common outcome (24.4%), followed by loss to follow-up (7.0%), and treatment failure (3.5%) (Halim, 2022). Ethiopia also reported, a high proportion of unfavourable treatment outcomes, with death (9.25%) being the highest, followed by loss to follow-up (6.94%) and treatment failure (3.1%) (Belachew *et al.*, 2022). Treating DR-TB is more challenging than treating drug-sensitive tuberculosis due to the need for a longer and more expensive therapy, which may come with potential adverse side effects (MOH, 2016).

Several factors are associated with unfavourable treatment outcomes among DR-TB patients. Elmi *et al.* (2015) found that HIV infection (AdjOR 1.09; 95% CI: 1.05, 1.75) and past TB treatment (AdjOR 4.87; 95% CI: 2.84, 8.38) were significant variables associated with unfavourable treatment outcomes. Khan *et al.* (2022) conducted a study in Pakistan involving 277 DR-TB patients and revealed that unsuccessful outcomes were statistically associated with being male (AdjOR 1.92; 95% CI: 1.10, 3.36), being in an age group above 60 years (AdjOR 3.34; 95% CI: 1.09, 10.1), having comorbidities (AdjOR 2.69; 95% CI: 1.35, 5.38), and a history of using second-line drugs (AdjOR 3.51; 95% CI: 1.35, 9.12).

In addition, based on the study conducted in Xi'an Province, China from 2017 to 2019 involving 446 DR-TB cases, Ma *et al*. (2022) found that age of more than 40 years (AdjOR 5.51; 95% CI: 2.52, 12.07), absence of fluoroquinolones in the regimen (AdjOR 3.31; 95% CI: 1.45, 7.51), and smear-positive status (AdjOR 4.0; 95% CI: 1.47, 10.8) were factors related with unfavourable treatment outcomes in DR-TB patients. Wrohan *et al.* (2022) conducted a retrospective cohort study in two provinces in Vietnam from 2014 to 2016 involving 662 participants and concluded the odds of treatment success were lower for male patients (AdjOR 0.56; 95% CI: 0.34, 0.90), for people living with HIV (AdjOR 0.44; 95% CI: 0.20, 1.00), and for patients treated for extensive antibiotic resistance (pre-XDR-/XDR-TB) (AdjOR 0.53; 95% CI: 0.29, 0.97), compared with others. In a retrospective study conducted at a South Korean tertiary referral hospital involving 195 patients with HR-TB cases, several factors were found to be associated with unfavourable outcomes, including smoking history (AdjOR 5.61; 95% CI: 1.69, 18.54) and positive culture at 2 months (AdjOR 7.85; 95% CI: 1.25, 49.51) (Kwak *et al*., 2020)

2.6 Conceptual Framework

The framework (Figure 1) shows the possible factors that may associate with treatment outcomes among drug-resistant TB cases. The factors are broadly classified into sociodemographic and clinical characteristics. Sociodemographic factors consisted of age, gender, ethnicity, nationality, level of education, marital status, and employment status. Meanwhile, clinical characteristics include comorbidities, current DR-TB treatment, treatment category, and social history. Treatment outcomes will be either favourable or unfavourable.

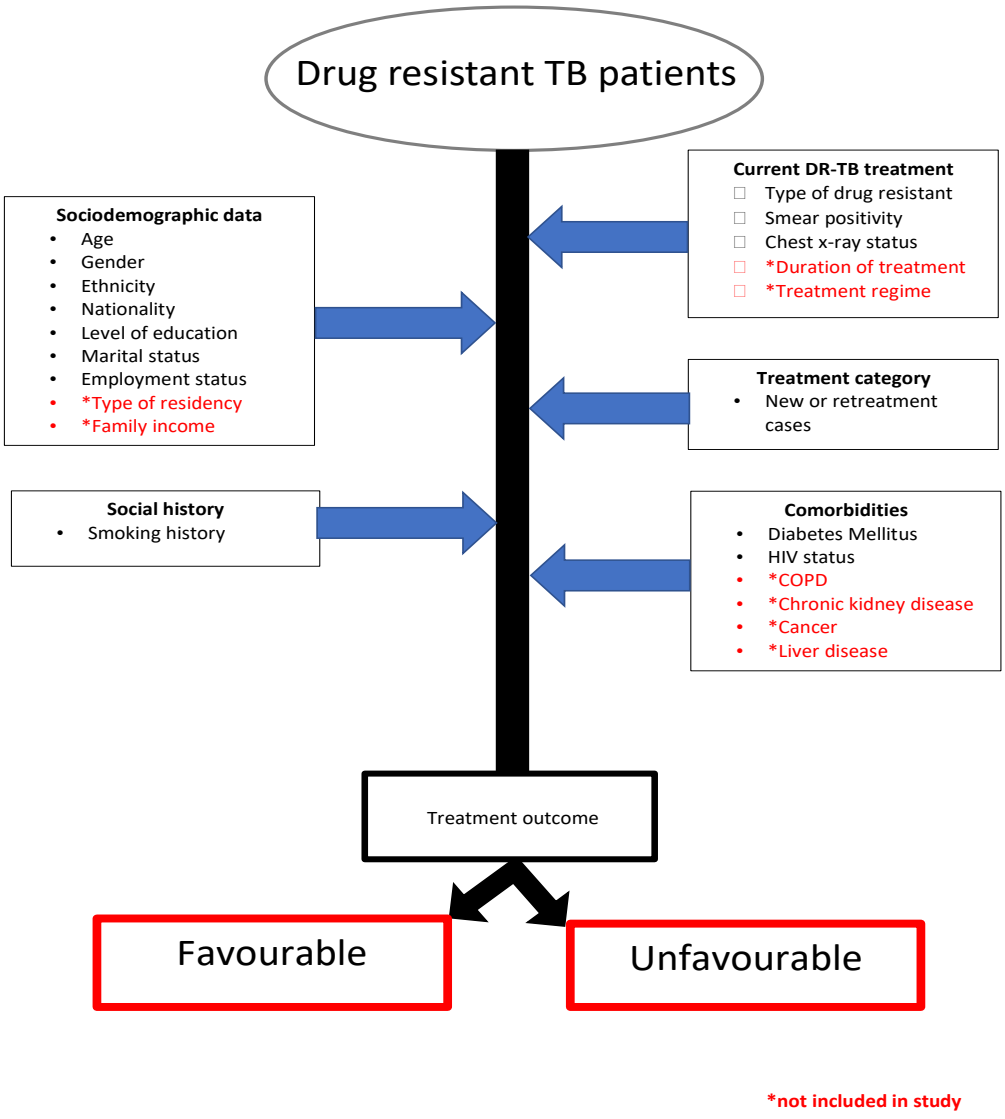


Figure 2.1 Conceptual framework for the factors associated with unfavourable treatment outcomes among drug resistant TB

3

METHODOLOGY

3.1 Study Design

This study has two components: prevalence rate and case-control analysis, utilizing secondary data obtained from the National Tuberculosis Surveillance Database (MyTB). The case group consists of individuals with drug-resistant tuberculosis (DR-TB) who experienced unfavourable treatment outcomes, while the control group comprises individuals with DR-TB who achieved favourable treatment outcomes. The ratio of cases to controls was 1:1.

3.2 Study Duration

This study started from November 2022 to June 2023.

3.3 Study Location

This study was carried out in Selangor and the Wilayah Persekutuan Kuala Lumpur (WPKL). Selangor, with 6.9 million population, is the state with the greatest Malaysian population composition, at 21.6% in 2020. Selangor has a population density of 880 people per square kilometre. Meanwhile, WPKL, with 1.9 million population, has the greatest population density, with 8,045 people per square kilometre (DOSM, 2022).

The male-to-female population ratio in both states is nearly identical, with 53.1% and 46.9% in Selangor and 53.4% and 46.6% in WPKL. Immigrants account for 8.1% (563,988 individuals) of the total population in Selangor, but WPKL has a greater proportion of immigrants at 10.5% (208,446 individuals). As a result, there are about 800,000 immigrants in these two states. In terms of public health care, Selangor has 13 hospitals, and WPKL has three (DOSM, 2022).

The data collection for this study was carried out in three main places: the Selangor State Health Department, Kuala Lumpur and Putrajaya State Health Department, and Institut Perubatan Respiratori (IPR). The locations of these three places are shown in Figure 3.1. IPR began in 1958 as a tuberculosis clinic on Jalan Pahang. In order to combat the TB epidemic in Malaysia, the Ministry of Health (MOH) changed the name of this facility to the National Tuberculosis Centre in 1961. The increase in the variety of respiratory services offered resulted in its rebranding as IPR in 1996 (MOH, 2021). As one of its core services, it handles most referrals for expert TB management, including DR-TB, primarily from Selangor and WPKL.

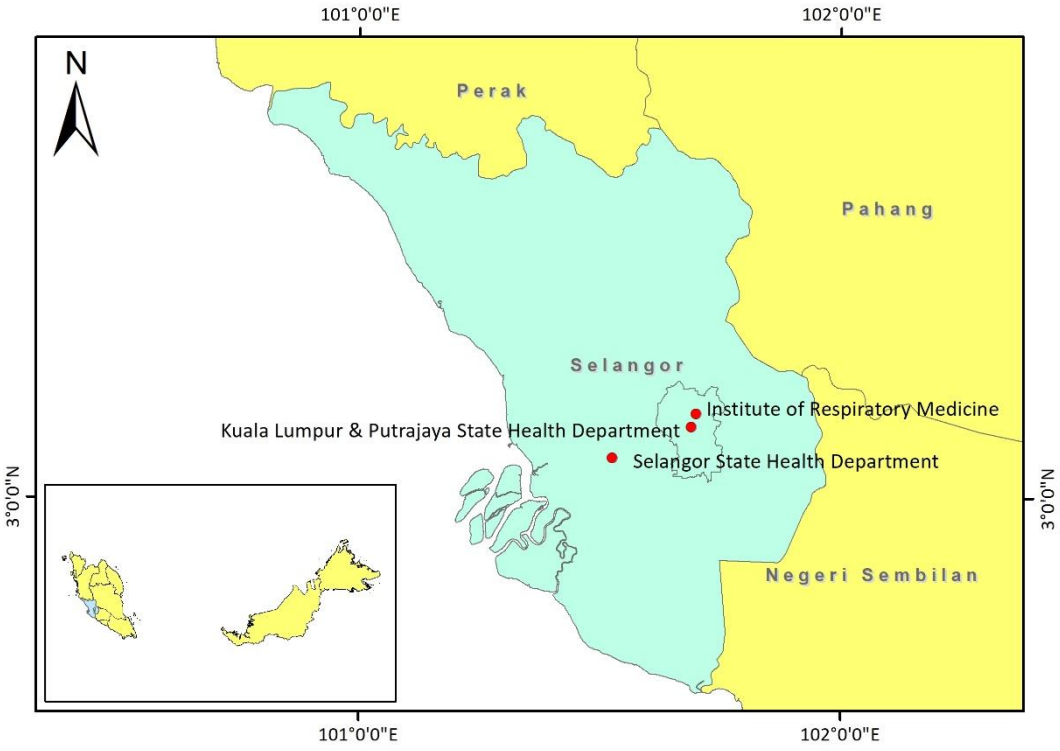


Figure 3.1 The locations of Selangor State Health Department, Kuala Lumpur and Putrajaya State Health Department and Institute of Respiratory Medicine

3.4 Study Population

3.4.1 Reference Population

DR-TB cases in Selangor and WPKL.

3.4.2 Source Population

DR-TB cases in Selangor and WPKL registered in MyTB from 2016 to 2020.

3.4.3 Sampling Frame

DR-TB cases in Selangor and WPKL registered in MyTB from 2016 to 2020, fulfilling inclusion and exclusion criteria.

3.5 Study Criteria

3.5.1 Inclusion Criteria

a. DR-TB cases registered in MyTB from 2016-2020.

b. Cases residing in Selangor and WPKL.

3.5.2 Exclusion Criteria

a. Missing or incomplete data of DR-TB cases > 30%. (The missing or incomplete data will interfere with independent data information and later affect the accuracy of data analysis).

b. Cases with ongoing DR-TB treatment, i.e. those who have not completed treatment.

3.6 Sample Size Calculation

The sample size was calculated in line with the objectives. For objective 1 (To determine the prevalence of DR-TB in Selangor and WPKL from 2016 to 2020 per 100,000 population), the sample size was estimated based on single proportion formula (as shown below) using a web sample size calculator (*https://wnarifin.github*). The estimated sample size is shown in Table 3.1.

$$n = \left(\frac{Z \ \left(1 - \frac{\alpha}{2}\right)}{\Delta} \right)^2 \ P(1-p)$$

Where,

n: number of samples

$Z_{1-\alpha/2:}$ level of confidence, set at 95%

α: Type I error, set at 0.05

Δ: Precision of estimation

P: The population proportion (from literatures, pilot study, experts)

Table 3.1 Sample size calculation for Objective 1

α	Δ	**P**	**n**	**n+10%***
0.05	0.0015	0.003	5107	5675

*Consider adding 10% to the sample size to account for data entry error, missing data, and outliers

The proportion was derived from research done in Sabah, Malaysia, by Goroh *et al.* (2020), which estimated the prevalence of MDR-TB infections to be 0.3%. The computed sample size was 5675 after accounting for an additional 10% of the potential of missing or incomplete data.

For objective 3 (To determine the association of sociodemographic and clinical characteristics with unfavourable treatment outcomes among drug-resistant tuberculosis (DR-TB) cases in Selangor and WPKL from 2016 to 2020), the online sample size calculator was used (https://wnarifin.github) to calculate the sample size based on the Two Independent Proportions formula. Table 3.2 shows the estimated sample size.

Table 3.2 Sample size calculation for Objective 3

Factors	P_0	P_1	m	n	n+ 10%*	Reference
Male	0.56	0.40	1	152	169	Khan *et al.*, 2022
Type of drug-resistant	0.40	0.55	1	173	193	Shariff *et al*., 2019
Past TB history	0.46	0.60	1	199	222	Elmi *et al.*, 2015
HIV co-infection	0.41	0.55	1	199	222	Wrohan *et al.*, 2022
Comorbid DM	0.21	0.35	1	161	179	Wrohan *et al.*, 2022
Smear positivity	0.64	0.50	1	196	218	Khan *et al.*, 2022
Smoking	0.35	0.50	1	170	189	Shariff *et al*., 2019

*Consider adding 10% to the sample size to account for data entry error, missing data, and outliers

P_0 = proportion of control (favourable treatment outcomes) obtained from the literature review

P_1 = estimated proportion of cases with unfavourable treatment outcomes

m = ratio of control to case

Power of study = 80%

$\alpha = 0.05$

3.7 Sampling Method and Subject Recruitment

The sample size estimated for Objective 1 was 5675, which represented the minimum required population size. This estimation is considered acceptable due to the fact that the population of Selangor and WPKL are approximately 7 million and 2 million, respectively, aligning well with the estimated sample size. All DR-TB cases in Selangor and WPKL registered in MyTB were included in determining the prevalence in a given year and in describing the sociodemographic and clinical characteristics. Meanwhile,

the largest sample size of 222 per group was required to answer Objective 3. For the case group, due to the limited number of cases with unfavourable outcomes, all cases were taken into the study. No sampling method was applied. The control group was chosen using a simple random sampling method from cases with favourable outcomes, as shown in the MyTB database.

3.8 Operational Definition

All the operational definitions used in this study follow the Notification and Reporting of Drug-Resistant TB (DR-TB) Cases, Ministry of Health Malaysia, 2020.

A) Drug-resistant tuberculosis

Drug-resistant TB is classified based on drug sensitivity testing (DST) in clinical isolates confirmed as *Mycobacterium tuberculosis* (MTB).

i) **Isoniazid-resistance tuberculosis (HR-TB):** resistance to isoniazid only and susceptibility to rifampicin confirmed in vitro.

ii) **Multidrug-resistance tuberculosis (MDR-TB):** resistance to at least both isoniazid and rifampicin.

iii) **Pre-extensively drug resistance tuberculosis (Pre-XDR-TB):** resistance that fulfilled the definition of MDR/RR-TB and that is also resistant to any fluoroquinolone.

iv) **Extensively drug-resistance tuberculosis (XDR-TB):** resistance that fulfilled the definition of MDR/RR-TB and that is also resistant to any fluoroquinolone and at least one additional Group A drugs (levofloxacin or moxifloxacin, bedaquiline and linezolid).

v) **Rifampicin-resistance tuberculosis (RR-TB):** resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to

other anti-TB drugs. It includes any resistance to rifampicin, in the form of mono-resistance, polydrug-resistance, MDR or XDR.

B) Treatment outcomes

i) **Cured**

Treatment completed as recommended without evidence of failure, AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.

ii) **Treatment completed**

Completed as recommended without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.

iii) **Treatment failed**

Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of the following:

- lack conversion by the end of the intensive phase or
- bacteriological reversion in the continuation phase after conversion to negative or
- evidence of additional acquired resistance to fluoroquinolones or second line injectable drugs or
- adverse drug reactions (ADRs)

iv) **Died**

A TB patient who dies for any reason during TB treatment.

v) **Lost to follow-up**

A TB patient whose treatment was interrupted for two (2) consecutive months or more.

vi) **Not evaluated**

A TB patient with no treatment outcome is assigned (includes case transferred out to another unit whose treatment outcome is unknown.

vii) **Treatment success**

The sum of cured and treatment completed.

C) Favourable treatment outcomes

Refers to the treatment success group, which includes TB patients with the outcomes of cured and treatment completed.

D) Unfavourable treatment outcomes

Refers to TB patients with the outcomes of treatment failure, death, and loss to follow-up.

