

Original Article

Development and validation of clinical prediction score for mortality in tuberculosis patients

Pattama Saisudjarit^{1,2}, Surasak Saokaew^{3,4,5*}, Acharaporn Duangjai⁶, Anurak Prasatkhetragarn^{1,7}, Sukrit Kanchanasurakit^{5,8,9} and Pochamana Phisalprapa^{10*}

¹Department of Applied Science, School of Sciences, University of Phayao, Phayao, Thailand; ²Medicine Staff Organization, Thap Khlo Hospital, Phichit, Thailand; ³Division of Social and Administration Pharmacy, Department of Pharmaceutical Care, School of Pharmaceutical Sciences, University of Phayao, Phayao, Thailand; ⁴Center of Excellence in Bioactive Resources for Innovative Clinical Applications, Chulalongkorn University, Bangkok, Thailand; ⁵Unit of Excellence on Clinical Outcomes Research and Integration (UNICORN), School of Pharmaceutical Sciences, University of Phayao, Phayao, Thailand; ⁶School of Medical Sciences, University of Phayao, Phayao, Thailand; ⁷School of Sciences, University of Phayao, Phayao, Thailand; ⁸Division of Clinical Pharmacy, Department of Pharmaceutical Care, School of Pharmaceutical Sciences, University of Phayao, Phayao, Thailand; ⁹Division of Pharmaceutical Care, Department of Pharmacy, Phrae Hospital, Phrae, Thailand; ¹⁰Division of Ambulatory Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

*Corresponding author: surasak.sa@up.ac.th (SS) and coco_a105@hotmail.com (PP)

Abstract

Tuberculosis (TB) remains a global and national public health concern, with mortality posing a significant challenge in treatment programs. The aim of this study was to develop a simple risk-scoring system to predict mortality among TB patients and assess its applicability in resource-limited settings. Data from TB patient registries in Phichit Province, Thailand, covering from January 1, 2017, to December 31, 2020, were used. Eligible participants were aged ≥ 18 years, having completed treatment or death. A risk score was developed and internally validated using logistic regression. Coefficients were used to assign weighted points to predictors and applied to a validation cohort to assess diagnostic performance. The performance was evaluated by generating a receiver operating characteristic (ROC) curve. The study included 2,196 participants, randomly allocated into derivation ($n=1,600$) and validation ($n=596$) cohorts. The risk score included Charlson Comorbidity Index scores (1–2 points and ≥ 3 points) and TB meningitis. It showed an area under ROC curve (AuROC) of 74.34% (95%CI: 70.80–77.88%) with good calibration (Hosmer-Lemeshow χ^2 : 0.53; $p=0.97$). Positive likelihood ratios for low (≤ 3) and high (≥ 6) risk were 1.06 (95%CI: 1.03–1.09) and 31.62 (95%CI: 7.23–138.37), respectively. In the validation cohort, AuROC was 79.50% (95%CI: 74.40–84.60%), with 75% and 100% certainty in low- and high-risk groups. In conclusion, this simple risk score, using routine data and two predictors, can predict mortality in TB patients. It may aid clinicians in planning appropriate care strategies. Nevertheless, the tool should undergo external validation before being implemented in clinical practice.

Keywords: Mortality, tuberculosis, risk score, prediction, screening tool

Introduction

Tuberculosis (TB) remains a formidable public health challenge at the global and national levels. As stated in the 2018 report published by the World Health Organization (WHO), the prevalence of TB cases reaches an alarming figure of approximately 10 million, corresponding to a rate of 132 individuals per 100,000 population [1]. Within this cohort, a staggering 1.2 million deaths result from TB cases unrelated to human immunodeficiency virus (HIV), while TB cases compounded with HIV infection account for 251,000 deaths, constituting a substantial 33% of all HIV-



associated mortalities [1]. Thailand has been designated as one of the 14 countries internationally burdened by the intersection of TB and HIV infection, as recognized by the WHO [1]. During 2016, Thailand experienced a collective count of 70,114 newly reported and recurring incidents of TB. An analysis of the gathered data unveiled a noteworthy outcome, indicating that a substantial portion of the afflicted individuals, precisely 82.9%, successfully achieved recuperation, whereas the mortality rate reached an alarming 8.1% [2]. TB patients in Phichit province have a high mortality rate of up to 17%, exceeding the national target of no more than 5% [2].

