

UNIVERSITI TEKNOLOGI MARA

**SURVIVAL ANALYSIS,
DEVELOPMENT & VALIDATION OF
TB-RELATED DEATH RISK SCORE
OF ADULT PULMONARY
TUBERCULOSIS IN SELANGOR,
MALAYSIA**

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ABSTRACT

Patients with Tuberculosis (TB) continue to die despite effective treatment. The study aimed to assess the 1-year survival, develop and validate a TB-related death predictive risk score on adult Pulmonary TB (PTB) patients on treatment. A retrospective cohort study was conducted using data of eligible adult PTB patients registered in Selangor, Malaysia between 1st January 2013 and 31st December 2019 obtained from Selangor's State Health Department. The survival function of the participants was assessed through the Kaplan–Meier method. Survival functions between and among groups within a variable were compared using Log-Rank tests. Out of 24570 enrolled participants, 595 (2.4%) died from TB. The mean survival time was 356.2 days and the 1-year survival rate was 96.9%. Sociodemographic and clinical TB-related death risk factors were determined through multivariable Cox Proportional Hazard model, TB-related death were significantly associated with far (adjusted Hazard Ratio (aHR) 9.98, 95%CI 4.28–23.28) and moderately advanced (aHR 3.23, 95%CI 1.43–7.31) radiological findings at diagnosis; concurrent TB meningitis (aHR 7.67, 95%CI 4.53–12.98) and miliary TB (aHR 6.32, 95%CI 4.10–9.74) involvement; HIV positive at diagnosis (aHR 2.81, 95%CI 2.21–3.57); Hulu Selangor (aHR 1.95, 95%CI 1.29–2.93), Klang (aHR 1.53, 95%CI 1.18–1.98) and Hulu Langat (aHR 1.31, 95%CI 1.03–1.68) residing districts; no formal education (aHR 1.70, 95%CI 1.23–2.35); unemployment (aHR 1.54, 95%CI 1.29–1.84), positive sputum smear AFB at diagnosis (aHR 1.51, 95%CI 1.22–1.85); rural residency (aHR 1.39, 95%CI 1.13–1.72); and advancing age (aHR 1.02, 95%CI 1.02–1.03). Subsequently, the data set was divided into development (registered patients between the years 2013 and 2017) and validation (patients between 2018 and 2019) data sets. A predictive model based on the determined TB-related death risk factors was developed using the development data set. The apparent model performance overall was good. The model was validated internally (using the simple bootstrap resampling method) and externally (using the validation data set). The model's predictive performance on internal validation (overall performance: R^2_D 0.38 (95%CI 0.33–0.42); discrimination: Harrell's C 0.75 (95%CI 0.73–0.78), Uno's C 0.76 (95%CI 0.73–0.78); calibration: observed-expected ratio 1.02 (95%CI 0.91–1.14), predictive index regression 1.12 (95%CI 1.09–1.15)) and external validation (overall performance: R^2_D 0.30 (95%CI 0.24–0.34); discrimination: Harrell's C 0.72 (95%CI 0.69–0.75), Uno's C 0.68 (95%CI 0.64–0.73); calibration (observed-expected ratio 0.97 (95%CI 0.87–1.08), predictive index regression 1.02 (95%CI 0.89–1.16)) were satisfactory. In summary, the study provides the latest information on TB-related death risk factors among local TB patients. Furthermore, the TB-Related Death Risk Score should assist clinicians in identifying high-risk TB patients for further management and improving patients's understanding of their own risk of TB-related death, encouraging their treatment adherence.

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CHAPTER ONE

INTRODUCTION

1.1 Preamble

Tuberculosis (TB) is an infectious disease predominantly caused by *Mycobacterium Tuberculosis*. The TB pathogen is usually transmitted into a human host through inhalation of TB-contaminated droplets, exhaled by active TB patients. However, the majority of human transmissions result in latent lung infections rather than clinical manifestations. Approximately ten per cent of those with latent infections progress to develop an active form of TB, which predominantly affects the lungs but may involve other organs. Typical symptoms of active TB infection include chronic cough, haemoptysis (coughing out blood or blood-streaked sputum), night sweating, fever and loss of weight (World Health Organization (WHO), 2020).

TB can be fatal to humans. In fact, TB has been one of the major causes of death in recent years and the main cause of death attributed to a single infectious agent since 2007 (Furin, Cox, & Pai, 2019; WHO, 2020; 2021a). Before the advent of TB chemotherapy, approximately 70% of smear-positive and 20% of smear-negative TB-infected individuals would succumb to TB (Mitchell, 2012). Moreover, almost half of TB-infected individuals will pass away from the disease within three years if not properly treated (Maher, 1999; Mitchell, 2012).

Deaths from TB (TB-related death) are an important public health concern. Due to the significant toll of TB mortality, the WHO declared the TB epidemic a worldwide emergency in 1993, designating the disease as a high priority among the global health challenges (Nathavitharana & Friedland, 2015; WHO, 1994). The declaration reinvigorated the global effort to combat TB, resulting in the widespread use of highly effective chemotherapy treatment, the application of Directly-Observed Treatment (DOT) to improve treatment adherence, and standardized TB management and control at nearly all national levels worldwide. The End TB Strategy, the current global strategy to end TB, signifies the world's vision of ending the TB epidemic once and for all. The strategy envisioned zero deaths from TB by targeting a 95% reduction of TB-related deaths by the year 2035 as compared to the 2015 reported cases (WHO, 2015b).