3.9 Research tools

The following research tools were used in this study.

i) National TB Surveillance Database – MyTB

All required anonymous dataset for this study was collected from National TB Surveillance Database (MyTB) involving three states managed by two separate state health departments: Selangor State Health Department and Kuala Lumpur and Putrajaya State Health Department. The electronic TB information system, MyTB 2.0, is a centralised TB database in Malaysia developed by Mr. Melvin bin Madarak and Sabah State Health Department in 2010. It was first introduced in 2011 and started its operation in 2012 (MOH, 2012b). It can be operated from the district health office level up to the Ministry of Health Malaysia headquarters, especially by enforcement officers, medical officers in charge of

the TB unit, epidemiology officers and medical officers of health. The users must have a username and password to access the data. It is very important in terms of preserving data confidentiality.

The system serves as a comprehensive platform for the management of both TB cases and contacts. It was based on the Tuberculosis Information System (TBIS). The system incorporates three main modules: TBIS 10A-1 for capturing initiation of TB treatment information, TBIS 10A-2 for recording monthly follow-up details of TB cases, and TBIS 10C for TB contact screening. MyTB contains various variables, including sociodemographic (name, gender, age, nationality, etc.), clinical (TB type, site of TB infection, previous TB history, etc.), laboratory parameters (sputum smear microscopy results, culture and sensitivity results, chest x-ray findings), treatment information (treatment start and completion date, treatment outcomes), follow-up status (follow-up visits, adverse drug reactions), and healthcare facility details (facility name, healthcare worker information).

ii) Line listing of DR-TB cases

Besides MyTB, the source of the data was the line listing of DR-TB cases that summarised information from TBIS 10G and DRTBIS 50A-1. Tuberculosis Information System (TBIS) 10G is specifically used for investigating TB cases that have failed first-line TB treatment, known as ‘gagal rawatan’. It provides a platform to gather relevant information pertaining to factors contributing to failed treatment. Meanwhile, the Drug-Resistance Tuberculosis Information System (DRTBIS) 50A-1 is designed to document information regarding the initiation of DR-TB treatment by respective treatment centres. It serves as a comprehensive database to capture essential details about the patients and their

treatment. The line listing is operated by the medical officer in charge of the TB/Leprosy Unit in the respective state health departments. Variables available are sociodemographic, clinical characteristics, registration category, risk factors, laboratory parameters, direct observed therapy short course (DOTS) information, and treatment outcomes.

iii) Proforma checklist

The desired data from MyTB and the line listing of DR-TB were extracted based on the Proforma Checklist (Appendix 1). The variables included in this study were broadly classified into sociodemographic and clinical characteristics.

iv) Population density for the state of Selangor and Wilayah Persekutuan Kuala Lumpur

The population statistics for these two states were obtained from the website of Department of Statistics Malaysia (DOSM) at http://www.dosm.gov.my/v1/index.php. to fulfil the first objective of this study.

3.10 Data Collection

The primary data sources for this study were the MyTB database and the line listing of DR-TB cases, with the latter serving as a data comparison to the registered cases in MyTB. The TB/Leprosy Unit is the gatekeeper for data access. Therefore, both state health directors were granted permission for data retrieval. In addition, permission was also obtained from the Director of the Institute of Respiratory Medicine in case of missing or inadequate data gathered from MyTb or line listing in those two state health departments. The Proforma Checklist was used as a guide to extract the desired data for this study. This interested variables were imported from MyTB into Microsoft Excel

format, and then the data was exported to IBM SPSS version 27 for data cleaning and analysis. Only the researcher has access to this password-protected document.

The data extracted were anonymised. In the data collection form, the case number refers to the subject identification number for this study. On subject data sheets, the subject number (such as 001, 002, 003) was used instead of personal identifiers. Personal identifiers such as name, registration numbers, address, identification card number, contact number, and registration number were not collected.

The variables included in this study encompass sociodemographic and clinical characteristics. Sociodemographic characteristics evaluated are age, gender, ethnicity, nationality, level of education, marital status, and employment status. The study also explored various clinical aspects, such as comorbidities, which include diabetes mellitus and HIV status; current DR-TB treatment including the type of drug-resistant TB, smear positivity, chest x-ray status, and DOTS supervision. The treatment category, whether cases are categorized as new or retreatment, was also considered. Lastly, the study investigates social history factors, with a focus on smoking history.

3.11 Statistical Analysis

IBM SPSS version 27 was used for data entry and analysis. The data was cleaned once it was entered. To discover any missing values, a preliminary data description was performed. The data set was reviewed for inaccuracies and corrected as necessary.

3.11.1 Prevalence of DR-TB in Selangor and WPKL from 2016 till 2020

For the first objective, the prevalence of DR-TB cases in Selangor and WPKL from 2016 to 2020 was calculated using the below formula. The results are presented as frequency (per 100,000 population).

$$\text{Prevalence} = \frac{\text{Total number of DR-TB cases in Selangor and WPKL in a given year}}{\text{Total population in Selangor and WPKL in a given year}} \times 100{,}000$$

3.11.2 Descriptive Statistics

Meanwhile, for the second objective, descriptive statistics were conducted for the sociodemographic (age, gender, ethnicity, nationality, level of education, marital status, employment status), clinical characteristics (comorbidities: diabetes mellitus and HIV status; current status of DR-TB: type of drug-resistant, chest x-ray status, and smear positivity; treatment category, DOTS supervision, and smoking status). With the exception of age, all data were categorical and summarised in frequency (n) and percentage (%). Treatment results were tallied for descriptive statistics and presented similarly to categorical data. Meanwhile, the numerical variable (age) was tested for data normality. Normally distributed data were presented as the mean and standard deviation (SD).

3.11.3 Factors associated with unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL

Simple and multiple logistic regression were used to examine factors associated with unfavourable treatment outcomes in DR-TB patients in Selangor and WPKL. Each variable was analysed. The outcome was a binary variable that was classified as "0" for favourable treatment outcomes and "1" for unfavourable treatment outcomes.

The independent variables were age, gender, ethnicity, nationality, level of education, marital status, employment status, diabetes mellitus status, HIV status, type of drug resistance, chest x-ray status, smear positivity, treatment category, DOTS supervision, and smoking status. Except for age, all variables were divided into two or more categories. Variables with a p-value of 0.25 or clinically relevant variables from the

univariable analysis were included in a preliminary model for multiple logistic regression to investigate factors associated with unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL. The p-value was set higher than the level of significance to allow for the inclusion of additional significant variables in the model. A preliminary main effect model was generated using the forward and backward likelihood ratios (LR). Best-fit, parsimonious, and biologically sound rules were used to select the significant variable in the model. Variance Inflation Factor (VIF) and tolerance in linear regression were used to measure multicollinearity. A tolerance of more than 0.1 and a VIF of less than 10 imply that the independent variables are not multicollinear. Meanwhile, each two-way interaction between the independent variables was examined individually.

The Hosmer-Lemeshow test, classification table, and area under the receiver operating characteristic (ROC) curve were then used to establish the goodness-of-fit model. The model was fit when the Hosmer-Lemeshow test was not significant (p-value > 0.05), the classification table had more than 80% correct answers, and the area under the ROC curve was equal to or greater than 0.70. The final model was then developed. The results were presented as adjusted odds ratios (OR) with 95% CI, Wald statistics, and a p-value. The significance threshold was set at a 0.05 p-value.

3.12 Ethical Consideration

3.12.1 Risk and Benefit to Study Participants

Secondary data was collected and analysed for this study. Private data such as name, identity card or passport number and phone number that has been collected by the health authority was not used in this study. The data was kept anonymous. Therefore, predispose subjects to minimal risk. This research provides no direct benefit to the

participants. On the other hand, the study findings may give a better understanding of illness prevalence and contributing factors. Hence, the health authorities can strategise more effective control and preventive TB program.

3.12.2 Risk-Benefit Assessment

As previously noted, the study methods pose little risk. The study's findings have the potential to improve treatment outcomes. The anticipated benefit outweighs the minimal risk to subjects.

3.12.3 Ethics of Study

Before commencing any research-related activities, the research protocol obtained ethical approval from the Medical Research and Ethics Committee of the Malaysian Ministry of Health (NMRR ID-23-00038-72L) and the Human Research Ethics Committee of Universiti Sains Malaysia (USM/JEPeM/22110712). The study adhered to the principles outlined in the Declaration of Helsinki and followed the guidelines set forth by the Malaysian Good Clinical Practice Guideline.

3.12.4 Subject Vulnerability

No subject vulnerability was involved in the study as secondary data was used. Therefore, Patient/Participant Information Sheet (PIS) and Consent Form (CF) assessments were not applicable to this study.

3.12.5 Privacy and Confidentiality

The Malaysian Ministry of Health (MOH) uses the MyTB system to assist the national TB control programme through data-driven decision-making. Hence, to meet the study objectives, only relevant data was extracted to ensure confidentiality. Permission for data access was obtained from the directors of the above-mentioned institutions in the study location. Only anonymous information was collected and analysed. The data in

the Excel sheet was encrypted, as was the laptop itself. The data was only accessible to researchers. The data were presented in groups, so the respondents could not be identified individually. The laptop was stored in a safe and locked compartment. The password-protected method was applied.

After the research was completed, the data on the computer was transferred to a thumb drive, and the data on the computer was erased. The thumb drive and any hardcopy data were kept in the investigators' secured office for at least three years after the study was completed.

3.12.6 Declaration of absence conflict of interest

No conflict of interest is declared.

3.12.7 Publication policy

No personal information will be shared, and individuals will not be identified when the research findings are published. Relevant permissions will be obtained prior to publication. Prior to publication, permission will be requested from the Malaysian Director General of Health.

3.13 Flowchart of the study

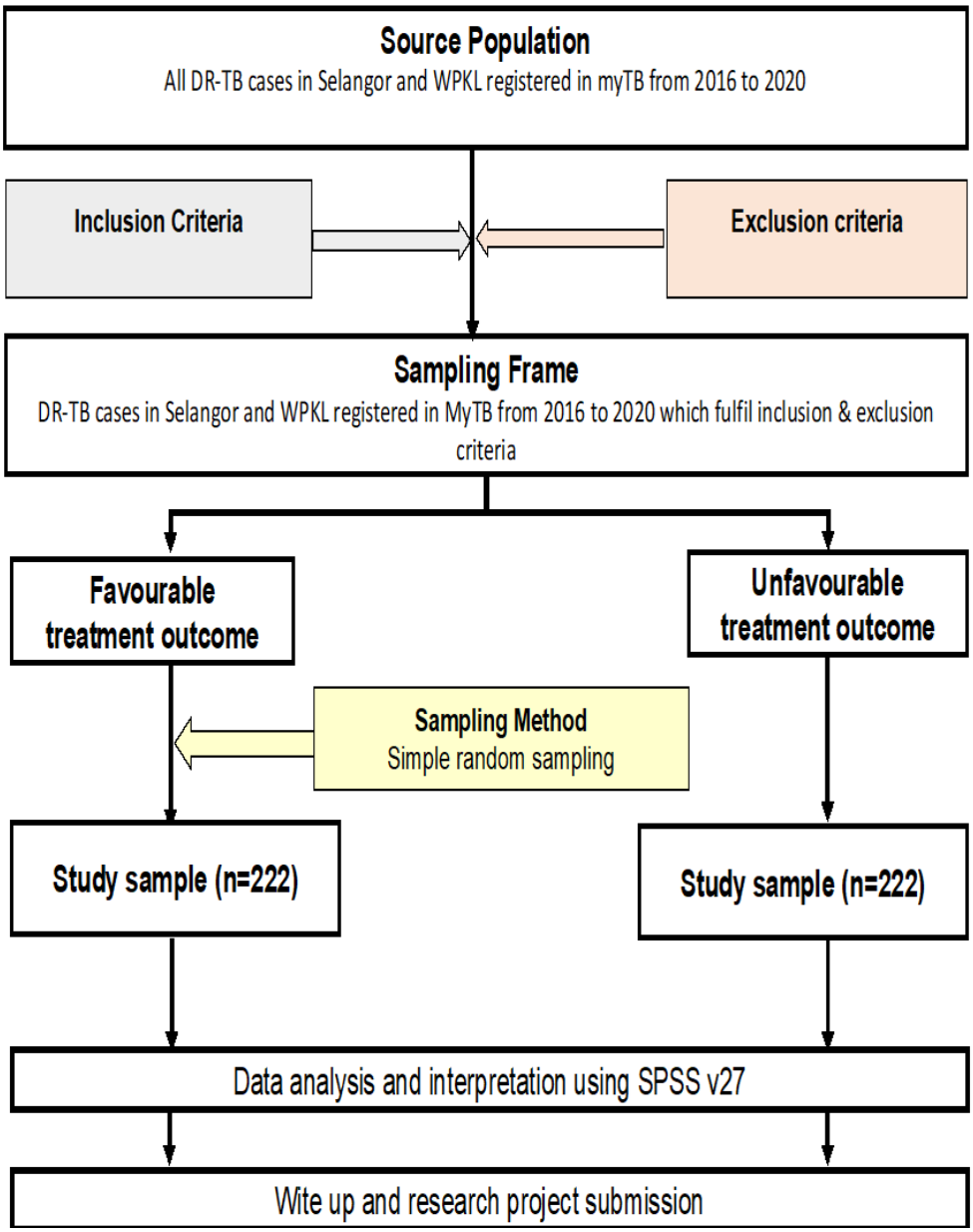


Figure 3.2 Flow chart of the study

4

RESULTS

During a five-year period from 2016 to 2020, a total of 444 cases of drug-resistant TB were notified and registered for the first time in the MyTB database for Selangor and WPKL. Among these cases, 19 were excluded due to missing data, ongoing treatment, change of diagnosis, or transfer out of the study area, leaving 425 who met the study requirements. Among the included cases, 181 were classified as unfavourable treatment outcomes, while 244 were favourable outcomes. Due to relatively small number of cases with unfavourable outcomes (case group), all of them were included in the study without applying any sampling technique. To ensure a representative sample of cases with favourable outcomes (control group), simple random sampling was used, resulting in the selection of 222 cases. Therefore, a total of 403 cases were included in this study.

4.1 Prevalence rate of DR-TB cases

The yearly number and calculated prevalence rate of DR-TB cases in Selangor and WPKL from 2016 to 2020 are shown in Table 4.1. Over five years, the frequency of DR-TB patients grew gradually. The prevalence rate of DR-TB rose steadily from 0.31 in 2016 to 1.83 in 2020. This suggests a concerning trend of increasing drug resistance in TB cases within the population during this period.

Table 4.1 Prevalence of DR-TB cases in Selangor and WPKL from 2016 to 2020

Year	No. of population	No. of DR-TB cases	Prevalence of DR-TB* (95% CI)
2016	8,060,000	25	0.31 (0.19, 0.45)
2017	8,170,000	45	0.55 (0.39, 0.74)
2018	8,270,000	102	1.23 (0.99, 1.49)
2019	8,290,000	119	1.44 (1.18, 1.72)
2020	8,290,000	152	1.83 (1.55, 2.14)

*Prevalence over 100,000 population

4.2 The Outcomes of DR-TB Cases

Figure 4.1 shows the proportion of DR-TB cases with favourable and unfavourable treatment outcomes in Selangor and WPKL from 2016 to 2020. DR-TB cases with favourable treatment outcomes outnumbered DR-TB cases with unfavourable treatment outcomes, accounting for 58.0% and 42.0%, respectively. Meanwhile, Figure 4.2 illustrates that of the 181 cases of unfavourable treatment outcomes among DR-TB patients, the majority was attributed to loss to follow-up (49.7%), followed by death (42.6%), with a smaller proportion resulting from treatment failure (7.7%).

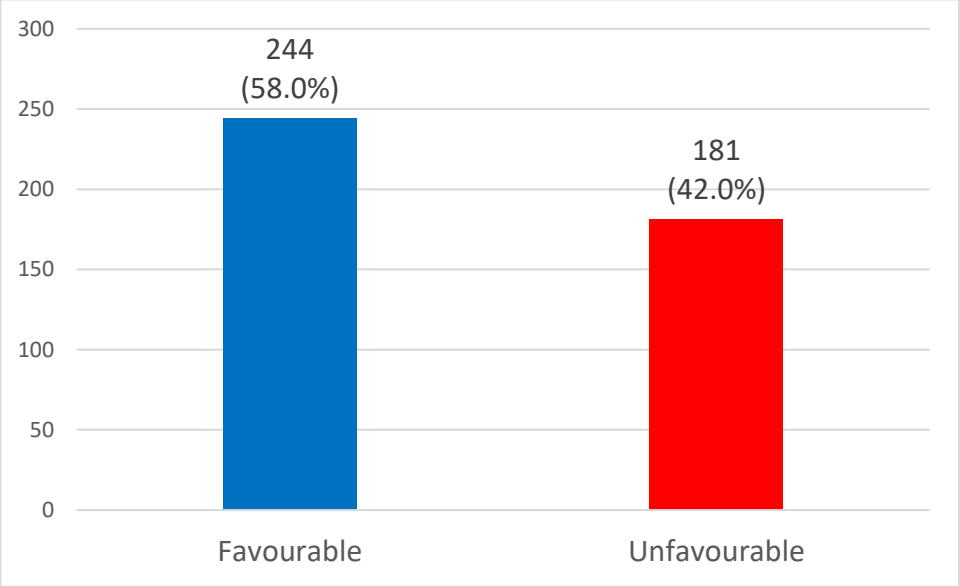


Figure 4.1 The proportion of favourable and unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL from 2016 to 2020

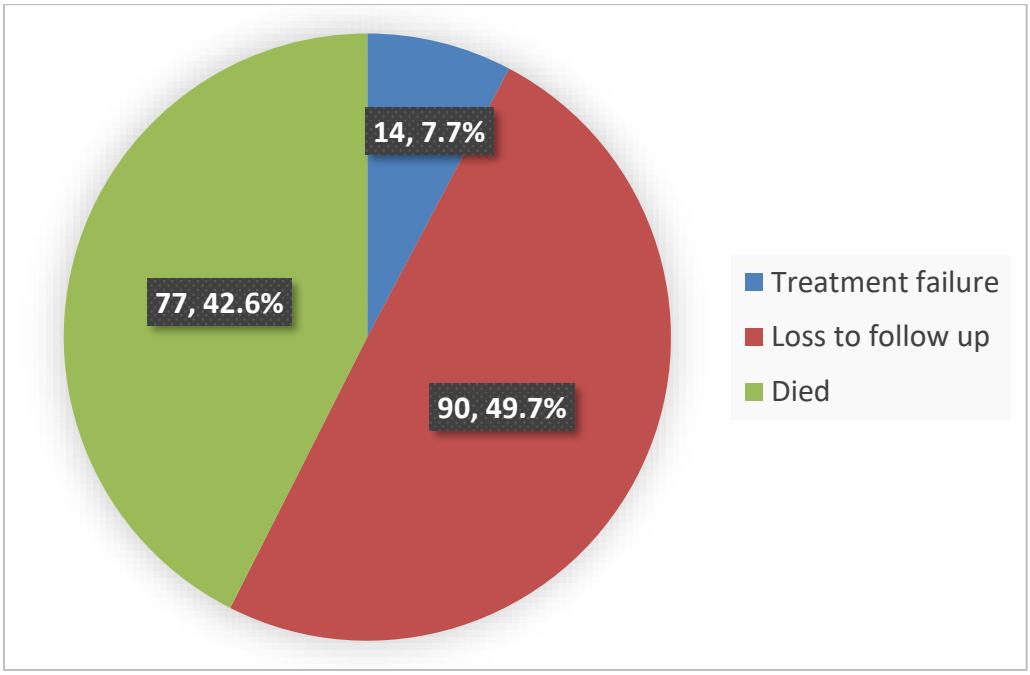


Figure 4.2 Categories of unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL from 2016 to 2020

4.3 Sociodemographic characteristics of DR-TB cases

The study comprised a total of 403 DR-TB patients. The ages ranged from 26 to 56 years old, with a mean of 40.95 (SD=14.93) years. Meanwhile, the bulk of the cases were male, with 287 cases (71.2%), while Malaysians predominated with 321 cases (79.7%), with 200 cases (49.6%) being Malays. Furthermore, the majority of the patients with education up to secondary school (51.6%), married (56.6%), and employed (52.6%), as presented in Table 4.2.