Several factors have consistently been associated with an increased risk of mortality among individuals with active TB. These factors include advanced age, male, delays in diagnosis and treatment, drug resistance, and the presence of comorbidities such as HIV co-infection, diabetes, renal disease, and chronic obstructive pulmonary disease (COPD) [3-7]. Existing mortality prediction models often rely on variables requiring specialized diagnostics, such as chest X-rays, sputum culture, or advanced laboratory markers such as cluster of differentiation 4 (CD4) count or sputum gene Xpert [7], which may be inaccessible in resource-limited settings. Treating TB patients requires the administration of multiple anti-TB drugs, which may cause severe adverse reactions, including hepatotoxicity [8,9], thereby significantly increasing the risk of mortality. Close monitoring of TB patients is essential. While TB treatment follows WHO recommendations [2], the decision regarding hospitalization for the initial two weeks or outpatient treatment from the start depends on the treating physician's discretion and available resources. The aim of this study was to develop a simple and practical risk-scoring system using routine clinical data to predict mortality in TB patients, enabling real-time risk stratification and supporting physicians in devising appropriate care strategies, particularly in resource-limited settings.

Methods

Setting

The study was conducted at hospitals in Phichit Province due to the high TB mortality rate in the region, using secondary data from the National Tuberculosis Information Program (NTIP) from January 1, 2017, to December 31, 2020. This study followed the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) Statement (see **Underlying data**).

Study population

Eligible subjects were new cases or relapsed TB patients diagnosed by clinicians following the TB practice guidelines established by WHO [2,10]. The follow-up schedule for patients involves an initial appointment at two weeks, followed by subsequent visits every 1 to 2 months, depending on the patient's condition and the physician's discretion. The final follow-up is scheduled at the conclusion of the treatment period, which extends for up to six months or until the attending physician confirms treatment completion. The inclusion criteria for this study consisted of patients who were 18 years of age or older and had either completed the treatment or experienced death as their outcome. Completed treatment was defined as TB patients diagnosed and treated according to the WHO guidelines having at least one negative sputum smear result during the course of treatment, and the final sputum smear result at the end of treatment is negative [2]. Patients who lost to follow-up and multidrug-resistant tuberculosis (MDR-TB) were excluded from the study. The study included a total of 2,196 patients who were then randomly divided into two groups: the derivation cohort, consisting of 1,600 patients, and the validation cohort, consisting of 596 patients. This approach ensures that the model is trained on a sufficiently large sample while still having an independent dataset for performance assessment. A common practice in predictive modeling is to allocate approximately 70–80% of the data for derivation and 20–30% for validation, which aligns with the distribution used in this study [11].

Study design and data collection

This retrospective cohort study sought to devise a simple screening tool that can precisely predict mortality among individuals with TB. The study utilized the NTIP to collect demographic information, clinical data, and laboratory data for the enrolled participants. The NTIP is a

nationwide TB database that collects medical records from hospitals across Thailand. It serves as a vital tool for monitoring and managing the disease across the country. The NTIP gathers data from various healthcare facilities involved in TB diagnosis, treatment, and prevention. This includes both public and private hospitals, as well as primary care units and community-based programs. The data encompasses demographic information, clinical characteristics, laboratory results, treatment outcomes, and other relevant details about TB patients. The Bureau of Tuberculosis, under the Ministry of Public Health of Thailand, is responsible for the overall management and maintenance of the NTIP system. They ensure data quality, security, and confidentiality, as well as provide training and support to healthcare personnel involved in data entry and utilization. Access to the NTIP data is restricted and controlled to protect patient privacy and confidentiality. Only authorized personnel, such as healthcare professionals, researchers, and public health officials, can request access to the data for specific purposes, such as research, program evaluation, and policy development.

Statistical analyses

Categorical data was presented in terms of frequencies and percentages, whereas continuous data was presented as the mean and standard deviation. Statistical significance was determined using two-tailed p -values, with a threshold of $p < 0.05$. All statistical analyses were performed using STATA software, version 16 (StataCorp LLC, Texas, USA).