Table 4.2 Sociodemographic characteristics of DR-TB cases in Selangor and WPKL from 2016 to 2020 (n=403)

Variables		Treatment outcomes, n (%)	
		Favourable (n=222)	Unfavourable (n=181)
Age* (years)		39.42 (15.17)	42.83 (14.44)
Gender			
	Female	83 (37.4)	33 (18.2)
	Male	139 (62.6)	148 (81.8)
Nationality			
	Malaysian	178 (80.2)	143 (79.0)
	Non-Malaysian	44 (19.8)	38 (21.0)
Ethnicity			
	Malay	116 (52.3)	84 (46.4)
	Chinese	31 (14.0)	27 (14.9)
	Indian	24 (10.8)	27 (14.9)
	Others[a]	51 (23.0)	43 (23.8)
Level of education			
	Tertiary	50 (22.5)	24 (13.3)
	Secondary	115 (51.8)	93 (51.4)
	Primary	16 (7.2)	19 (10.5)
	No formal education	41 (18.5)	45 (24.9)
Marital status			
	Single/Divorced	80 (36.0)	93 (51.4)
	Married	142 (64.0)	88 (48.6)
Employment status	Unemployed	94 (42.3)	97 (53.6)
	Employed	128 (57.7)	84 (46.4)

*Mean (SD)
[a]Indigenous peoples, Bumiputera Sabah and Sarawak, Non-Malaysian

4.4 Clinical Characteristics of DR-TB Cases

Among patients with DR-TB, patient with diabetic was 22.5% and 24.9% favourable treatment outcomes and unfavourable treatment outcomes, respectively. Meanwhile, HIV-positive DR-TB cases with unfavourable treatment outnumbered HIV-positive DR-TB cases with favourable treatment outcomes. A higher proportion of individuals with unfavourable treatment outcomes for DR-TB were smokers compared to those

with favourable treatment outcomes. For the treatment category, the new cases outnumbered those in the favourable treatment outcomes group, while the retreatment cases outnumbered those in the unfavourable treatment outcomes group.

These findings also imply that the majority of patients with both favourable and unfavourable DR-TB treatment outcomes had positive smear results. However, the number of negative smear results was slightly higher among individuals with favourable treatment outcomes compared to those with unfavourable treatment outcomes. Additionally, a small percentage of individuals did not undergo a smear test, which may have influenced their treatment outcomes. Most patients with favourable and unfavourable treatment outcomes for DR-TB had minimal lesions on chest x-ray. However, a higher proportion of individuals with unfavourable treatment outcomes had moderate to far advanced lesions compared to those with favourable treatment outcomes. Among individuals with favourable treatment outcomes, the majority had HR-TB, followed by RR-TB and MDR/Pre-XDR/XDR-TB in descending order. Conversely, among individuals with unfavourable treatment outcomes, MDR/Pre-XDR/XDR-TB cases predominated, with HR-TB having the least number of cases. The majority of patients in both the favourable and unfavourable treatment outcomes groups received DOTS supervision from healthcare workers. Family members also played a significant role in providing supervision, but to a lesser extent. A small percentage of individuals had no supervision or received supervision from other sources. Details on the clinical characteristics of DR-TB cases are summarised in Table 4.3.

Table 4.3 Clinical characteristics of DR-TB cases in Selangor and WPKL from 2016 to 2020 (n=403)

Variables		Treatment outcomes, n (%)	
		Favourable (n=222)	**Unfavourable (n=181)**
Diabetes mellitus			
	No	172 (77.5)	136 (75.1)
	Yes	50 (22.5)	45 (24.9)
HIV status			
	Negative	209 (94.1)	148 (81.8)
	Positive	13 (5.9)	33 (18.2)
Treatment category			
	New case	122 (55.0)	79 (43.6)
	Retreatment case	100 (45.0)	102 (56.4)
Smear positivity			
	Negative	31 (14.0)	27 (14.9)
	Positive	185 (83.3)	149 (82.3)
	Not done	6 (2.7)	5 (2.8)
Chest x-ray status			
	No lesion	11 (5.0)	6 (3.3)
	Minimal	134 (60.4)	87 (48.1)
	Moderate/Far advanced	77 (34.6)	88 (48.6)
DOTS supervision			
	Healthcare workers[a]	145 (65.3)	122 (67.4)
	Family members	72 (32.4)	46 (25.4)
	No supervision/ others[b]	5 (2.3)	13 (7.2)
DR-TB status			
	HR-TB	100 (45.0)	38 (21.0)
	RR-TB	49 (22.1)	64 (35.4)
	MDR/Pre-XDR/ XDR-TB	73 (32.9)	79 (43.6)
Smoking status			
	No	155 (69.8)	104 (57.5)
	Yes	67 (30.2)	77 (42.5)

[a]including virtual DOTS
[b]DOTS by other than healthcare workers and family members
DOTS = Directly observed treatment, short-course

4.5 Factors associated with unfavourable treatment outcomes of DR-TB cases

Simple and multiple logistic regression was used to determine the factors associated with unfavourable treatment outcomes among DR-TB cases in Selangor and Wilayah Persekutuan Kuala Lumpur (WPKL).

4.5.1 Simple logistic regression analysis (Univariable analysis)

There was a significant association between sociodemographic characteristics and unfavourable treatment outcomes for the majority of variables, including age, gender, level of education, marital status, and employment status. Meanwhile, for the clinical characteristics, HIV status, smoking status, treatment category, DOTS supervision, and DR-TB category statistically had a significant association with unfavourable treatment outcomes. Table 4.4 shows details of univariable analysis using simple logistic regression.

Table 4.4 Simple logistic regression for factors associated with unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL from 2016 to 2020 (n=403)

Variables	Crude OR (95% CI)	Wald statistics (df)	*P*-value
Age* (years)	1.02 (1.00, 1.03)	5.15 (1)	**0.023**
Gender			
Female	1		
Male	2.68 (1.68, 4.26)	17.24 (1)	**<0.001**
Nationality			
Malaysian	1		
Non-Malaysian	1.08 (0.66, 1.75)	0.09 (1)	0.771
Ethnicity			
Malay	1		
Chinese	1.20 (0.67, 2.16)	0.38 (1)	0.538
Indian	1.55 (0.84, 2.88)	1.96 (1)	**0.162**
Others	1.16 (0.71, 1.91)	0.37 (1)	0.546
Level of education			
Tertiary	1		
Secondary	0.44 (0.23, 0.83)	6.32 (1)	**0.012**
Primary	0.74 (0.45, 1.22)	1.41 (1)	**0.235**
No formal education	1.08 (0.49, 2.38)	0.04 (1)	0.845
Marital status			
Married	1		
Single/Divorced	1.88 (1.26, 2.79)	9.49 (1)	**0.002**
Employment status			
Unemployed	1		
Employed	0.64 (0.43, 0.94)	5.04 (1)	**0.025**
Diabetes mellitus			
No	1		
Yes	1.14 (0.72, 1.81)	0.30 (1)	0.582
HIV status			
Negative	1		
Positive	3.59 (1.82, 7.04)	13.72 (1)	**<0.001**
Smoking status			
No	1		
Yes	1.71 (1.14, 2.58)	6.59 (1)	**0.010**

Treatment category			
New case	1		
Retreatment case	1.58 (1.06, 2.34)	5.08 (1)	**0.024**
Smear positivity			
Negative	1		
Positive	0.93 (0.53, 1.62)	0.08 (1)	0.784
Not done	0.95 (0.26, 3.49)	0.01 (1)	0.947
Chest x-ray status			
No lesion	1		
Minimal	1.19 (0.43, 3.34)	0.11 (1)	0.425
Moderate/Far advanced	1.75 (0.61, 5.01)	1.94 (1)	0.740
DOTS supervision			
Healthcare workers	1		
Family members	0.76 (0.49, 1.18)	1.49 (1)	**0.222**
No supervision/others	3.09 (1.07, 8.91)	4.36 (1)	**0.037**
DR-TB category			
HR-TB	1		
RR-TB	3.44 (2.03, 5.82)	21.07 (1)	**<0.001**
MDR/Pre-XDR/XDR-TB	2.85 (1.74, 4.65)	17.48 (1)	**<0.001**

OR = Odds ratio
CI = Confidence interval
*Mean (SD)
DOTS = Directly observed treatment, short-course

4.5.2 Multiple logistic regression analysis

During multiple logistic regression analysis, all significant variables and variables with a *p*-value of less than 0.25 from univariable analysis and clinically important variables were included. The selected variables were as follows:

- Age
- Gender
- Ethnicity
- Level of education
- Marital status
- Employment status

- HIV status
- Smoking status
- Treatment category
- Chest x-ray status
- Diabetes mellitus
- DOTS supervision
- DR-TB category

A preliminary main effect model was generated after comparing models using backward and forward LR. However, the enter approach was used to manually delete variables with *p*-values greater than 0.05 that had been preserved using backward LR. Gender, marital status, level of education, HIV status, and DR-TB category were the five variables in the preliminary main effect model. A collinearity diagnostic was performed to check for multicollinearity, and no multicollinearity was found between these independent variables, as proven by tolerance values greater than 0.1 and VIF values less than 10. All potential two-way interactions were also investigated, and no significant interactions were found in the model (The SPSS output for collinearity diagnostic and examination of all possible two-way interactions between study factors are provided in Appendix 7). As a result, a preliminary final model was established.

The fitness of the preliminary model was assessed, and the results were as below:

a) The Hosmer and Lemeshow goodness-of-fit is not significant, with a *p*-value of 0.859, indicating that the model is fit and no significant difference between the observed and the expected probability.
b) However, the classification table shows that only 66.7% are correctly classified.

c) Meanwhile, the area under the receiver operating characteristic (ROC) curve is 0.728 (95% CI: 0.679, 0.777), indicating the model accurately discriminate 72.8% of the cases (Figure 4.3).

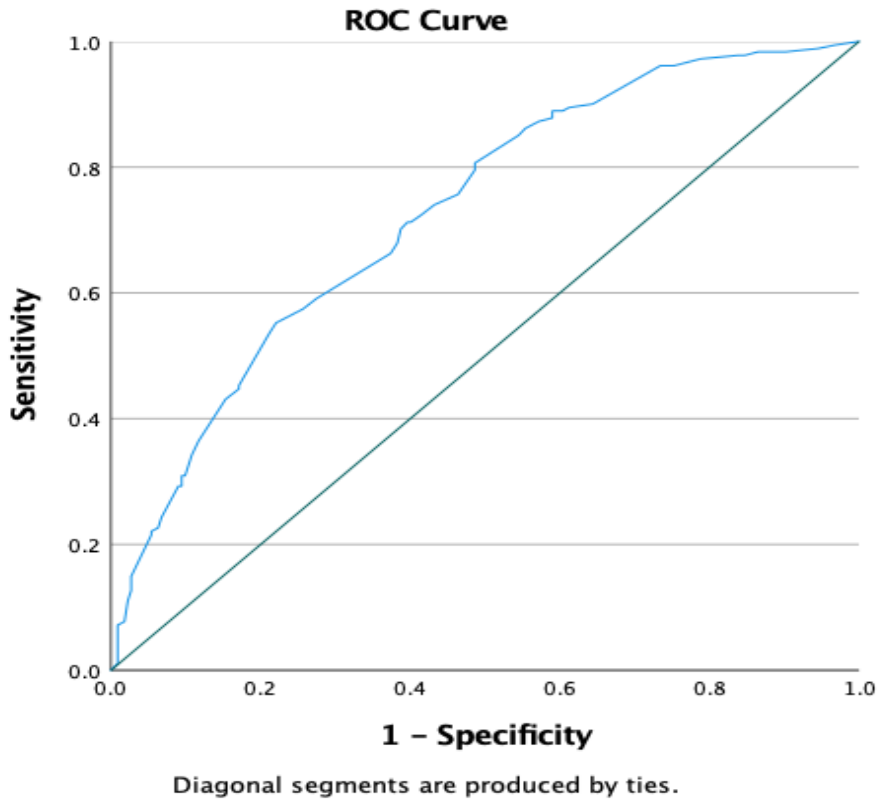


Figure 4.3 The Receiver Operation Characteristics (ROC) curve of the final model

The final model for the factors associated with unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL is presented in Table 4.5. The significant factors associated with unfavourable treatment outcomes among DR-TB cases were male (AdjOR 2.38; 95% CI: 1.44, 3.94; p = 0.001), single or divorced (AdjOR 1.61; 95% CI: 1.03, 2.49; p = 0.035), receive no formal education (AdjOR 3.09; 95% CI: 1.49, 6.41; p = 0.002), HIV positive (AdjOR 2.87; 95% CI: 1.40, 5.87; p = 0.004) and DR-TB category for RR-TB (AdjOR 3.34; 95% CI: 1.90, 5.86; p = <0.001) and MDR/ Pre-XDR/ XDR-TB (AdjOR 2.57; 95% CI: 1.52, 4.33; p = <0.001) when other variables were controlled.

Table 4.5 Multiple logistic regression for factors associated with unfavourable treatment outcomes among DR-TB cases in Selangor and WPKL from 2016 to 2020 (n=403)

Variables	B	Adjusted OR (95% CI)	*p*-value
Gender			
Female		1	
Male	0.87	2.38 (1.44, 3.94)	0.001
Marital status			
Married		1	
Single/Divorced	0.47	1.61 (1.03, 2.49)	0.035
Level of education			
Tertiary		1	
Secondary	0.59	1.81 (0.97, 3.41)	0.064
Primary	0.74	2.09 (0.84, 5.15)	0.112
No formal education	1.13	3.09 (1.49, 6.41)	0.002
HIV status			
Negative		1	
Positive	1.05	2.87 (1.40, 5.87)	0.004
DR-TB category			
HR-TB		1	
RR-TB	1.21	3.34 (1.90, 5.86)	<0.001
MDR/Pre-XDR/XDR-TB	0.94	2.57 (1.52, 4.33)	<0.001

B = Regression coefficient
OR = Odds ratio
CI = Confidence interval
Constant = -2.493
Enter method was applied
No multicollinearity and no significant interaction were observed
Hosmer-Lemeshow test, $p = 0.859$
The classification table was 66.7% correctly classified
The area under the Receiver Operating Characteristics (ROC) curve was 72.8%

The interpretation for the final model is as follows:

i. Male DR-TB patients have 2.39 times the odds of ending up with unfavourable treatment outcomes compared to female DR-TB patients (AdjOR 2.38; 95% CI: 1.44, 3.94; $p = 0.001$) when other variables were adjusted.

ii. DR-TB patients who are single or divorced had 1.61 times the odds of unfavourable treatment outcomes compared to married patients (AdjOR 1.61; 95% CI: 1.03, 2.49; $p = 0.035$) when other variables were adjusted.

iii. DR-TB patients with no formal education have 3.09 times the odds compared to those with a tertiary level of education of ending up with unfavourable treatment outcomes (AdjOR 3.09; 95% CI: 1.49, 6.41; $p = 0.002$) when adjusted for other variables.

iv. DR-TB cases with underlying HIV positive have 2.87 times the odds of having poor treatment outcomes compared to non-HIV DR-TB cases (AdjOR 2.87; 95% CI: 1.40, 5.87; $p = 0.004$) when other variables were controlled.

v. Monoresistant RR-TB cases have 3.34 times the odds of ending up with unfavourable treatment outcomes compared to monoresistant HR-TB cases (AdjOR 3.34; 95% CI: 1.90, 5.86; $p = <0.001$) when adjusted for other variables.

vi. Patients with MDR/ Pre-XDR/ XDR-TB have 2.57 times the odds of having unfavourable treatment outcomes compared to monoresistant HR-TB cases (AdjOR 2.57; 95% CI: 1.52, 4.33; $p = <0.001$) when other variables were adjusted.