Model development

Variables with potential influence on the outcome were identified and integrated into the model development process. The extracted data encompassed the following aspects: (1) demographic information encompassing age, sex, and weight (kg); and (2) clinical data encompassing registration type (new case, relapse, treatment after loss of follow-up, treatment after failure, and others), HIV infection status, TB type (intrapulmonary, extrapulmonary, or both), and comorbidities. The identification of comorbidities relied on the 2016 version of the International Classification of Diseases 10th revision (ICD-10), using codes J44.0-J44.9 (for chronic obstructive pulmonary disease), N18.0-N18.9 (for chronic kidney disease (CKD)), K70.1-K77.8 (for liver disease), and E10.0-E14.9 (for diabetes mellitus). Each patient in the study population was assigned a Charlson comorbidity index (CCI) score (see **Underlying data**), quantifying the level of underlying comorbidity at the time of diagnosis. The CCI scores were categorized as 0, 1–2, and ≥ 3 [12], and laboratory data encompassed sputum acid-fast bacillus (AFB) testing.

Through univariable logistic regression, a comparison was made between the identified variables for TB patients who died and those who completed treatment. The findings were summarized using odds ratios (ORs), 95% confidence intervals (95% CIs), and p -values. Variables with a p -value < 0.2 or determined to be clinically significant were chosen for the subsequent multivariable stepwise logistic regression analysis [13]. Variables with a p -value below 0.05 were deemed eligible for incorporation into the model. Significant variable coefficients from the multivariable analysis were weighted and transformed into item scores by dividing each regression coefficient by the smallest one in the model and then rounding to the nearest integer [14,15]. To assess the discriminative performance of the prediction score created, a receiver operating characteristic (ROC) curve was generated and a Hosmer-Lemeshow goodness of fit test was performed [16]. Threshold scores were selected to categorize TB patients into three risk groups: low, moderate, and high risk of mortality. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR-) were computed [17,18].

Model validation

For internal validation, this study used a simple split method in which the dataset was split into derivation and validation cohorts at random in a 3:1 ratio. Missing data was handled using complete-case analysis. The performance and accuracy of the score were assessed by replicating the evaluation conducted in the derivation cohort using the validation cohort. The validation cohort was used to validate the score, and its performance was evaluated by generating an ROC curve.

Results

Characteristics of TB patients

Among the initial cohort of 2,350 TB patients, 154 individuals (6.6%) exhibited outcomes other than completion or death (see **Underlying data**). Consequently, the final analytical sample was composed of 2,196 patients, within which 399 individuals (18.2%) experienced mortality during treatment (**Figure 1**). A comprehensive overview of the general characteristics of the TB patient cohort is presented in **Table 1**. Among the 2,196 patients included in the analysis, the mean age was 56.7 years, with 35.3% of patients aged 65 years or older, and a substantial majority of 70.9% comprising male individuals. The average weight was recorded as 51.1 kg, and a minority of 3.2% weighed 35 kg. Diabetes mellitus emerged as the most prevalent comorbid condition within the study population.

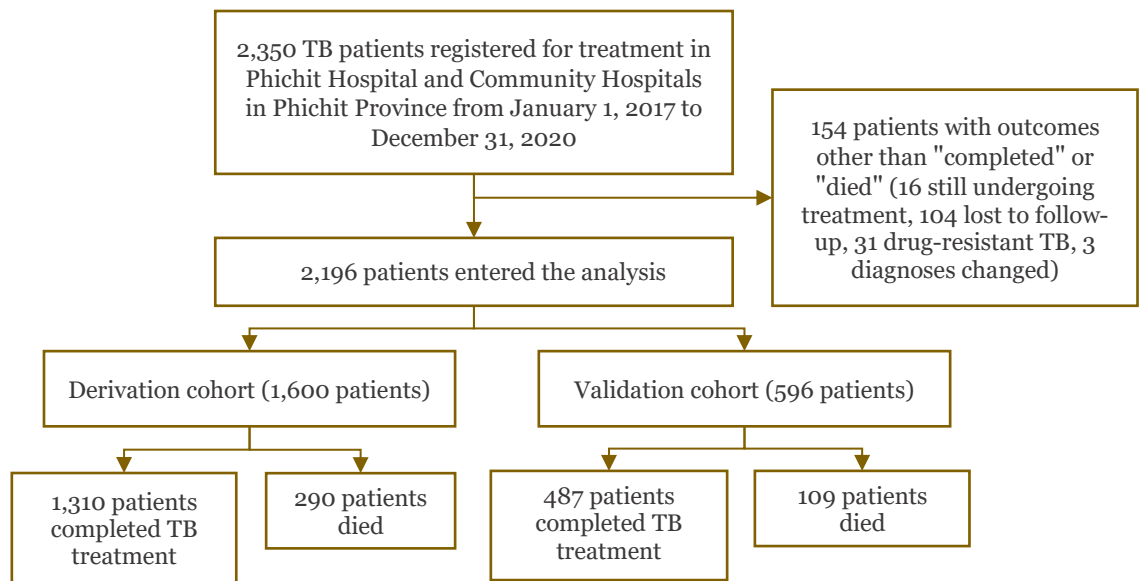


Figure 1. Flowchart of the study populations.

Predictors of mortality in TB patients

The results of the univariable analysis conducted on the derivation cohort, indicating the presence of eight predictors associated with mortality, are presented in **Table 2**. These predictors included age ≥ 65 years (OR: 3.01; 95%CI: 2.32–3.91, $p < 0.001$), weight < 35 kg (OR: 1.87; 95%CI: 1.03–3.39; $p = 0.039$), COPD (OR: 2.29; 95%CI: 1.26–4.15; $p = 0.006$), CKD (OR: 2.74; 95%CI: 1.53–4.89; $p = 0.001$), liver disease (OR: 6.71; 95%CI: 2.53–17.77; $p < 0.001$), positive HIV status (OR: 1.25; 95%CI: 1.14–1.39; $p < 0.001$), TB meningitis (OR: 14.52; 95%CI: 5.71–36.93; $p < 0.001$), and CCI ≥ 3 points (OR: 2.30; 95%CI: 1.33–3.99; $p = 0.003$).

Model development

The final model retained two variables, CCI and TB meningitis, and the scoring system for predicting mortality in TB patients involved assigning points to each factor during the calculation process. These factors included the CCI with 1–2 points (assigned a value of 1 for "yes" and 0 for "no"), CCI with ≥ 3 points (assigned a value of 3 for "yes" and 0 for "no"), and the presence of TB meningitis (assigned a value of 4 for "yes" and 0 for "no"). The points assigned to each factor were determined based on the weighted coefficients, and they were rounded to the nearest whole number. This process yields the corresponding assigned scores, as indicated in **Table 3**. The final multivariable analysis identifies CCI scores and TB meningitis as significant predictors of mortality in TB patients. Higher CCI scores (≥ 1) and the presence of TB meningitis were strongly associated with increased mortality risk. TB meningitis had the highest impact, as indicated by its largest coefficient. Based on these findings, a weighted risk score was developed, assigning 1 point for CCI (1–2), 3 points for CCI (≥ 3), and 4 points for TB meningitis, allowing for effective risk stratification using routine clinical data.

Table 1. Clinical and demographic characteristics of tuberculosis (TB) patients (n=2,196)