5

DISCUSSIONS

The most vulnerable and underprivileged people in society are frequently affected by DR-TB (MOH, 2016). The unpleasant drug reactions caused by the disease's therapy, the exorbitant costs they suffer while seeking care and during treatment, the stigma associated with the condition and the ensuing discrimination all further impair their quality of life and financial circumstances. Besides clinical factors, sociodemographic and socioeconomic background should never be overlooked or ignored as an indicator of favourable treatment outcomes. However, the rate of favourable treatment outcomes among DR-TB cases globally is concerning. To address this challenge, stakeholders and various agencies must actively collaborate in continuous efforts. Therefore, this study was designed to determine factors associated with unfavourable treatment outcomes among DR-TB cases, which may contribute some value to our national TB policy-making.

5.1 DR-TB prevalence in Selangor and WPKL

The findings of the current study, based on secondary data obtained from the National Tuberculosis Surveillance Database (MyTB), indicate an increase in the prevalence of DR-TB cases in Selangor and WPKL. The prevalence ranges from 0.31 to 1.83 per 100,000 population. It is important to note that Selangor has the highest population, while WPKL has the highest population density in Malaysia, as reported by the Department of Statistics in 2022. Additionally, according to statistics from the Ministry of Health (MOH) Malaysia, Selangor and WPKL were ranked as the 1st and 3rd states, respectively, with the highest number of DR-TB cases in a report by Halim in 2022. The low number of cases observed during the initial two-year period of the

study could lead to an underestimated prevalence rate in these two states. This could be attributed to the low number of DR-TB cases being notified and registered in the MyTB database during that time. Similar issues were encountered by Elmi *et al.* (2015) when they conducted a case-control study to determine risk factors associated with MDR-TB between January 2010 and January 2014. Due to the limited number of MDR-TB cases, all cases were included in the study. Five referral TB hospitals in Peninsular Malaysia, including the Institute of Respiratory Medicine, were selected based on the highest prevalence of MDR-TB in each centre.

Findings from some other studies have reported the DR-TB prevalence within the range of 3–5%. For instance, Amin *et al.* (2021) reported a prevalence of 3.8% in Ethiopia, while Al Ammari *et al.* (2018) and Sambas *et al.* (2020) reported rates of 4.4% and 5.0%, respectively, both from Saudi Arabia. Additionally, from 2010 to 2012, the prevalence of DR-TB at one hospital in Bangkok, Thailand, was found to be 2.6% (Jitmuang *et al.*, 2015).

Meanwhile, one local study revealed that MDR-TB prevalence was 0.3% of TB cases, as Goroh *et al.* (2020) reported. The study used a retrospective record review of 33,193 TB cases from the MyTB database reported in Sabah, Malaysia, between 2012 and 2018. MDR/RR-TB was found in an estimated 3.3% of new TB cases and 18% of retreated TB patients worldwide in 2019. There were an estimated 465,000 (range, 400,000-535,000) incident cases of RR-TB, with 78% having MDR-TB. The highest part of the global load was contributed by India (27%), China (14%), and the Russian Federation (8%). Meanwhile, HR-TB was found in an estimated 13.1% of new cases and 17.4% of previously treated patients during the same year (WHO, 2020a). Another study in East Africa found that the pooled prevalence of MDR-TB

among newly diagnosed and retreatment cases was 4% and 21%, respectively (Molla *et al.*,2022).

Meanwhile, in Indonesia, MDR/RR-TB rates among new and retreatment cases were reported to be 2.8% and 16%, respectively (Chadha, 2018). Conversely, Thailand recorded an estimated 2.2% of new TB cases with MDR/RR-TB and 24% of retreatment cases with MDR/RR-TB (Bhatia, 2018). For WPR, the notification rate for MDR/RR-TB out of total TB cases was reported at about 2.32% in 2020, slightly higher than the global rate of 2.15% (WHO, 2021a). According to the Western Pacific Regional Framework to End TB (2021–2030), there were around 101, 000 people with MDR/RR-TB (5.2 per 100 000 population) in 2019. In 2021, the overall incidence of MDR/RR-TB in Malaysia was 1.6 per 100,000 population, with 0.94% of new cases and 19.0% of retreatment cases (WHO, 2022b).

In Malaysia, TB is one of the infectious diseases that must be notified under mandatory notifiable disease surveillance. The Prevention and Control of Infectious Disease Act 1988 requires the act of reporting or notifying infectious diseases. The Regulations for the Prevention and Control of Infectious Diseases (Notice Form) were gazetted in 1993 (MOH, 2017). The national TB surveillance is bolstered further by the MyTB electronic TB information system, which was started way back in 2012. The number of DR-TB patients grew significantly from 2018 onwards, possibly due to clear instructions based on a MOH circular requiring improved notification. TB unit in the respective state health department also improved their DR-TB documentation through proper line listing and regular data updates with district health offices as well as treatment centres.

5.2 Treatment Outcomes of DR-TB Cases in Selangor and WPKL

The global surveillance and treatment of DR-TB are based on three primary categories: RR-TB, MDR-TB, and MDR-TB with added fluoroquinolone resistance. Treatment for all types of DR-TB requires a second-line regimen, which typically lasts between nine and 20 months. Counselling and monitoring for adverse effects are essential components of the treatment process. The duration of treatment can be adjusted based on the patient's response, with the shorter MDR-TB regimen typically lasting 9–12 months. In Malaysia, the enrolment rate of DR-TB cases in second-line treatment was 84.4% overall, with Selangor and WPKL achieving rates of 86.0% and 79.3%, respectively, in 2020. In this study, HR-TB was also counted as one category of DR-TB despite not being monitored by the WHO. Isoniazid-resistant and rifampicin-susceptible TB were found in 11% (range, 6.5–15%) of all incident cases of TB (WHO, 2020a). People with HR-TB may be overlooked in situations where diagnostic algorithms prioritise detecting rifampicin resistance, resulting in their not receiving the recommended modified treatment regimen (WHO, 2020a).

In 2018, the global favourable treatment rate or also known as treatment success rate for DR-TB was 55%. (WHO, 2021). Favourable treatment is indicated as either cured or treatment completed. Several studies from various countries found out higher favourable treatment rate compared to global data: Khan *et al.* (2022) with 63.9% (Pakistan), Wrohan *et al.* (2022) with 65.5% (Vietnam) and Belachew *et al.* (2022) with 77.12% (Ethiopia). Conversely, Indonesia reported a lower favourable treatment rate, which was about 50% (46.6% cure and 3.6% completed treatment) and Thailand stood up with a favourable treatment rate ranging from 58% to 60% for the same cohort as Indonesia (in the year 2018) (Chadha, 2018; Bhatia, 2018). On the other hand, studies conducted in our countries showed even poorer results. Goroh *et*

al. (2020) showed the rate was 36% (range: 25–45%), and Elmi *et al.* (2015) reported 17.1%.

This study found that 58% of DR-TB cases in Selangor and WPKL ended up with favourable treatment outcomes. Meanwhile, of the 181 cases of unfavourable treatment outcomes among DR-TB patients, the majority was attributed to loss to follow-up (49.7%), followed by death (42.6%), with a smaller proportion resulting from treatment failure (7.7%). In another study conducted in Vietnam by Wrohan *et al*. (2022), among the 211 cases that experienced unfavourable treatment outcomes, loss to follow-up also the most prevalent at 50.7%, followed by treatment failure at 25.6% and death at 23.7%. Conversely, in Ethiopia, a different scenario was observed, with a smaller pool of cases (n = 75) ending up with unfavourable treatment outcomes. In this context, the highest proportion was attributed to death, accounting for 48.0%, as opposed to 36.0% for loss to follow-up, and 16.0% for treatment failure (Belachew *et al.*, 2022).

The observation that loss to follow-up has the highest percentage among unfavourable treatment outcomes in this study raises several critical considerations. Loss to follow-up might reflect challenges related to treatment adherence. Factors such as socioeconomic status, access to healthcare, patient education, and support systems could contribute to individuals discontinuing their treatment prematurely. Issues within the healthcare system, such as inadequate patient tracking mechanisms, long waiting times, or insufficient support services, may become other factors. Stigma associated with TB and its treatment, along with societal attitudes towards the disease, could deter patients from continuing treatment. DR-TB is more challenging to treat than drug-sensitive tuberculosis due to the longer and more expensive therapy

required, along with potentially adverse side effects (MOH, 2016). Therefore, strategies such as decentralising treatment services, providing financial support for transportation or treatment costs, and establishing support group should be considered (Kliiman & Altraja, 2010; Wingfield *et al.*, 2017).

Loss to follow-up essentially means that a portion of the study participants did not complete their treatment, and as a result, their exact outcomes are not known. This can introduce data bias in the study results, as the outcomes of those lost to follow-up might differ from those who complied with the treatment regime. The individual lost to follow-up might have experienced improvements, deterioration, or adverse events that remain unaccounted for.

In this context, loss to follow-up is a situation that can potentially be rectified by enhancing mechanisms to track and follow up with patients who have missed appointments or treatments. Addressing this issue is crucial, as taking steps to minimise loss to follow-up will help prevent irreversible consequences such as death or treatment failure. Therefore, focusing on improving treatment adherence and implementing effective defaulter tracking mechanisms should be the primary goals of future public health interventions in these two states.

5.3 Sociodemographic Characteristics of DR-TB Cases

The distribution of age is important in infectious diseases like TB because it determines vulnerability and risk, transmission dynamics, demographic changes and trends, and prevention and control measures. This study reveals that the range of ages for DR-TB cases in Selangor and WPKL was between 26 and 56 years old, with a mean (SD) of 40.95 (14.93) years. In both groups, the disease mostly affected adult patients between 24 and 56. One retrospective cohort study for DR-TB surveillance

analysis carried out in Saudi Arabia came out with the finding of a mean age of 36.6 years (SD=15.90) (Al Ammari *et al*., 2018). Other similar studies found a younger age, with a mean age of 32.7 years (SD=12.70) (Amin *et al*., 2021) in Ethiopia and 29.55 years (SD=12.00) in India (Waghmare *et al*., 2017). Meanwhile, in studies on DR-TB from our neighbouring countries, the mean age was recorded at 43.87 years (SD=15.12) in Thailand (Jitmuang *et al*., 2015) and 43.60 years (SD=11.10) in Indonesia (Burhan, 2022). On the other hand, another study from Vietnam mentioned the age characteristic in terms of the median, which was 43.00 [interquartile range (IQR) 32–55] (Wrohan *et al*., 2022). Based on a study comprising five referral TB hospitals in Peninsular Malaysia from January 2010 to January 2014, Elmi *et al.* (2015) determined that the median (IQR) age of DR-TB patients was 40.40 (14.75). According to the aforementioned studies, most DR-TB cases were therefore in their prime earning years or working years, which can indicate whether there is a greater likelihood of transmission taking place at work as opposed to at home. It may affect how productive people are at work, result in higher medical expenses, and place a very crippling financial load on them.

In terms of gender, the majority of DR-TB patients were male, accounting for 287 cases (71.2%). This finding is similar to earlier studies that found male predominance in various nations, including Saudi Arabia (Al Ammari *et al.*, 2018), Vietnam (Wrohan *et al.*, 2022), and China (Ma *et al*., 2022). Males are considered at higher risk compared to females, probably due to their vulnerability and risk in terms of underlying comorbidities such as HIV infection, diabetes mellitus, and chronic obstructive pulmonary disease (COPD), which are predominant in males; behavioural risk factors like smoking, illicit drug and alcohol abuse (Rajendran *et al*., 2020; Molla *et al*., 2022); socio-cultural factors, for example occupational-related factors in certain

male-predominant professions such as mining and construction (Amin *et al*., 2021); and also health-seeking behaviour patterns as most male patients delay seeking treatment, resulting in delayed diagnosis and treatment initiation. The above-mentioned factors were discussed in one study pertaining to gender differentials in TB (Marcoa, 2018). However, gender disparities in the healthcare workforce, in which women represent almost 70% of employment globally compared to men, can predispose female workers to infectious diseases, including TB (Boniol, 2019). In addition, healthcare professionals, particularly those working in high-risk TB locations such as medical or respiratory wards, chest clinics, health clinics and laboratories, are regarded as a high-risk vocation for TB transmission (MOH, 2012a).

Malaysians predominate with 321 cases (79.7%), and most of them were Malays with 200 cases (49.6%). Another similar study conducted by Elmi *et al.* (2015) also revealed the same result with Malays predominance at 46.2%. Given the study's focus on DR-TB in Selangor and WPKL, it is expected that the majority of the cases were from the local population. The finding that Malays account for 49.6% of the cases, despite constituting a larger proportion (approximately 60%) of the Malaysian population, could potentially be attributed to various factors. It is crucial to bear in mind that the distribution of diseases within certain groups may not always precisely mirror the demographic distribution. Sampling variability, regional distribution, socioeconomic factors, migration, and differences in cultural practices and lifestyles are among the contributing factors leading to variations in disease prevalence among different ethnic groups.

Meanwhile, most non-citizens were Burmese and Indonesian, constituting 42.7% and 34.1%, respectively. These two countries were categorised as high-burden

TB countries, including DR-TB (WHO, 2021a). The influx of foreign workers especially from endemic TB neighbouring countries in various sectors, especially in manufacturing, construction, plantation, agriculture, and food and beverage, which constitutes about 20% of the country's workforce, predisposes to the rising threat of DR-TB in our country (Shariff M. *et al*., 2016; ILO, 2023). Selangor and WPKL, which are recognised as the hub of Malaysia's economy with rapid urbanisation and industrialisation, are where this issue is also emphasised. Up to June 2022, Malaysia has 2.1 million foreigners working in various industries (DOSM, 2022). It is made worse by the fact that the exact numbers of foreigners are unknown: there are illegal or unpermitted foreign employees without proper health screening, and there is also a population of refugees and asylum seekers mainly from the Myanmar, Indonesia, and the Philippines.

Furthermore, a significant proportion of the cases (51.6%) had received education up to the secondary school, totalling 208 cases. Similar findings can be seen in the study by Amin *et al.* (2021) in Eastern Ethiopia involving 395 respondents, with most (33.7%) of them attended secondary school, and also one study in Bangladesh involving 148 participants, which showed 39.9% (Siddik, 2018). The development of DR-TB is influenced by a complex interplay of various factors, including the level of education (Molla *et al.*, 2022). The level of education determines adherence to treatment, awareness and knowledge regarding disease, health-seeking behaviour, and socioeconomic status, which is often linked to employment, financial capacity, accessibility to healthcare services, and living conditions.

In this study, the majority of DR-TB patients were married, with 228 cases (56.6%), compared to those who were single and divorced. The findings are consistent

with a previous retrospective observational study conducted at the Programmatic Management of Drug-Resistant Tuberculosis (PMDT) unit at the Pakistan Institute of Medical Sciences, Islamabad, Pakistan (PIMS), which included 277 respondents, but in a much higher proportion, 80.9%. Another study that was carried out in China recorded 65.5% of married cases out of 446 cases (Ma *et al*., 2022). Marital status is vital concerning social support. A supportive spouse or partner can provide emotional, financial, and practical assistance, such as in DOTS, leading to better treatment adherence and outcomes. However, one study in Ethiopia found that marital status was not related to the occurrence of MDR-TB (Desissa *et al*., 2018).

Poor and overcrowded living circumstances may facilitate the spread of tuberculosis. Thus, MDR-TB preventive initiatives should prioritise these lower socioeconomic family groupings (He, 2011). These poor living conditions are rooted in financial constraints, often associated with low levels of education and unemployment (WHO, 2010). This current study found that most DR-TB cases were employed, representing 212 cases (52.6%). This finding is consistent with the results of research done in Ethiopia (64.9%), one of the nations with the highest prevalence of DR-TB (Desissa *et al*., 2018).

5.4 Clinical Characteristics of DR-TB Cases

Meanwhile, for comorbidities, 95 cases (23.6%) of DR-TB patients were diabetics, and 46 cases (11.4%) were HIV positive. Comparing this finding with another local study by Elmi *et al.* (2015), the results were 26.7% and 5.7%, respectively. The difference in the percentage of HIV positive DR-TB cases between this study and the study by Elmi *et al*. (2015) could be attributed to several factors. One potential explanation is the variation in the study populations and settings. The prevalence of

HIV varies based on geographic locations, populations studied, and changes in the HIV epidemic over time. Another study in Saudi Arabia involving 2098 patients from the MDR-TB and RR-TB categories revealed an even lower percentage of DR-TB with diabetes mellitus (DM) and HIV-positive individuals (12.7% and 2.1%, respectively). Other studies revealed 7.6% of comorbid DM and 14.7% of HIV-positive (Amin *et al*., 2021) in Ethiopia and 11.4% and 7.0%, respectively, for one study in Vietnam (Wrohan *et al*., 2022).

Comparing study figures between local and other countries from different continents, our study showed a higher percentage for both diabetes mellitus and HIV. The comorbidities can significantly impact the treatment outcomes of DR-TB in terms of a weakened immune system leading to more severe disease, an increased risk of treatment failure, and higher mortality. Besides that, there is an issue of potential drug interactions between anti-retroviral therapy (ART) and second-line anti-TB, which requires vigilant monitoring for the efficacy and safety of both treatment regimens. According to the updated National TB Control Programme, it is essential to test HIV status in new TB patients and to undertake TB screening in newly diagnosed HIV patients. This practice enables early HIV detection and timely ART initiation, improving HIV-infected TB patients' treatment results (MOH, 2016b). Concurrent DR-TB treatment with either HIV or diabetes poses a great challenge and is complex, often involving multiple medications and strict adherence requirements. Diabetes, on the other hand, can specifically mask and complicate the diagnosis of TB, leading to a delay in diagnosis that results in late treatment initiation, subsequently causing poor treatment response and more advanced disease. Diabetes increased the likelihood of contracting tuberculosis by two- to threefold when compared to non-diabetic controls.