Characteristics	All patients (n=2,196)	Derivation cohort (n=1,600)		Validation cohort (n=596)	
	n (%)	Dead (n=290)	Completed (n=1,310)	Dead (n=109)	Completed (n=487)
		n (%)	n (%)	n (%)	n (%)
Age, mean $\pm$ standard deviation (SD)	56.7 $\pm$ 16.8	64.4 $\pm$ 16.2	55.0 $\pm$ 16.4	65.0 $\pm$ 15.9	54.8 $\pm$ 16.5
$\geq$ 65 years	774 (35.3)	165 (56.9)	399 (30.5)	62 (56.9)	148 (30.4)
<65 years	1,422 (64.7)	125 (43.1)	911 (69.5)	47 (43.1)	339 (69.6)
Sex					
Male	1,556 (70.9)	206 (71.0)	935 (71.4)	73 (67.0)	342 (70.2)
Female	640 (29.1)	84 (29.0)	375 (28.6)	36 (33.0)	145 (29.8)
TB type					
Intrapulmonary	1,872 (85.3)	246 (84.8)	1,123 (85.7)	90 (82.6)	413 (84.8)
Extrapulmonary	304 (13.8)	39 (13.5)	177 (13.5)	18 (16.5)	70 (14.4)
Both	20 (0.9)	5 (1.7)	10 (0.8)	1 (0.9)	4 (0.8)
Type of register					
New	1,960 (89.3)	252 (86.9)	1,172 (89.5)	94 (86.2)	442 (90.8)
Relapse	177 (8.1)	29 (10.0)	107 (8.2)	11 (10.1)	30 (6.2)
Treatment after loss of follow-up	29 (1.3)	6 (2.1)	14 (1.1)	1 (0.9)	8 (1.6)
Treatment after failure	12 (0.5)	1 (0.3)	7 (0.5)	0	4 (0.8)
Other	18 (0.8)	2 (0.7)	10 (0.8)	3 (2.8)	3 (0.6)
Weight (kg), mean $\pm$ SD	51.1 $\pm$ 11.0	48.6 $\pm$ 12.3	51.7 $\pm$ 10.9	47.9 $\pm$ 10.5	51.7 $\pm$ 10.4
<35 kg.	70 (3.2)	16 (5.1)	40 (3.1)	5 (4.6)	9 (1.9)
COPD	72 (3.3)	17 (5.9)	35 (2.8)	7 (6.4)	13 (2.7)
CKD	71 (3.2)	19 (6.6)	33 (2.5)	8 (7.3)	11 (2.3)
Liver disease	27 (1.2)	10 (3.5)	8 (0.6)	9 (8.3)	0 (0.00)
DM	295 (13.4)	46 (15.9)	170 (13.0)	20 (18.4)	59 (12.1)
HIV status (+)	203 (9.2)	43 (14.8)	103 (7.9)	17 (15.6)	40 (8.2)
AFB smear (+)	942 (42.9)	131 (45.2)	537 (41.01)	45 (41.3)	229 (47.0)
TB meningitis	32 (1.5)	18 (6.2)	6 (0.5)	6 (5.5)	2 (0.4)
CCI scores					
0	493 (22.5)	22 (7.6)	338 (25.8)	4 (3.7)	129 (26.5)
1–2	809 (36.8)	67 (23.1)	518 (39.5)	24 (22.0)	200 (41.1)
$\geq$ 3	894 (40.7)	201 (69.3)	454 (34.7)	81 (74.3)	158 (32.4)

AFB: Acid-fast bacillus; CCI: Charlson comorbidity index; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; HIV: human immunodeficiency virus

Table 2. Univariable analysis of risk factors associated with death in tuberculosis (TB) patients (n=1,600)

Variable	Derivation cohort (n=1,600)		
	Odds ratio	95% confidence interval	p-value
Age ≥65 years	3.01	2.32–3.91	<0.001
Male	0.98	0.74–1.30	0.908
Extrapulmonary TB*	1.13	0.82–1.55	0.458
Relapse TB infection	1.26	0.81–1.94	0.294
Weight <35 kg.	1.87	1.03–3.39	0.039
COPD	2.29	1.26–4.15	0.006
CKD	2.74	1.53–4.89	0.001
Liver disease	6.71	2.53–17.77	<0.001
DM	1.26	0.88–1.80	0.204
HIV status (+)	1.25	1.14–1.39	<0.001
AFB smear (+)	1.07	0.90–1.27	0.455
TB meningitis	14.52	5.71–36.93	<0.001
CCI scores			
1–2 points	1.45	0.81–2.62	0.214
≥3 points	2.30	1.33–3.99	0.003

AFB: acid-fast bacillus; CCI: Charlson comorbidity index; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; HIV: human immunodeficiency virus

*Reference group is intrapulmonary TB

The risk scoring system was established by determining the threshold through the analysis of the discrimination plot and the performance of parameters, allowing for the identification of patients at risk of mortality. Cutoff scores of 3 and 6 were chosen to classify patients into three risk categories: low-risk (≤ 3 points), moderate-risk (4–5 points), and high-risk (≥ 6 points). The high-risk group correctly predicted death in 87.5% of TB patients. Predicting the presence of death exhibited moderate accuracy (PPV of 87.5%). In the low-risk group, patients without death were accurately identified in 75.0% of cases. Excluding the presence of death demonstrated moderate accuracy (NPV of 75.0%). The correct prediction rate for the presence or absence of death was $(1,304+14)/(1,576+16)=82.8\%$. The incorrect prediction rate was $(272+2)/(1,576+16)=17.2\%$ (Table 4). With this scoring system and the two cutoff points, the score effectively differentiated between patients with and without death, demonstrating good validity (AuROC: 74.34%; 95%CI: 70.80–77.88%) (Figure 2A) and a well-calibrated predictive model (Hosmer-Lemeshow χ^2 : 0.53; $p=0.97$).

Table 3. Multivariable analysis and risk score for death in tuberculosis (TB) patients

Predictors	Coefficient	95%CI	Transformed coefficients	Assigned score
Charlson comorbidity index (CCI)				
1–2 points	0.67	0.17–1.18	1	1
≥3 points	1.89	1.43–2.36	2.81	3
TB meningitis	2.54	1.56–3.53	3.78	4

CI: confidence interval

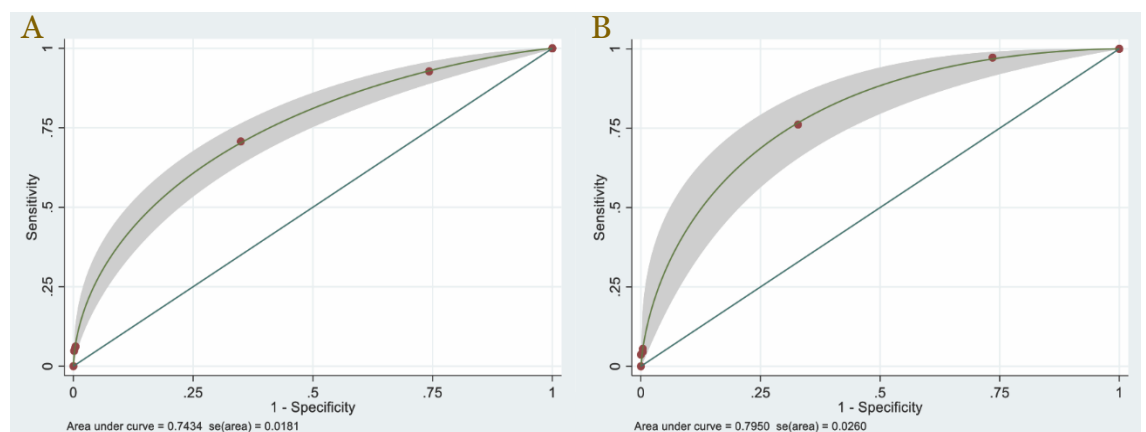


Figure 2. Receiver operator characteristic (ROC) curve of the scoring system in predicting death in tuberculosis patients. (A) derivation cohort (n=1,600); and (B) validation cohort (n=596).

Table 4. Distribution of risk of death in tuberculosis patients, diagnostic performance and interpretation in derivation cohort (n=1,600)

Derivation (n=1,600)	Low (score ≤3)	Moderate (score 4–5)	High (score ≥6)	Total
Total	1,576	8	16	1,600
Completed	1,304	4	2	1,310
Dead	272	4	14	290
Diagnostic performance				
Sensitivity	99.54%		4.83%	
Specificity	6.21%		99.85%	
Positive predictive value	82.74%		87.50%	
Negative predictive value	75.00%		82.58%	
Accuracy	82.62%		82.62%	
Likelihood ratio (+)	1.06 (95%CI: 1.03–1.09)		31.62 (95%CI: 7.23–138.37)	
Likelihood ratio (-)	0.07 (95%CI: 0.03–0.18)		0.95 (95%CI: 0.93–0.98)	
Interpretation	Absence of death (75.00% certainty)		Presence of death (87.50% certainty)	

Model validation

The ROC curve demonstrated similarities between the derivation and validation cohorts, with AuROC values of 74.34% (95%CI: 70.80–77.88%) and 79.50% (95%CI: 74.40–84.60%), respectively (**Figure 2**). In the high-risk group, TB patients were consistently predicted to have mortality, achieving a high predictive accuracy of 100% (PPV of 100%). In the low-risk group, the absence of death was correctly identified in 75.0% of patients, indicating a moderate accuracy in predicting survival (NPV of 75.0%). The overall accuracy in predicting the presence or absence of death was calculated as (485+4)/(588+4), resulting in an accuracy rate of 82.4%. Conversely, the error rate was calculated as (103+0)/(588+4), yielding an error rate of 17.4% (**Table 5**). The association between the risk score and the probability of death, with higher scores associated with increased mortality risk is presented in **Figure 3**.