In addition, weakened immunity in individuals with diabetes may lead to the emergence of active tuberculosis from latent infection (Molla *et al*., 2022).

Concerning the smear status, most cases were smear positive (82.9%) during the initial diagnosis of TB. Smear positive (OR = 5.8, 95% CI 1.8 to 18.5) is one of the independent risk factors for MDR-TB among previously treated patients, as reported by Law *et al.* (2008). Furthermore, a positive AFB smear was usually associated with a high mycobacterial load, which could cause severe disease and be associated with unfavourable outcomes, as shown by Jitmuang *et al*. (2015), which had a percentage of positive AFB smears of 55.3% in the study. Meanwhile, Wrohan *et al.* (2021), with 63.2% of positive AFB smears and Khan *et al*. (2021), with 61.7%. As a result, sputum samples for culture and sensitivity must be sent at diagnosis to establish the presence of *Mycobacterium tuberculosis* and rule out DR-TB, particularly in immunocompromised patients (MOH, 2016b). This practice aligns with MOH Malaysia policy, which mandates all bacteriologically confirmed TB cases (cases with AFB smear positive, Xpert MTB/RIF positive, and line probe assay positive) to be sent for MTB culture and sensitivity. However, DST for several first-line and most second-line anti-TB medications does not identify drug sensitivity with 100% accuracy (MOH, 2016).

In the study, almost 20% of cases with smear-negative TB and no sputum were diagnosed as DR-TB. Smear-negative PTB was responsible for 27.9% of all PTB cases in Malaysia in 2020, which can be attributed to immunosuppression, early illness, or poor specimen quality (MOH, 2022). Compared to mycobacterial culture, chest X-ray (CXR) is a sensitive method for diagnosing and eliminating PTB, with sensitivity ranging from 87% to 98% (Sarmiento OL, 2003). Besides CXR, mycobacterial culture

and Xpert MTB/RIF improve diagnostic accuracy (MOH, 2022). Malaysia also supports using of Xpert MTB/RIF to detect rifampicin resistance in adults and children since it provides faster results than culture (MOH, 2016a). Rapid diagnosis and treatment and adequate infection control strategies are critical for better overall treatment results and disease prevention (MOH, 2012).

Upon diagnosis, the lesion on CXR findings was classified as minimal, moderate, or advanced (MOH, 2012). As mentioned above, CXR remains the primary modality for diagnosing PTB in children and adults. The distinctive feature of PTB is consolidation with cavitation, especially for adult-type PTB; however, any abnormality must be considered (Churchyard, 2010; MOH, 2012). In this study, most cases had a minimal lesion (54.8%) on initial CXR. However, it is not surprising that a normal CXR can be seen in up to 15% of patients with established primary TB (Burrill, 2007). Furthermore, TB detection using CXR improved by 1.23-fold (95% CI: 1.02,1.48) when interpreted by trained personnel compared to inexperienced personnel (Abubakar, 2010). The severity of abnormalities on CXR can indicate disease progression and a potential risk factor for drug resistance. However, the severity of abnormal findings on CXR alone is not the sole determinant of DR-TB development; individual susceptibility and host factors such as immune status, comorbidities, and past TB history may also play a role. One study encompassing 1354 participants from various countries found that the radiological severity of illness on CXR before therapy in smear-positive PTB patients is very weakly related to the bacterial load (Murthy *et al.*, 2018).

For each treatment category, the number of new and retreatment cases was almost equal to 50%. Meanwhile, other local studies revealed almost similar findings,

with 53.3% and 46.7%, respectively, but fewer patients (Elmi *et al*., 2015). One research in Saudi Arabia comprising 2098 patients found a substantially greater proportion of DR-TB cases with no history of prior TB therapy (6.8% versus 93.2%) (Al Ammari *et al*., 2018). In contrast, research with 1443 individuals in Russia discovered a greater prevalence of DR-TB among previously treated TB cases (64.6%) compared to new cases (34.8%), while another study in Ethiopia showed the same result with 65.8% and 34.2%, respectively (Desissa *et al*., 2018). Other low- to middle-income countries have observed a greater prevalence of DR-TB in previously treated TB patients compared to newly diagnosed TB patients (Massi *et al.,* 2011; Sethi *et al.,* 2013).

According to research in Indonesia, the higher prevalence of DR-TB among previously treated TB patients is due to the fact that drug susceptibility testing (DST) coverage was higher among previously treated TB patients than newly diagnosed TB patients. This trend is observed internationally (81% versus 59%) and in Indonesia (100% versus 16%). As a result of higher testing rates, DR-TB is more likely to be discovered in previously treated TB patients (Burhan *et al.,* 2022). Hence, Strategy 5 of our National TB Control Programme 2016–2020 demands 100% DST coverage for all bacteriologically proven TB patients, whether new or retreatment cases.

Drug resistance is often the result of insufficient, incomplete, or prolonged antibiotic usage. The increasing trend of DR-TB in Malaysia is attributable to increased immigrants, resulting in endemicity (Aziah, 2004). In our study, MDR-TB predominates the DR-TB category with a total of 147 cases (36.5%), followed by HR-TB (n = 138, 34.2%), and RR-TB (n = 113, 28.0%). The analysis showed four cases of pre-XDR-TB and one case of XDR-TB. There are not many studies comparing this

group of types of DR-TB, as the WHO captures two main categories, MDR-TB and RR-TB, to be monitored and reported. WHO recommended that the proportion of DR-TB cases at the national level be viewed in the context of the country's TB epidemic (WHO, 2020a).

According to our national data, the HR-TB proportion was the largest (45.2%), followed by RR-TB (31.3%) and MDR-TB (21.1%), as reported in 2020 (Halim, 2022). In previous research conducted in Malaysia in 2015, 215 cases of MDR-TB were recorded in the national TB surveillance in Malaysia as a whole in 2011 and 2012. Three individuals with XDR-TB had strains resistant to second-line medicines such as amikacin, kanamycin, and capreomycin. Rifampicin had the highest degree of resistance, followed by isoniazid (Elmi *et al*., 2015). According to Goble *et al*. (1993), this condition arose when widely used rifampicin, which was initially introduced as an anti-TB medication in 1971, came into contact with isoniazid-resistant organisms, resulting in rifampicin resistance. As a result, the growing number of patients resistant to both isoniazid and rifampicin poses a concern in this research. This is also the case in a few other countries, like Pakistan, where MDR/RR-TB accounts for 95.67% of 277 samples, compared to isoniazid monoresistance of 2.89% (Khan *et al*., 2022), and Vietnam, where 88.0% of the cases evaluated were MDR/RR-TB (Wrohan *et al*., 2022).

The WHO has identified DOT as a critical element in effectively treating TB (WHO, 2011). Anti-TB medicine consumption that is directly monitored by healthcare workers, trained family members, or, in certain locations, trained community volunteers or a non-governmental organisation (NGO) is referred to as directly observed treatment (DOT). The DOT supervisor will sign the TB treatment booklet

after observing the patient correctly taking the prescribed anti-TB medication. DOT supervision is considered accomplished during the intensive phase once 80% of the prescribed daily doses are successfully administered and supervised (Avoi and Liaw, 2021). The National Tuberculosis Control Programme 2016–2020 targets 1% of patients receiving DOT from community volunteers or NGOs through collaborations between the health and social sectors. DOT should be patient-centred, considering the patient's unique traits and preferences. DOT was reportedly practised in Malaysia at 97% (93% to 100%) (MOH, 2012). In our study, the majority of the cases (66.3%) were supervised by healthcare workers, including virtual DOT, followed by family members (29.3%) and others (1.2%). Sadly, 3.2% of cases had no DOT supervision from any of the above-mentioned personnel or organisations. Poor compliance is one of the most well-known factors associated with an unfavourable outcome, according to Jitmuang *et al*. (2015), who found that 27% of patients with MDR-TB and 14.5% of people with non-MDR-TB who did not attend at least 80% of the DOT had poor treatment outcomes. Patients who got DOT for the whole treatment period had better outcomes than those with limited observation or self-administered therapy (Orenstein, 2009).

5.5 Factors associated with unfavourable treatment outcomes of DR-TB

Gender, marital status, level of education, HIV status, and DR-TB category were the significant risk factors associated with unfavourable treatment outcomes among DR-TB patients in Selangor and WPKL found in this study. When other variables were adjusted for in the multivariable analysis, male DR-TB patients had 2.38 times the chances of having poor treatment outcomes as compared to female DR-TB patients (AdjOR 2.38; 95% CI: 1.44, 3.94; $p = 0.001$).

Males usually have a higher prevalence of certain comorbidities that can impact treatment outcomes in DR-TB. Higher rates of smoking, illicit drug abuse, and alcohol consumption among males, as well as being immunocompromised due to certain diseases like HIV and diabetes mellitus and other comorbidities such as chronic obstructive pulmonary disease (COPD), which in turn prolongs the treatment duration and ends up in unfavourable sequelae. Previous local studies support this conclusion (Kaur *et al*., 2022; Liew *et al*., 2015; Tok *et al*., 2020) and also in Pakistan (Khan *et al.*, 2022). Furthermore, male patients are associated with frequent loss of follow-up throughout therapy (Jiménez-Corona et al., 2006). Treatment adherence becomes a huge challenge for them due to work responsibilities, fear of stigmatisation, and poor social support (Bogale *et al.*, 2021). Male patients are the primary breadwinners in various cultures worldwide. Loss of employment or time away from work to attend clinic appointments result in a significant income reduction for them, placing their family under a catastrophic financial burden. This may result in voluntary withdrawal from therapy to prioritise their work and ensure their household needs (Wrohan *et al*., 2022). Societal expectations of masculinity also hinder men from seeking healthcare and treatment compliance. Poor adherence to therapy can result in treatment failure, relapse, the development of further medication resistance, and even mortality (MOH, 2016a).

The next factor associated with unfavourable treatment outcomes among DR-TB patients in Selangor and WPKL is marital status. We found that patients who are single or divorced have 1.61 times the odds of unfavourable treatment outcomes compared to married patients (AdjOR 1.61; 95% CI: 1.03, 2.49; $p = 0.035$) when other variables were adjusted. Social support is the utmost important explanation behind this finding. Marriage often provides a built-in support system, including emotional, financial, and

practical support. Tola *et al.* (2015) revealed that being unmarried is one factor associated with psychological distress among TB patients (AdjOR 4.29; 95% CI: 2.45, 7.53). Married individuals have a spouse who can accompany them to the clinic appointments, or at least be a driver to send them there, given the limited parking, usually in healthcare settings. They can also become DOT supervisors when trained and certified, coupled with emotional support throughout treatment.

Furthermore, married individuals may hinder high-risk behaviours such as smoking, alcohol consumption and substance abuse, which can disrupt good treatment outcomes. A healthy lifestyle, such as regular exercise and a healthy-balanced diet practised by one of the family members, may influence others to behave the same way. The same finding was retrieved by Ma *et al.* (2022) when univariate analysis revealed unmarried as one of the independent factors for unfavourable treatment outcomes. Being single or divorced is usually associated with a lack of immediate social support which can impact treatment adherence. They need to settle their routine on their own. This is where psychological factors come in place and influence their treatment response. Being single or divorced may contribute to higher stress levels, loneliness and even depression secondary to disease. One cross-sectional study comprising 338 TB inpatients in China discovered that the prevalence of depression and anxiety among TB patients was 47.9 and 42.6%, respectively. Furthermore, 38.5% of patients had both anxiety and depression symptoms. Patients with anxiety or depression have a lower cell immune state and higher inflammatory responses than those who do not have symptoms. Divorce or widowhood, medication resistance, and a higher systemic immune inflammation index (SII) were all linked to depression or anxiety symptoms (Liu *et al.*, 2022).

The level of education is one of the determinants of achieving favourable treatment outcomes. DR-TB patients with no formal education have 3.09 times the odds compared to those with a tertiary level of education of ending up with unfavourable treatment outcomes (AdjOR 3.09; 95% CI: 1.49, 6.41; $p = 0.002$) when adjusted for other variables. This conclusion aligns with previous research findings (Tok *et al*., 2020; Azura *et al.,* 2011). Those who pursued a university education had a lower chance of receiving an adverse treatment result. This might be attributed to improved knowledge, which would result in better nutrition, early treatment initiation, and good adherence to therapy (Bogale *et al*., 2021). However, individuals with lower levels of education may have a limited understanding of the importance of treatment adherence or face challenges comprehending treatment instructions. This can lead to non-adherence, which increases the risk of developing drug resistance.

Higher educational attainment improves health outcomes by reducing ignorance and increasing understanding of drug management and its implications (Muture *et al*., 2011). Furthermore, individuals with a higher level of education can improve their communication skills and advocate for themselves to receive quality healthcare, enabling better collaboration with healthcare providers, which in turn improves their treatment endpoint. Educated individuals often have better access to healthcare information, resources, and appropriate medical care. Hence, it is valuable to empower continuous health education in the community to reduce unfavourable treatment outcomes because of different educational backgrounds. Targeted education campaigns through various platforms and technologies can be used nowadays, and efforts to improve treatment outcomes should be tailored to each patient individually because every patient is unique. Education creates awareness, which drives treatment adherence motivation (Azura *et al*., 2011).

Another significant finding in our study is HIV co-infection. The number of people living with HIV (PLHIV) was predicted to reach 87,000 in 2019, with 3,564 newly diagnosed. In Malaysia in 2020, the incidence of HIV-TB co-infection was 1,700 (5.2/100,000 population) (MOH, 2022). We discovered that DR-TB cases with HIV co-infection are nearly three times more likely to have unfavourable treatment outcomes than HIV-negative DR-TB cases (AdjOR 2.87; 95% CI: 1.40, 5.87; p = 0.004). This observation is consistent with the findings of numerous previous studies.

The endemicity of HIV in Malaysia has contributed to a rise in the TB burden (Kaur *et al*., 2022). Most HIV-infected patients (especially those with low CD4 counts) are impoverished, have no carer, or are hospitalised regularly due to recurring medical conditions, most of which are caused by opportunistic infections. As a result, this group is at risk of developing primary and/or secondary medication resistance (Jitmuang *et al*., 2015). Antiretroviral therapy (ART) is recommended for all patients with HIV and DR-TB, regardless of CD4 cell count, as soon as anti-TB medication is initiated (MOH, 2016a). Patients getting concurrent HIV/TB therapy, on the other hand, are at a higher risk of developing adverse effects from those drugs than patients who are not receiving HIV treatment (WHO, 2014). The toxicity of drugs, which causes discomfort, raises the chance of voluntary withdrawal from treatment, posing a significant risk of loss to follow-up. In addition, both diseases are stigmatised, which can lead to social alienation and discrimination (Wrohan *et al*., 2022; Ahmad *et al*., 2018). Meanwhile, retrospective cohort research conducted in Malaysia from 2014 to 2017 discovered that the risks of all-cause death were seven times greater in TB patients who were HIV-positive compared to HIV-negative TB patients (Tok *et al*., 2020).

We also found a significant association between unfavourable treatment outcomes in the DR-TB category for both RR-TB and MDR-TB. Drug-resistant strains of Mycobacterium tuberculosis are well-known in many parts of the world and hinder the success of TB control programmes (Ismail and Bulgiba, 2013). Compared to monoresistant HR-TB patients, those with RR-TB and MDR-TB/pre-XDR-TB/XDR-TB have 3.34 times and 2.57 times the chances of unfavourable treatment outcomes, respectively. In general, patients with more than one type of drug resistance are more likely to end up with unfavourable treatment outcomes. Wrohan *et al.* (2022) found that patients with RR- or MDR-TB were more likely to achieve therapeutic success than those with pre-XDR-TB or XDR-TB. This is consistent with estimates of global treatment success rates of just 56% and 30% for MDR-TB and XDR-TB patients, respectively, due to the longer and more sophisticated treatment regimen required (Wrohan *et al*., 2022). This will particularly limit future treatment options, increase the possibility of acquiring subsequent drug resistance, expose the patient to potentially more toxic regimens, and contribute to ongoing community transmission as the patient is still infectious.

XDR-TB patients were reported to have a 50% greater risk of mortality than MDR-TB patients, and their treatment options are highly restricted since second-line medications are less effective, more toxic, and more costly than first-line drugs (Elmi, 2015a). In addition, treatment duration in individuals with confirmed rifampicin susceptibility but isoniazid resistance is shorter than in RR-TB and MDR-TB. The recommended treatment lasts six months, including three first-line anti-TB drugs plus one fluoroquinolone (MOH, 2016a). A shorter duration of treatment provides fewer side effects from anti-TB treatment and therefore increases treatment adherence.

On the other hand, several other factors that are usually identified as significant associated factors and clinically important based on literature reviews, namely age, diabetes mellitus, smoking, and DOT supervision, were not significantly associated in this current study. Variations in the characteristics and demographics of the study population, differences in study design and analysis, confounding variables, a small sample size, and random chance are the factors and limitations when interpreting the lack of significance in this particular study. Further research, larger sample sizes, and improved methodologies might yield different results.

In addition, this study did not include several other factors, such as place of residency, household income, history of TB contact, other comorbidities (cancer, COPD, chronic liver disease, chronic kidney disease), duration of treatment, treatment regime, and other high-risk behaviours (substance abuse, alcohol consumption), due to limitations in data availability and time constraints. This situation is associated with selection bias, specifically information bias or measurement bias. In this case, the bias arises because the absence of these important variables can potentially lead to an incomplete understanding of the complex interactions influencing the study's outcomes. However, it is important to see the DOT supervision factor as an important element in treatment adherence. Furthermore, in line with current technology, video-assisted treatment (VOT) can be seen as an alternative to in-person or face-to-face DOT for selected patients where available facilities are more flexible, more convenient, and time and cost-saving (MOH, 2022).