Table 5. Distribution of risk of death in tuberculosis patients, diagnostic performance and interpretation in validation cohort (n=596)

Validation (n=596)	Low (score ≤3)	Moderate (score 4–5)	High (score ≥6)	Total
Total	588	4	4	596
Completed	485	2	0	487
Dead	103	2	4	109
Diagnostic performance				
Sensitivity	99.59%		3.67%	
Specificity	5.50%		100.00%	
Positive predictive value	82.48%		100.00%	
Negative predictive value	75.00%		82.26%	
Accuracy	82.38%		82.38%	
Likelihood ratio (+)	1.05 (95%CI: 1.01–1.10)		-	
Likelihood ratio (-)	0.07 (95%CI: 0.02–0.36)		0.96 (95%CI: 0.93–1.00)	
Interpretation	Absence of death (75.00% certainty)		Presence of death (100.00% certainty)	

Discussion

This study provides evidence of the effectiveness of the TB mortality risk score in predicting mortality in TB patients. This study created and verified a prognostic scoring system for TB mortality, utilizing two frequently accessible demographic and clinical characteristics collected during a patient's initial healthcare facility visit. Consequently, our scoring model enables the timely provision of the patient's death prognosis to clinicians and healthcare workers. Through the utilization of the model's three risk groups—low, moderate, and high-risk groups—clinicians and healthcare workers gain access to a dependable and user-friendly tool for guiding treatment decisions, delivering essential medical support, and allocating follow-up resources, including

prompt treatment and intensified medical support. All TB patients require timely initiation of standard treatment in accordance with national and WHO guidelines [2]. High-risk patients necessitate the highest level of care, including immediate hospitalization, intensive monitoring, and enhanced medical support. Moderate-risk patients can derive advantages from vigilant monitoring and timely intervention to prevent the worsening of their health status. TB patients classified as low-risk should receive treatment and management following established protocols.

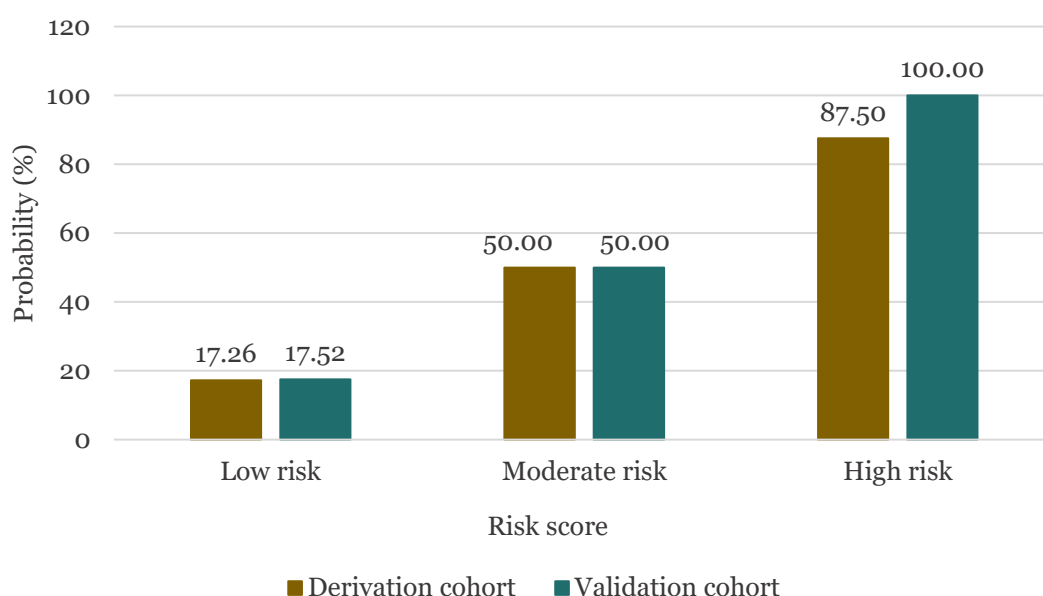


Figure 3. Percentage of predicting death in tuberculosis patients by risk score.