5.6 Strengths and Limitation

5.6.1 Strengths

This study involved a retrospective record review with a case-control design using secondary data from MyTB. This kind of study design allows us to study multiple exposures that may relate to a single outcome, which is the treatment outcome. MyTB is considered a valid and reliable source of information because it has become a tool for TB surveillance in Malaysia. Data entry is usually performed by dedicated, well-trained staff in each district health office and is user-friendly. The data source was complemented by line-listings from both the studied states and the Institute of Respiratory Medicine. Our investigation recruited all registered DR-TB patients in MyTB from the most recent years with complete treatment results. Even though our research findings are neither unusual nor novel compared to past studies, they may provide the most up-to-date information and helpful input to the existing TB control plan in these two states and the country in general. The study's findings may be used to enhance DR-TB management among all stakeholders and suggest future steps to guarantee that we remain on track to meet the indicators in our national TB action plan. This study is easily reproducible by other researchers in different demographics and periods for further improvement.

5.6.2 Limitations

Despite the encouraging findings, a few limitations were encountered during this study. The assumed coverage of the MyTB database would ideally be 100% of all TB cases within the studied region. However, given the limitations and challenges of data collection, entry errors, especially by a new or untrained user, and potential inconsistencies, achieving true 100% coverage and accuracy might not be guaranteed. As mentioned above, some necessary variables are not available in MyTB, which can

contribute extra knowledge about DR-TB. In addition, the number of cases couldn't reach the calculated sample size due to the small number of cases in the early two years of the study period. Therefore, all DR-TB cases with unfavourable treatment outcomes were taken into account. Proper documentation and improvement in DR-TB notification only started in 2018 through a clear written circular from MOH, with dedicated staff taking care of data at the state level in the TB Unit.

As this is a case-control study, it merely describes the strength of the connection between the variable and the desired result. The findings have no temporal relationship. The exposure obtained following the diagnosis.

6

CONCLUSION AND RECOMMENDATION

6.1 Conclusion

The prevalence of DR-TB cases in Selangor and WPKL has shown an upward trend from 2016 to 2020, with rates ranging from 0.31 to 1.83 per 100,000 population. DR-TB cases with unfavourable treatment outcomes accounted for 42%, with loss to follow-up predominating at 21.0%. The mean (SD) for DR-TB cases for these five years was 40.95 (14.93), with the majority of them (71.2%) being male, Malaysian citizens (79.7%), Malays (49.6%), having formal education up to secondary school (56.6%), married (56.6%), and employed (52.6%). Meanwhile, for clinical characteristics, the number of new and retreatment cases was almost equal to 50%. Most cases were smear positive (82.9%) and had minimal lesions on initial CXR findings (54.8%). MDR-TB predominates as the type of DR-TB (36.5%), and healthcare workers supervised the majority of the cases (66.3%). One out of five DR-TB cases were diabetics (23.6%), HIV-positive DR-TB cases were recorded at 11.4%, and more than one-third of DR-TB cases were smokers (35.7%). Furthermore, being male, single or divorced, having no formal education, having HIV co-infection, being diagnosed as RR-TB, and being diagnosed as MDR/ Pre-XDR/ XDR-TB were the significant risk factors associated with unfavourable treatment outcomes among DR-TB cases.

This finding may provide guidance to policymakers for DR-TB control and prevention, especially for the national TB strategic plan onward. We hope that future studies will look into other parameters as well as drive efforts to start capturing additional significant variables in the surveillance database for all TB cases.

6.2 Recommendations

6.2.1 TB Control and Prevention Program

The increasing DR-TB trend, especially pre-XDR and XDR-TB, should capture everyone's attention regarding the future global threat and limited treatment options. Therefore, prevention is crucial rather than focusing solely on treatment strategies. The associated factors found in this study should be considered in addressing policy actions for tuberculosis control.

Male-friendly approach, considering their unique characteristics regarding their accountabilities, perceptions, and risk-taking behaviours, and eliminating stigma among the community to facilitate their treatment adherence. More flexible approaches, such as extended service hours to cater for working patients and VOT despite in-person DOT, are among the strategies to be highlighted. Health education is the core component of disease control and prevention. Information on disease and treatment should be intensified in a more understandable, simple, and technologically advanced way using various mediums in order to ensure treatment adherence. Strong social partnerships involving family members, the community, and related NGOs must be established to create a sense of belonging and a supportive environment for DR-TB patients. Furthermore, mandatory testing of HIV status among new TB patients and conducting TB screening among newly diagnosed HIV patients should be practised by all healthcare providers. This practice allows for an early diagnosis of HIV and a timely start of ART, improving the treatment outcome of the HIV-infected TB patient.

MyTB as a surveillance tool should be reviewed from time to time, and additional significant variables should be added based on suggestions from recent studies. In addition, continuous staff training, regular meetings between treatment centres,

including private medical centres and district health offices, and regular audits of the entered data should be planned accordingly by TB unit state health departments.

Last but not least, besides focusing on managing active TB cases, TB screening through contact tracing must go hand in hand as an effort for early detection, prompt diagnosis and treatment, and prevention of TB spread in the community.

6.2.2 Future Research

Future quantitative studies should look into other associated factors that contribute to unfavourable treatment outcomes among DR-TB patients but are not captured in the database alone. Meanwhile, qualitative studies may explore patients' knowledge, attitude, and practice towards DR-TB treatment. It is also suggested to identify a method of improving communication on treatment outcome updates between treatment centres and respective district health offices in order to keep track of defaulters and transfer cases from one centre to another other than traditional ways.

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APPENDICES

APPENDIX 1

PROFORMA CHECKLIST
MAKLUMAT ASAS KES *DRUG - RESISTANT TB* (DR-TB)

NO. KES:
TAHUN DIAGNOSA:

<table>
<tr><th colspan="2">A) SOSIODEMOGRAFI PESAKIT</th></tr>
<tr><td>1) UMUR:</td><td>2) JANTINA:
☐ LELAKI
☐ PEREMPUAN</td></tr>
<tr><td colspan="2">3) WARGANEGARA: YA / TIDAK
JIKA BUKAN WARGANEGARA,
NEGARA ASAL: _____</td></tr>
<tr><td>4) BANGSA:
☐ MELAYU
☐ CINA
☐ INDIA
☐ LAIN-LAIN _____</td><td>5) TARAF PERKAHWINAN:
☐ BUJANG
☐ BERKAHWIN
☐ DUDA/JANDA</td></tr>
<tr><td>6) TARAF PENDIDIKAN (JIKA BERUMUR 7 TAHUN KE ATAS):
☐ TIADA
☐ SEKOLAH RENDAH
☐ SEKOLAH MENENGAH
☐ DIPLOMA/PRA-UNIVERSITI/SIJIL
☐ IJAZAH & KE ATAS
☐ LAIN-LAIN _____</td><td>7) STATUS BEKERJA:
☐ YA
☐ TIDAK</td></tr>
</table>

8) PEKERJAAN:	

B) MAKLUMAT KLINIKAL	
9) KATEGORI KES: ☐ **KES BARU** ☐ **KES DIRAWAT SEMULA**	**10) STATUS KAHAK AWAL RAWATAN:** ☐ **POSITIF** ☐ **NEGATIF** ☐ **TIDAK DIBUAT**
11) STATUS X-RAY DADA SEMASA DIAGNOSA: ☐ ***NO LESION*** ☐ ***MINIMAL*** ☐ ***MODERATELY ADVANCED*** ☐ ***FAR ADVANCED*** ☐ ***NOT DONE***	**12) JENIS KERINTANGAN ANTI-TIBI:** ☐ ***HR-TB*** ☐ ***RR-TB*** ☐ ***MDR-TB*** ☐ ***PRE XDR-TB*** ☐ ***XDR-TB***
13) PEMANTAUAN DOTS OLEH: ☐ **PETUGAS KESIHATAN** ☐ **AHLI KELUARGA** ☐ **LAIN-LAIN** ☐ **TIADA PEMANTAUAN**	**14) PENGHIDAP KENCING MANIS:** ☐ **YA** ☐ **TIDAK**
15) STATUS HIV: ☐ **POSITIF** ☐ **NEGATIF** ☐ **UJIAN TIDAK DIBUAT**	**16) MEROKOK:** ☐ **YA** ☐ **TIDAK**

APPENDIX 2

UNIVERSITI SAINS MALAYSIA ETHICAL APPROVAL LETTER

Jawatankuasa Etika
Penyelidikan Manusia USM (JEPeM)

Human Research Ethics Committee USM (HREC)

Universiti Sains Malaysia
Kampus Kesihatan
16150 Kubang Kerian, Kelantan. Malaysia.
Tel. : +609 - 767 3000/2354/2362
Fax. : + 609 - 767 2351
Email : jepem@usm.my
Laman Web : www.jepem.kk.usm.my
www.usm.my

15th January 2023

Dr. Mohd Fahmin Kamarul Zaman
Department of Community Medicine
School of Medical Sciences
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.

JEPeM Code : USM/JEPeM/22110712
Protocol Title: Prevalence and Factors Associated with Unfavourable Treatment Outcomes Among Drug Resistant Tuberculosis (DR-TB) Cases in Selangor and Wilayah Persekutuan Kuala Lumpur (WPKL).

Dear Dr.,

We wish to inform you that your study protocol has been reviewed and is hereby granted approval for implementation by the Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia (JEPeM-USM). Your study has been assigned study protocol code **USM/JEPeM/22110712**, which should be used for all communications to JEPeM-USM in relation to this study. This ethical approval is valid from **15th January 2023** until **14th January 2024.**

Study Site: Selangor and Wilayah Persekutuan Kuala Lumpur (WPKL).

The following researchers are also involved in this study:
1. Dr. Mohd Yusof Sidek
2. Assoc. Prof. Dr. Nik Rosmawati Nik Husain
3. Dr. Zamzurina Abu Bakar

The following documents have been approved for use in the study.
1. Research Proposal

In addition to the abovementioned documents, the following technical documents were included in the review on which this approval was based:
1. Data Collection Form (Proforma Checklist)

While the study is in progress, we request you to submit to us the following documents:
1. Application for renewal of ethical approval 60 days before the expiration date of this approval through submission of **JEPeM-USM FORM 3(B) 2019: Continuing Review Application Form.**
2. Any changes in the protocol, especially those that may adversely affect the safety of the participants during the conduct of the trial including changes in personnel, must be submitted or reported using **JEPeM-USM FORM 3(A) 2019: Study Protocol Amendment Submission Form.**
3. Revisions in the informed consent form using the **JEPeM-USM FORM 3(A) 2019: Study Protocol Amendment Submission Form.**
4. Reports of adverse events including from other study sites (national, international) using the **JEPeM-USM FORM 3(G) 2019: Adverse Events Report.**
5. Notice of early termination of the study and reasons for such using **JEPeM-USM FORM 3(E) 2019.**
6. Any event which may have ethical significance.

JEPeM
JAWATANKUASA ETIKA PENYELIDIKAN MANUSIA

7. Any information which is needed by the JEPeM-USM to do ongoing review.
8. Notice of time of completion of the study using **JEPeM-USM FORM 3(C) 2019: Final Report Form.**

Please note that forms may be downloaded from the JEPeM-USM website: **www.jepem.kk.usm.my**

JEPeM-USM is in compliance with the Declaration of Helsinki, International Conference on Harmonization (ICH) Guidelines, Good Clinical Practice (GCP) Standards, Council for International Organizations of Medical Sciences (CIOMS) Guidelines, World Health Organization (WHO) Standards and Operational Guidance for Ethics Review of Health-Related Research and Surveying and Evaluating Ethical Review Practices, EC/IRB Standard Operating Procedures (SOPs), and Local Regulations and Standards in Ethical Review.

Thank you.

"BERKHIDMAT UNTUK NEGARA"

ASSOC. PROF. DR. AZLAN HUSIN
Chairperson
Jawatankuasa Etika Penyelidikan (Manusia) JEPeM
Universiti Sains Malaysia

APPENDIX 3

MEDICAL RESEARCH AND ETHICS COMMITTEE'S ETHICAL APPROVAL LETTER

JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
(*Medical Research & Ethics Committee*)
KEMENTERIAN KESIHATAN MALAYSIA
d/a Kompleks Institut Kesihatan Negara
Blok A, No 1, Jalan Setia Murni U13/52,
Seksyen U13, Bandar Setia Alam,
40170 Shah Alam, Selangor. Tel: 03-3362 8888/8205

Ref : 23-00038-72L (2)
Date: 06-March-2023

MOHD FAHMIN BIN KAMARUL ZAMAN
UNIVERSITI SAINS MALAYSIA

Dear Sir/ Mdm,

ETHICS INITIAL APPROVAL: NMRR ID-23-00038-72L (IIR)
PREVALENCE AND FACTORS ASSOCIATED WITH UNFAVOURABLE TREATMENT OUTCOMES AMONG DRUG RESISTANT TUBERCULOSIS (DR-TB) CASES IN SELANGOR AND WILAYAH PERSEKUTUAN KUALA LUMPUR (WPKL)

This letter is made in reference to the above matter.

2. The Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (MOH) has provided ethical approval for this study. Please take note that all records and data are to be kept strictly **CONFIDENTIAL** and can only be used for the purpose of this study. All precautions are to be taken to maintain data confidentiality. Permission from the District Health Officer / Hospital Administrator / Hospital Director and all relevant heads of departments / units where the study will be carried out must be obtained prior to the study. You are required to follow and comply with their decision and all other relevant regulations.

3. The investigators and study sites involved in this study are:

JABATAN KESIHATAN WILAYAH PERSEKUTUAN KUALA LUMPUR & PUTRAJAYA
Mohd Fahmin Bin Kamarul Zaman (Principal Investigator)
Mohd Yusof bin Sidek

INSTITUTE OF RESPIRATORY MEDICINE
Zamzurina Abu Bakar

JABATAN KESIHATAN NEGERI SELANGOR
Nik rosmawati Nik Husain

4. The following study documents have been received and reviewed with reference to the above study:

Documents received and reviewed with reference to the above study:

1. Study Protocol Version 3, dated 17-February-2023
2. Clinical Form Report / Data Collection Form Version 1, dated 30-November-2022
3. Investigator's documents : Declaration of Conflict of Interest (COI), IA-HOD-IA, and CV:
    a) Mohd Fahmin Bin Kamarul Zaman (Principal Investigator)
    b) Mohd Yusof bin Sidek
    c) Zamzurina Abu Bakar
    d) Nik rosmawati Nik Husain

5. Please note that ethical approval is valid until **05-March-2024**. The following are to be reported upon receiving ethical approval. Required forms can be obtained from the National Medical Research Regisry (NMRR) website:

   i. **Continuing Review Form** has to be submitted to MREC within 2 month (60 days) prior to the expiry of ethical approval.
   ii. **Study Final Report** upon study completion to the MREC.
   iii. Ethical approval is required in the case of **amendments / changes** to the **study documents/ study sites/ study team.** MREC reserves the right to withdraw ethical approval if changes to study documents are not completely declared.

6. This study involves the following methods:

   i. Retrospective
   ii. Secondary Data

7. Please take note that the reference number for this letter must be stated in all correspondence related to this study to facilitate the process.

Comments (if any): NIL

Project Sites:
JABATAN KESIHATAN WILAYAH PERSEKUTUAN KUALA LUMPUR & PUTRAJAYA
INSTITUTE OF RESPIRATORY MEDICINE
JABATAN KESIHATAN NEGERI SELANGOR

Decision by Medical Research & Ethics Committee:
(√) Approved
( ) Disapproved

Date of Approval : 06-March-2023

DR NURAIN BINTI MOHD NOOR
Chairperson
Medical Research & Ethics Committee
Ministry of Health Malaysia
MMC No: 31576

JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
(*Medical Research & Ethics Committee*)
KEMENTERIAN KESIHATAN MALAYSIA
d/a Kompleks Institut Kesihatan Negara
Blok A, No 1, Jalan Setia Murni U13/52,
Seksyen U13, Bandar Setia Alam,
40170 Shah Alam, Selangor. Tel: 03-3362 8888/8205

Ref : 23-00038-72L (1)
Date: 06-Mac-2023

MOHD FAHMIN BIN KAMARUL ZAMAN
UNIVERSITI SAINS MALAYSIA

Dato'/ Tuan/ Puan,

SURAT KELULUSAN ETIKA: NMRR ID-23-00038-72L (IIR)
PREVALENCE AND FACTORS ASSOCIATED WITH UNFAVOURABLE TREATMENT OUTCOMES AMONG DRUG RESISTANT TUBERCULOSIS (DR-TB) CASES IN SELANGOR AND WILAYAH PERSEKUTUAN KUALA LUMPUR (WPKL)

Dengan hormatnya perkara di atas adalah dirujuk.

2. Bersama dengan surat ini dilampirkan surat kelulusan saintifik dan etika bagi projek ini. Segala rekod dan data subjek adalah SULIT dan hanya digunakan untuk tujuan kajian dan semua isu serta prosedur mengenai *data confidentiality* mesti dipatuhi. Kebenaran daripada Pengarah Hospital / Institusi di mana kajian akan dijalankan mesti diperolehi terlebih dahulu sebelum kajian dijalankan. Dato' / Tuan / Puan perlu akur dan mematuhi keputusan tersebut dan undang-undang lain yang berkaitan.

3. Penyelidik- penyelidik dan lokasi kajian yang terlibat ialah:

   JABATAN KESIHATAN WILAYAH PERSEKUTUAN KUALA LUMPUR & PUTRAJAYA
   Mohd Fahmin Bin Kamarul Zaman (Penyelidik Utama)
   Mohd Yusof bin Sidek

   INSTITUTE OF RESPIRATORY MEDICINE
   Zamzurina Abu Bakar

   JABATAN KESIHATAN NEGERI SELANGOR
   Nik rosmawati Nik Husain

4. Dokumen kajian yang berikut telah diterima dan dinilai:

1. Study Protocol Version 3, dated 17-February-2023 2. Clinical Form Report / Data Collection Form Version 1, dated 30-November-2022 3. Investigator's documents : Declaration of Conflict of Interest (COI), IA-HOD-IA, and CV: a) Mohd Fahmin Bin Kamarul Zaman (Penyelidik Utama) b) Mohd Yusof bin Sidek c) Zamzurina Abu Bakar d) Nik rosmawati Nik Husain

5. Adalah dimaklumkan bahawa kelulusan ini adalah sah sehingga **05-Mac-2024.** Tuan/Puan perlu menghantar dokumen-dokumen seperti berikut selepas mendapat kelulusan etika. Borang-borang berkaitan boleh dimuat turun daripada laman web *National Medical Research Registry (NMRR)*.

   i. ***Continuing Review Form*** selewat-lewatnya dalam tempoh 2 bulan (60 hari) sebelum tamat tempoh kelulusan ini bagi memperbaharui kelulusan etika.
   ii. ***Study Final Report*** pada penghujung kajian.

iii. Mendapat kelulusan etika sekiranya terdapat pindaan ke atas sebarang dokumen kajian / lokasi kajian / penyelidik. Pihak JEPP mempunyai hak untuk menarik balik kelulusan etika sekiranya terdapat perubahan dokumen kajian yang tidak diisytiharkan.

6. Kajian tersebut hanya melibatkan pengumpulan data melalui:

   i. Retrospektif
   ii. Data Sekunder

7. Sila ambil maklum bahawa sebarang urusan surat-menyurat berkaitan dengan penyelidikan ini haruslah dinyatakan **nombor rujukan surat** ini untuk melicinkan urusan yang berkaitan.

Sekian terima kasih.

Komen (Jika ada) : **NIL**

Lokasi Kajian:
JABATAN KESIHATAN WILAYAH PERSEKUTUAN KUALA LUMPUR & PUTRAJAYA
INSTITUTE OF RESPIRATORY MEDICINE
JABATAN KESIHATAN NEGERI SELANGOR

Keputusan Jawatankuasa Etika dan Penyelidikan Perubatan:
☎ ☽ ♋
( ) Tidak Lulus

Tarikh kelulusan etika : 06-Mac-2023

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

Saya yang menjalankan amanah,

.....
DR NURAIN BINTI MOHD NOOR
Pengerusi
Jawatankuasa Etika & Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

NH/Approval2023/Mrecshare

APPENDIX 4

DIRECTOR OF INSTITUT PERUBATAN RESPIRATORI APPROVAL LETTER

Jabatan Perubatan Masyarakat
Department of Community Medicine

Pusat Pengajian Sains Perubatan

Kampus Kesihatan
Universiti Sains Malaysia,
16150 Kubang Kerian,
Kelantan, Malaysia.
Tel : 609 767 3000 Samb.: 6621
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Ruj : PPSP/JPM/MPH/23
Tarikh : 8 Mac 2023

Dr. Nurhayati binti Mohd Marzuki
Pengarah,
Institut Perubatan Respiratori,
Hospital Kuala Lumpur,
Jalan Pahang,
50586 Kuala Lumpur,
Wilayah Persekutuan Kuala Lumpur.
(U/P: Dr. Zamzurina binti Abu Bakar
En. Mohamad Azam bin Mohamad Yusop)

Puan,

MEMOHON KEBENARAN UNTUK MENGAKSES DATA BAGI TUJUAN PENYELIDIKAN

Dengan segala hormatnya, perkara di atas adalah dirujuk.

2. Sukacita dimaklumkan bahawa satu penyelidikan bertajuk *Prevalence and Factors Associated with Unfavourable Treatment Outcomes among Drug Resistant Tuberculosis (DR-TB) Cases in Selangor and Wilayah Persekutuan Kuala Lumpur (WPKL)* **(NMRR ID-23-00038-72L)** akan dilakukan oleh calon Sarjana Kesihatan Awam, Dr. Mohd Fahmin bin Kamarul Zaman yang juga merupakan penyelidik utama.

3. Oleh yang demikian, pihak jabatan memohon agar pelajar tersebut dibenarkan untuk mengakses data bagi tujuan penyelidikan. Bersama-sama surat ini disertakan surat kelulusan dari pihak Jawatankuasa Etika Penyelidikan Perubatan Kementerian Kesihatan Malaysia (KKM) dan Jawatankuasa Etika Penyelidikan Manusia (JEPeM) Universiti Sains Malaysia (USM) untuk rujukan pihak Puan.

4. Segala kerjasama dan perhatian daripada pihak Puan amatlah dihargai dan didahului dengan ucapan ribuan terima kasih.

Sekian.

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

PROF MADYA DR. KAMARUL IMRAN MUSA
Ketua Jabatan

s.k. Prof. Madya Dr. Mohd Nazri bin Shafei (Ketua Kursus Projek Penyelidikan)
Dr. Mohd Yusof Sidek (Penyelia Utama Projek Penyelidikan Calon)
Prof. Madya Dr. Nik Rosmawati Nik Husain (Penyelia Bersama Projek Penyelidikan Calon)

INSTITUT PERUBATAN RESPIRATORI
(HOSPITAL KUALA LUMPUR)
JALAN PAHANG ,
50590 KUALA LUMPUR.

Tel: 03- 4023 2966
Fax: 03- 4021 8807
Email : ipr@moh.gov.my

Ruj. Kami : IPR.100-07/09(6)
Tarikh : 15 Mac 2023

PROF. MADYA DR KAMARUL IMRAN MUSA
Ketua Jabatan Perubatan Masyarakat
Kampus Kesihatan
Universiti Sains Malaysia
16150 Kubang Kerian
KELANTAN

Prof Madya,

KEBENARAN UNTUK MENGAKSES DATA BAGI TUJUAN PENYELIDIKAN

Adalah saya dengan hormatnya merujuk perkara di atas dan surat PPSP/JPM/MPH/23 bertraikh 8 Mac 2023 berkaitan.

2. Dimaklumkan bahawa, permohonan pihak Prof Madya untuk mengakses data bagi tujuan penyelidkan bertajuk :**PREVALENCE AND FACTORS ASSOCIATED WITH UNFAVOURABLE TREATMENT OUTCOME AMONG DRUG RESISTANT TUBERCULOSIS (DR-TB) CASES IN SELANGOR AND WILAYAH PERSEKUTUAN KUALA LUMPUR (WPKL) - NMRR ID-23-00038-72L** adalah **DILULUSKAN**.

3. Sehubungan dengan itu, sokongan dari pihak Prof Madya adalah dimohon untuk sentiasa mematuhi Prosedur Operasi Standard (SOP) dan peraturan yang telah ditetapkan oleh Institut Perubatan Respiratori (IPR) sepanjang berada di Institut ini.

Sekian, terima kasih.

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

(DR. GNANAMALAR JOHN)
b.p. Pengarah
Institut Perubatan Respiratori
Hospital Kuala Lumpur

s.k : **CIK NURUL SA'ADAH BINTI JAAFAR**
Ketua
Unit Rekod Perubatan
Institut Perubatan Respiratori
Hospital Kuala Lumpur

APPENDIX 5

DIRECTOR OF SELANGOR STATE HEALTH DEPARTMENT APPROVAL LETTER

Jabatan Perubatan Masyarakat
Department of Community Medicine
Pusat Pengajian Sains Perubatan
Kampus Kesihatan
Universiti Sains Malaysia,
16150 Kubang Kerian,
Kelantan, Malaysia.
Tel : 609 767 3000 Samb.: 6621
Faks : 609 767 6654
Website: www.medic.usm.my/jpm

Ruj : PPSP/JPM/MPH/23
Tarikh : 8 Mac 2023

YBhg. Dato' Indera Dr. Sha'ari bin Ngadiman
Pengarah,
Jabatan Kesihatan Negeri Selangor,
No.1, Wisma Sunway,
Jalan Tengku Ampuan Zabedah C 9/C,
Seksyen 9, 40100 Shah Alam,
Selangor.
(U/P: Dr. Harishah binti Talib
Dr. Annabella Ruth Edwin)

YBhg. Dato',

MEMOHON KEBENARAN UNTUK MENGAKSES DATA BAGI TUJUAN PENYELIDIKAN

Dengan segala hormatnya, perkara di atas adalah dirujuk.

2. Sukacita dimaklumkan bahawa satu penyelidikan bertajuk *Prevalence and Factors Associated with Unfavourable Treatment Outcomes among Drug Resistant Tuberculosis (DR-TB) Cases in Selangor and Wilayah Persekutuan Kuala Lumpur (WPKL)* **(NMRR ID-23-00038-72L)** akan dilakukan oleh calon Sarjana Kesihatan Awam, Dr. Mohd Fahmin bin Kamarul Zaman yang juga merupakan penyelidik utama.

3. Oleh yang demikian, pihak jabatan memohon agar pelajar tersebut dibenarkan untuk mengakses data bagi tujuan penyelidikan. Bersama-sama surat ini disertakan surat kelulusan dari pihak Jawatankuasa Etika Penyelidikan Perubatan Kementerian Kesihatan Malaysia (KKM) dan Jawatankuasa Etika Penyelidikan Manusia (JEPeM) Universiti Sains Malaysia (USM) untuk rujukan pihak YBhg. Dato'.

4. Segala kerjasama dan perhatian daripada YBhg. Dato' amatlah dihargai dan didahului dengan ucapan ribuan terima kasih.

Sekian.

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

PROF MADYA DR. KAMARUL IMRAN MUSA
Ketua Jabatan

s.k. Prof. Madya Dr. Mohd Nazri bin Shafei (Ketua Kursus Projek Penyelidikan)
Dr. Mohd Yusof Sidek (Penyelia Utama Projek Penyelidikan Calon)
Prof. Madya Dr. Nik Rosmawati Nik Husain (Penyelia Bersama Projek Penyelidikan Calon)

JABATAN KESIHATAN NEGERI SELANGOR
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Jalan Tengku Ampuan Zabedah C 9/C,
Seksyen 9, 40100 Shah Alam,
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Portal Rasmi : www.jknselangor.moh.gov.my

Ruj Kami : JKNS/KA/Q-712/04-01 Jld ɔɔ(12)
Tarikh : 14 April 2023

Dr. Mohd Fahmin bin Kamarul Zaman
Jabatan Perubatan Masyarakat,
Kampus Kesihatan,
Universiti Sains Malaysia
16150 Kubang Kerian,
Kelantan

Tuan,

MAKLUMBALAS PERMOHONAN MENGGUNAKAN FASILITI JABATAN KESIHATAN NEGERI SELANGOR UNTUK MENJALANKAN PENYELIDIKAN BERTAJUK "NMRR ID-23-00038-72L (IIR) - *PREVALENCE AND FACTORS ASSOCIATED WITH UNFAVOURABLE TREATMENT OUTCOMES AMONG DRUG RESISTANT TUBERCULOSIS (DR-TB) CASES IN SELANGOR AND WILAYAH PERSEKUTAN KUALA LUMPUR (WPKL)*"

Dengan hormatnya saya merujuk kepada perkara di atas.

2. Sukacita dimaklumkan bahawa Bahagian Kesihatan Awam, Jabatan Kesihatan Negeri Selangor **tiada halangan** untuk membenarkan tuan menjalankan penyelidikan yang **"NMRR ID-23-00038-72L (IIR) - *Prevalence And Factors Associated With Unfavourable Treatment Outcomes Among Drug Resistant Tuberculosis (DR-TB) Cases In Selangor And Wilayah Persekutan Kuala Lumpur (WPKL)*"** di :

2.1 Unit Kawalan Penyakit Tibi/Kusta, Bahagian Kesihatan Awam, Jabatan Kesihatan Negeri Selangor

3. Walaupun begitu berdasarkan pembentangan yang dijalankan pada 5 April 2023, pihak tuan adalah diminta untuk mempertimbangkan cadangan di bawah bagi memastikan factor yang dikaji oleh tuan adalah menyeluruh. Cadangan tersebut adalah :

3.1 Memasukkan *Directly Observed Therapy* (DOT) sebagai salah satu faktor yang akan dikaji

4. Oleh itu, pihak tuan perlu menghubungi Dr Annabella Edwin daripada Unit Kawalan PenyakitTibi/Kusta, Bahagian Kesihatan Awam, Jabatan Kesihatan Negeri Selangor melalui emel annabellaedwin@gmail.com / annabella@moh.gov.my atau di talian 03-5123 7333 (ext: 356).

MAKLUMBALAS PERMOHONAN MENGGUNAKAN FASILITI JABATAN KESIHATAN NEGERI SELANGOR UNTUK MENJALANKAN PENYELIDIKAN BERTAJUK "NMRR ID-23-00038-72L (IIR) - *PREVALENCE AND FACTORS ASSOCIATED WITH UNFAVOURABLE TREATMENT OUTCOMES AMONG DRUG RESISTANT TUBERCULOSIS (DR-TB) CASES IN SELANGOR AND WILAYAH PERSEKUTAN KUALA LUMPUR (WPKL)*"

Kerjasama pihak tuan juga dipohon agar tidak mengganggu perkhidmatan dan mematuhi etika sewaktu menjalankan penyelidikan di fasiliti yang terlibat. **Kelulusan dan kebenaran bagi menjalankan penyelidikan ini adalah sehingga 5 Mac 2024**. Jika pihak tuan memerlukan lebih masa untuk menjalankan penyelidikan maka pihak tuan perlu mendapatkan kebenaran tempoh lanjutan tersebut daripada Jawatankuasa Etika dan Penyelidikan Perubatan, Kementerian Kesihatan Malaysia dan memaklumkan semula perkara ini kepada pihak kami selepas kebenaran tempoh lanjutan diterima.

Kerjasama dan perhatian pihak tuan adalah dihargai dan didahului dengan ucapan terima kasih.

Sekian.

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

(DR. WAN NORAINI BINTI WAN MOHAMED NOOR)

Pakar Perunding Perubatan Kesihatan Awam
Timbalan Pengarah Kesihatan Negeri (Kesihatan Awam)
Jabatan Kesihatan Negeri Selangor

s.k:-

Ketua Unit Kawalan Penyakit Tibi/Kusta
Bahagian Kesihatan Awam, JKNS

APPENDIX 6

DIRECTOR OF WPKL AND PUTRAJAYA STATE HEALTH DEPARTMENT APPROVAL LETTER

Jabatan Perubatan Masyarakat
Department of Community Medicine

Pusat Pengajian Sains Perubatan

Kampus Kesihatan
Universiti Sains Malaysia,
16150 Kubang Kerian,
Kelantan, Malaysia.
Tel : 609 767 3000 Samb.: 6621
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Website: www.medic.usm.my/jpm

Ruj : PPSP/JPM/MPH/23
Tarikh : 8 Mac 2023

Dr. Nor'Aishah binti Abu Bakar
Pengarah,
Jabatan Kesihatan WP Kuala Lumpur dan Putrajaya,
Jalan Cenderasari,
50590 Kuala Lumpur,
Wilayah Persekutuan Kuala Lumpur.
(U/P: Dr. Rohaya binti Ramli
Dr. Shuhaily binti Ishak)

Puan,

MEMOHON KEBENARAN UNTUK MENGAKSES DATA BAGI TUJUAN PENYELIDIKAN

Dengan segala hormatnya, perkara di atas adalah dirujuk.

2. Sukacita dimaklumkan bahawa satu penyelidikan bertajuk *Prevalence and Factors Associated with Unfavourable Treatment Outcomes among Drug Resistant Tuberculosis (DR-TB) Cases in Selangor and Wilayah Persekutuan Kuala Lumpur (WPKL)* **(NMRR ID-23-00038-72L)** akan dilakukan oleh calon Sarjana Kesihatan Awam, Dr. Mohd Fahmin bin Kamarul Zaman yang juga merupakan penyelidik utama.

3. Oleh yang demikian, pihak jabatan memohon agar pelajar tersebut dibenarkan untuk mengakses data bagi tujuan penyelidikan. Bersama-sama surat ini disertakan surat kelulusan dari pihak Jawatankuasa Etika Penyelidikan Perubatan Kementerian Kesihatan Malaysia (KKM) dan Jawatankuasa Etika Penyelidikan Manusia (JEPeM) Universiti Sains Malaysia (USM) untuk rujukan pihak Puan.

4. Segala kerjasama dan perhatian daripada pihak Puan amatlah dihargai dan didahului dengan ucapan ribuan terima kasih.

Sekian.

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

PROF MADYA DR. KAMARUL IMRAN MUSA
Ketua Jabatan

s.k. Prof. Madya Dr. Mohd Nazri bin Shafei (Ketua Kursus Projek Penyelidikan)
Dr. Mohd Yusof Sidek (Penyelia Utama Projek Penyelidikan Calon)
Prof. Madya Dr. Nik Rosmawati Nik Husain (Penyelia Bersama Projek Penyelidikan Calon)

JABATAN KESIHATAN WILAYAH PERSEKUTUAN
KUALA LUMPUR DAN PUTRAJAYA
Jalan Cenderasari
50590 KUALA LUMPUR
MALAYSIA

Tel : 03-2268 7333
Fax : 03-2268 7555
Laman Web : jknkl.moh.gov.my

Ruj. Kami : Bil.(20)dlm.JKWPKL/203/4 Bhg.15
Tarikh : 17 Mac 2023

YBrs. Prof. Madya Dr. Kamarul Imran Musa
Ketua Jabatan
Jabatan Perubatan Masyarakat
Kampus Kesihatan Universiti Sains Malaysia
16150 Kubang Kerian
Kelantan

YBrs. Prof. Madya Dr,

MAKLUMBALAS PERMOHONAN KEBENARAN UNTUK MENGAKSES DATA BAGI TUJUAN PENYELIDIKAN

TAJUK KAJIAN : ***PREVALANCE AND FACTORS ASSOCIATED WITH UNFAVOURABLE TREATMENT OUTCOMES AMONG DRUG RESISTANT TUBERCULOSIS (DR-TB) CASES IN*** **SELANGOR** ***AND*** **WILAYAH PERSEKUTUAN KUALA LUMPUR (WPKL)**

Dengan segala hormatnya merujuk kepada perkara di atas dan surat YBrs. Prof. Madya Dr no. rujukan PPSP/JPM/MPH/23 bertarikh 08 Mac 2023 adalah berkaitan.

2. Sukacita dimaklumkan bahawa pihak kami **tiada halangan** untuk membenarkan YBrs. Prof. Madya Dr menjalankan penyelidikan seperti di atas mulai 20 Mac 2023 sehingga 05 Mac 2024 di Jabatan Kesihatan Wilayah Persekutuan Kuala Lumpur dan Putrajaya.

3. Untuk makluman, YBrs. Prof. Madya Dr dimohon agar mematuhi perkara-perkara berikut semasa menjalankan kajian di fasiliti kesihatan Jabatan Kesihatan Wilayah Persekutuan Kuala Lumpur & Putrajaya:

3.1 Sebarang bentuk kajian yang dijalankan tidak mengganggu kelancaran perkhidmatan klinik dan tugas hakiki pegawai yang terlibat.

3.2 Memastikan penyelidik mematuhi *Standard Operation Procedure* (SOP) berkaitan COVID-19 semasa melakukan kajian di fasiliti kesihatan.

3.3 Perlu mengikuti segala perundangan dan prosedur yang telah ditetapkan oleh Kerajaan Malaysia, Kementerian Kesihatan Malaysia (KKM), Pejabat Kesihatan Daerah (PKD) dan Klinik Kesihatan.

3.4 Membentangkan hasil kajian kepada pihak kami setelah kajian selesai.

...1/2

MAKLUMBALAS PERMOHONAN KEBENARAN UNTUK MENGAKSES DATA BAGI TUJUAN PENYELIDIKAN

TAJUK KAJIAN : ***PREVALANCE AND FACTORS ASSOCIATED WITH UNFAVOURABLE TREATMENT OUTCOMES AMONG DRUG RESISTANT TUBERCULOSIS (DR-TB) CASES IN*** **SELANGOR *AND* WILAYAH PERSEKUTUAN KUALA LUMPUR (WPKL)**

3.5 Memberikan sesalinan hasil kajian kepada pihak kami sebagai bahan bacaan dan rujukan pegawai-pegawai di Jabatan ini.

3.6 Sebarang penerbitan atau diseminasi hasil penyelidikan tersebut sama ada melalui penulisan, pengiklanan, pembentangan atau untuk ke media perlu mendapat kelulusan Ketua Pengarah Kesihatan Malaysia terlebih dahulu.

YBrs. Prof. Madya Dr boleh merujuk kepada garis panduan Institut Kesihatan Negara mengenai penyelidikan di institusi dan fasiliti Kementerian Kesihatan Malaysia (Pindaan 01/2015).

4. Untuk perbincangan lanjut, YBrs. Prof. Madya Dr boleh berhubung terus dengan Ketua Unit Tibi dan Kusta (No. Telefon: 03-22687303) sebelum penyelidikan bermula bagi memastikan kelancaran penyelidikan tersebut. Kerjasama dan perhatian YBrs. Prof. Madya Dr amat dihargai dan didahulukan dengan ucapan terima kasih.

Sekian.

"MALAYSIA MADANI"
"BERKHIDMAT UNTUK NEGARA"

Pakar Perunding Perubatan Kesihatan Awam
Pengarah Kesihatan Negeri
Jabatan Kesihatan Wilayah Persekutuan
Kuala Lumpur & Putrajaya

s.k - Timbalan Pengarah Kesihatan Negeri (Kesihatan Awam)
- Ketua Unit Tibi dan Kusta JKWPKL&P

AzeeyAmin\kuratibabenarankajian\15032023

APPENDIX 7

SPSS OUTPUT FOR COLLINEARITY DIAGNOSTICS AND EXAMINATION OF ALL POSSIBLE TWO-WAY INTERACTIONS

a) SPSS Output for Collinearity Diagnostics

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B		Collinearity Statistics	
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound	Tolerance	VIF
1	(Constant)	.054	.061		.878	.380	-.066	.174		
	Gender	.193	.052	.176	3.728	.000	.091	.295	.982	1.018
	HIV Status	.234	.074	.150	3.148	.002	.088	.381	.966	1.036
	DR-TB Category	.098	.028	.167	3.507	.001	.043	.153	.967	1.034
	Marital status	.098	.048	.098	2.041	.042	.004	.193	.956	1.046
	Level of education	.066	.023	.134	2.854	.005	.021	.111	.997	1.003

a. Dependent Variable: Treatment status

b) SPSS Output for Examination of All Possible Two-Way Interaction between Independent Variables

i) Gender*HIV status

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	1.088	.276	15.509	1	.000	2.968	1.727	5.101
	HIV Status(1)	22.141	14650.699	.000	1	.999	4.130E+9	.000	.
	DR-TB Category			20.199	2	.000			
	DR-TB Category(1)	1.229	.290	18.007	1	.000	3.419	1.938	6.033
	DR-TB Category(2)	.951	.269	12.507	1	.000	2.589	1.528	4.387
	Marital status(1)	.446	.227	3.859	1	.049	1.561	1.001	2.436
	Level of education			8.618	3	.035			
	Level of education(1)	.465	.324	2.068	1	.150	1.592	.845	3.002
	Level of education(2)	.588	.465	1.598	1	.206	1.800	.723	4.480
	Level of education(3)	1.065	.372	8.186	1	.004	2.900	1.398	6.015
	Gender(1) by HIV Status (1)	-21.521	14650.699	.000	1	.999	.000	.000	.
	Constant	-2.558	.399	40.998	1	.000	.077		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, Gender * HIV Status .

ii) Gender*DR-TB category

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	1.116	.505	4.888	1	.027	3.053	1.135	8.211
	HIV Status(1)	1.067	.366	8.490	1	.004	2.905	1.418	5.953
	DR-TB Category			8.394	2	.015			
	DR-TB Category(1)	1.722	.594	8.386	1	.004	5.593	1.744	17.934
	DR-TB Category(2)	1.022	.565	3.270	1	.071	2.778	.918	8.405
	Marital status(1)	.472	.225	4.412	1	.036	1.604	1.032	2.492
	Level of education			9.683	3	.021			
	Level of education(1)	.603	.323	3.478	1	.062	1.828	.970	3.445
	Level of education(2)	.749	.462	2.629	1	.105	2.114	.855	5.228
	Level of education(3)	1.151	.374	9.474	1	.002	3.162	1.519	6.581
	DR-TB Category * Gender			1.322	2	.516			
	DR-TB Category(1) by Gender(1)	-.681	.674	1.021	1	.312	.506	.135	1.896
	DR-TB Category(2) by Gender(1)	-.090	.638	.020	1	.888	.914	.262	3.191
	Constant	-2.699	.522	26.695	1	.000	.067		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, DR-TB Category * Gender .

iii) Gender*marital status

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.748	.334	5.024	1	.025	2.114	1.099	4.067
	HIV Status(1)	1.061	.366	8.408	1	.004	2.888	1.410	5.916
	DR-TB Category			20.071	2	.000			
	DR-TB Category(1)	1.209	.287	17.702	1	.000	3.349	1.907	5.881
	DR-TB Category(2)	.949	.266	12.686	1	.000	2.584	1.532	4.356
	Marital status(1)	.255	.454	.317	1	.574	1.291	.530	3.142
	Level of education			9.029	3	.029			
	Level of education(1)	.604	.323	3.500	1	.061	1.830	.972	3.446
	Level of education(2)	.720	.463	2.420	1	.120	2.054	.829	5.086
	Level of education(3)	1.114	.373	8.921	1	.003	3.048	1.467	6.333
	Gender(1) by Marital status(1)	.288	.521	.306	1	.580	1.334	.480	3.703
	Constant	-2.409	.420	32.846	1	.000	.090		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, Gender * Marital status .

iv) Gender*level of education

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	1.161	.609	3.631	1	.057	3.194	.967	10.543
	Level of education			7.362	3	.061			
	Level of education(1)	.726	.604	1.446	1	.229	2.067	.633	6.754
	Level of education(2)	2.596	1.048	6.138	1	.013	13.410	1.720	104.554
	Level of education(3)	1.219	.645	3.570	1	.059	3.384	.956	11.984
	HIV Status(1)	1.006	.370	7.379	1	.007	2.736	1.324	5.655
	DR-TB Category			20.388	2	.000			
	DR-TB Category(1)	1.225	.289	17.907	1	.000	3.403	1.930	6.002
	DR-TB Category(2)	.971	.269	13.037	1	.000	2.639	1.558	4.470
	Marital status(1)	.514	.229	5.049	1	.025	1.672	1.068	2.619
	Gender * Level of education			4.361	3	.225			
	Gender(1) by Level of education(1)	-.206	.720	.082	1	.775	.814	.198	3.339
	Gender(1) by Level of education(2)	-2.280	1.169	3.806	1	.051	.102	.010	1.011
	Gender(1) by Level of education(3)	-.120	.789	.023	1	.879	.887	.189	4.166
	Constant	-2.723	.542	25.205	1	.000	.066		

a. Variable(s) entered on step 1: Gender, Level of education, HIV Status, DR-TB Category, Marital status, Gender * Level of education .

v) HIV status*DR-TB category

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.911	.262	12.110	1	.001	2.487	1.489	4.154
	HIV Status(1)	.480	.777	.381	1	.537	1.616	.352	7.415
	DR-TB Category			19.240	2	.000			
	DR-TB Category(1)	1.307	.302	18.685	1	.000	3.693	2.042	6.679
	DR-TB Category(2)	.796	.277	8.270	1	.004	2.217	1.289	3.816
	Marital status(1)	.445	.229	3.775	1	.052	1.560	.996	2.444
	Level of education			10.576	3	.014			
	Level of education(1)	.633	.330	3.677	1	.055	1.884	.986	3.600
	Level of education(2)	.635	.477	1.767	1	.184	1.886	.740	4.807
	Level of education(3)	1.211	.375	10.428	1	.001	3.357	1.610	7.000
	DR-TB Category * HIV Status			6.384	2	.041			
	DR-TB Category(1) by HIV Status(1)	-.391	.974	.161	1	.688	.676	.100	4.563
	DR-TB Category(2) by HIV Status(1)	2.005	1.107	3.282	1	.070	7.428	.848	65.032
	Constant	-2.514	.401	39.331	1	.000	.081		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, DR-TB Category * HIV Status .

vi) HIV status*marital status

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.875	.258	11.504	1	.001	2.400	1.447	3.979
	HIV Status(1)	.681	.523	1.692	1	.193	1.975	.708	5.509
	DR-TB Category			18.474	2	.000			
	DR-TB Category(1)	1.172	.288	16.506	1	.000	3.228	1.834	5.682
	DR-TB Category(2)	.905	.268	11.392	1	.001	2.473	1.462	4.183
	Marital status(1)	.406	.234	3.000	1	.083	1.501	.948	2.377
	Level of education			9.660	3	.022			
	Level of education(1)	.633	.327	3.737	1	.053	1.883	.991	3.578
	Level of education(2)	.789	.466	2.858	1	.091	2.200	.882	5.490
	Level of education(3)	1.154	.375	9.457	1	.002	3.170	1.520	6.615
	HIV Status(1) by Marital status(1)	.735	.759	.940	1	.332	2.086	.472	9.228
	Constant	-2.476	.397	38.974	1	.000	.084		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, HIV Status * Marital status .

vii) HIV status*level of education

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.946	.264	12.801	1	.000	2.576	1.534	4.325
	HIV Status(1)	.561	.714	.617	1	.432	1.752	.432	7.107
	DR-TB Category			21.457	2	.000			
	DR-TB Category(1)	1.302	.292	19.820	1	.000	3.676	2.072	6.520
	DR-TB Category(2)	.940	.270	12.094	1	.001	2.561	1.507	4.351
	Marital status(1)	.529	.228	5.403	1	.020	1.698	1.087	2.653
	Level of education			9.832	3	.020			
	Level of education(1)	.486	.348	1.950	1	.163	1.626	.822	3.216
	Level of education(2)	.449	.499	.811	1	.368	1.567	.590	4.163
	Level of education(3)	1.182	.394	8.989	1	.003	3.262	1.506	7.065
	HIV Status * Level of education			3.684	3	.298			
	HIV Status(1) by Level of education(1)	.862	.895	.927	1	.336	2.367	.410	13.687
	HIV Status(1) by Level of education(2)	20.921	17495.237	.000	1	.999	1.219E+9	.000	.
	HIV Status(1) by Level of education(3)	-.999	1.073	.866	1	.352	.368	.045	3.018
	Constant	-2.528	.404	39.188	1	.000	.080		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, HIV Status * Level of education .

viii) DR-TB category*marital status

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.879	.258	11.636	1	.001	2.409	1.454	3.993
	HIV Status(1)	1.033	.370	7.775	1	.005	2.808	1.359	5.804
	DR-TB Category			12.193	2	.002			
	DR-TB Category(1)	1.254	.365	11.783	1	.001	3.504	1.712	7.169
	DR-TB Category(2)	.784	.349	5.051	1	.025	2.190	1.105	4.340
	Marital status(1)	.353	.417	.718	1	.397	1.424	.629	3.225
	Level of education			9.255	3	.026			
	Level of education(1)	.593	.322	3.381	1	.066	1.809	.962	3.403
	Level of education(2)	.703	.464	2.300	1	.129	2.020	.814	5.014
	Level of education(3)	1.124	.372	9.113	1	.003	3.076	1.483	6.379
	DR-TB Category * Marital status			.829	2	.661			
	DR-TB Category(1) by Marital status(1)	-.098	.587	.028	1	.868	.907	.287	2.868
	DR-TB Category(2) by Marital status(1)	.356	.546	.425	1	.515	1.427	.490	4.161
	Constant	-2.452	.413	35.331	1	.000	.086		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, DR-TB Category * Marital status .

ix) DR-TB category*level of education

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.845	.259	10.678	1	.001	2.329	1.403	3.867
	HIV Status(1)	.947	.372	6.496	1	.011	2.578	1.245	5.340
	DR-TB Category			3.712	2	.156			
	DR-TB Category(1)	1.256	.764	2.704	1	.100	3.510	.786	15.681
	DR-TB Category(2)	1.422	.769	3.419	1	.064	4.144	.918	18.704
	Marital status(1)	.449	.226	3.938	1	.047	1.567	1.006	2.443
	Level of education			3.317	3	.345			
	Level of education(1)	.932	.681	1.876	1	.171	2.541	.669	9.648
	Level of education(2)	-19.257	16074.079	.000	1	.999	.000	.000	.
	Level of education(3)	1.318	.725	3.302	1	.069	3.734	.902	15.466
	DR-TB Category * Level of education			3.057	6	.802			
	DR-TB Category(1) by Level of education(1)	-.094	.857	.012	1	.913	.911	.170	4.882
	DR-TB Category(1) by Level of education(2)	19.829	16074.079	.000	1	.999	408883462	.000	.
	DR-TB Category(1) by Level of education(3)	.059	.984	.004	1	.952	1.061	.154	7.296
	DR-TB Category(2) by Level of education(1)	-.793	.844	.882	1	.348	.453	.087	2.366
	DR-TB Category(2) by Level of education(2)	20.443	16074.079	.000	1	.999	755346440	.000	.
	DR-TB Category(2) by Level of education(3)	-.549	.939	.342	1	.558	.577	.092	3.634
	Constant	-2.650	.652	16.536	1	.000	.071		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, DR-TB Category * Level of education .

x) Marital status*level of education

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.922	.264	12.220	1	.000	2.513	1.499	4.213
	HIV Status(1)	1.049	.368	8.108	1	.004	2.855	1.387	5.877
	DR-TB Category			20.448	2	.000			
	DR-TB Category(1)	1.226	.289	18.015	1	.000	3.408	1.935	6.002
	DR-TB Category(2)	.966	.268	12.984	1	.000	2.628	1.554	4.446
	Marital status(1)	.640	.578	1.228	1	.268	1.897	.611	5.890
	Level of education			8.034	3	.045			
	Level of education(1)	.625	.493	1.610	1	.205	1.868	.711	4.907
	Level of education(2)	.862	.648	1.768	1	.184	2.368	.665	8.436
	Level of education(3)	1.444	.549	6.923	1	.009	4.238	1.445	12.427
	Level of education * Marital status			1.426	3	.699			
	Level of education(1) by Marital status(1)	-.006	.654	.000	1	.993	.994	.276	3.580
	Level of education(2) by Marital status(1)	-.264	.941	.079	1	.779	.768	.121	4.856
	Level of education(3) by Marital status(1)	-.663	.748	.786	1	.375	.515	.119	2.232
	Constant	-2.645	.514	26.454	1	.000	.071		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education, Level of education * Marital status .

c) SPSS Output for Preliminary Final Model

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.868	.257	11.416	1	.001	2.383	1.440	3.944
	HIV Status(1)	1.053	.365	8.313	1	.004	2.867	1.401	5.865
	DR-TB Category			19.913	2	.000			
	DR-TB Category(1)	1.205	.287	17.595	1	.000	3.335	1.900	5.855
	DR-TB Category(2)	.943	.266	12.541	1	.000	2.567	1.523	4.326
	Marital status(1)	.473	.224	4.446	1	.035	1.605	1.034	2.492
	Level of education			9.416	3	.024			
	Level of education(1)	.595	.322	3.418	1	.064	1.813	.965	3.407
	Level of education(2)	.735	.462	2.532	1	.112	2.085	.843	5.153
	Level of education(3)	1.129	.372	9.225	1	.002	3.093	1.493	6.411
	Constant	-2.493	.395	39.784	1	.000	.083		

a. Variable(s) entered on step 1: Gender, HIV Status, DR-TB Category, Marital status, Level of education.