The final model utilized CCI scores and TB meningitis as predictor variables. The threshold value was established through the evaluation of specificity, sensitivity, accuracy, positive likelihood ratio, and negative likelihood ratio. Patients were classified into three categories, namely low-risk (score ≤ 3), moderate-risk (score 4 to 5), and high-risk (score ≥ 6), according to their TB mortality risk score. Importantly, the score demonstrated strong predictive capability in assessing mortality. The CCI score was originally utilized to assess the likelihood of death in hospitalized patients within a one-year duration. Since the study utilized retrospective data, CCI scores were determined based on patients' baseline characteristics without tracking changes over time. CCI was a tool used to assess multiple comorbidities in patients, focusing on conditions that may impact the treatment and outcomes of the primary disease being treated, such as diabetes, liver disease, and HIV/AIDS [12].

Advancing age, for instance, has been widely reported to be associated with higher mortality risk in patients with TB [19-23], especially patients older than 65 years [7,24]. Advancing age is associated with multiple organ degeneration and low immunity. TB increases the number of HIV and progresses to AIDs faster [2]. Coinfection with HIV has also been established as a powerful determinant of death in TB patients [7,22,24,25]. Patients with liver disease are at high risk of death [26]. Due to the common side effect of TB medicines—hepatitis—patients with underlying liver disease experience more severe side effects. TB meningitis is a major organ infection with a high risk of death [24,27].

This study stands out by employing a simplified risk score obtained from routine data collection. This risk score for TB mortality serves as a valuable resource for predicting mortality upon initial diagnosis. Notably, the score relies on only two clinical parameters, enhancing its memorability and obviating the necessity for further laboratory tests, thereby contributing to cost reduction.

Numerous prognostic models have been developed to predict mortality in TB patients. Several predictors, including older age, sex, diabetes, HIV co-infection, malnutrition, alcohol abuse, and respiratory failure, have been identified as risk factors associated with poor outcomes in TB patients [13,19-21,24,27-30]. The model presented in this study is a simple one, consisting

of only two variables. While the model performed well in this study, its predictive performance should be compared to other TB mortality prediction systems. Existing models, such as those incorporating chest X-rays, sputum culture results, or more comprehensive laboratory markers, report similar AuROC values ranging from 75% to 80% [24,29] but often require specialized diagnostics that are inaccessible in resource-limited settings. In contrast, this model relies exclusively on routine clinical data, making it more practical and scalable for broader applications. Most of the research in Thailand has focused on identifying factors associated with TB mortality [31-33], but few studies have developed predictive models to stratify patient risk.

Our study has several limitations. Firstly, the deaths of TB patients were categorized as all-cause deaths, which may lead to misclassification. In Thailand, the NTIP records deaths without specifying the cause. Secondly, certain key variables known to influence TB mortality, such as body mass index and CD4 count, were unavailable in the NTIP database. As a result, weight was used as a proxy for malnutrition, and HIV status served as a general indicator of immunosuppression. Additionally, routine laboratory testing for TB does not typically include CD4 count measurement. Thirdly, retrospective designs are vulnerable to biases, such as selection and information bias, which can distort results if patient records are incomplete or if the cohort isn't representative of the general TB population. Despite these challenges, this study design can still offer valuable insights and serve as a basis for developing a mortality prediction score. However, the quality of data collected and the number of variables available are sometimes limited by the reliance on routine data.

Furthermore, incorporating socioeconomic status variables and other lifestyle factors such as alcohol consumption, smoking, and physical activity could provide a more comprehensive understanding of the factors influencing patient outcomes. These variables may have significant predictive value and could enhance the model's ability to accurately forecast patient prognosis. External validation through testing this tool in other populations or conducting prospective studies will enhance its credibility and utility while expanding its applicability and generalizability across diverse contexts and settings. Additionally, the use of all-cause mortality instead of TB-specific mortality may lead to misclassification. However, this limitation was unavoidable due to the nature of routine data collection. Future studies should explore methods to refine mortality classification for improved accuracy.

Conclusion

This study developed a risk score to predict mortality in TB patients at the time of diagnosis, providing a simple tool for early risk stratification and clinical decision-making. The developed risk score, based on routine data collection and consisting of CCI scores and TB meningitis, can be utilized to predict mortality in TB patient care. This risk score has the potential to assist clinicians in planning appropriate care for TB patients. The risk score could be integrated into existing TB management protocols and electronic health record (EHR) systems. Utilizing existing NTIP data for predicting mortality risk in TB patients has significant potential. Integrating the two predictors, CCI and TB meningitis, into NTIP's analytical framework enables automatic risk score calculation within the system. This approach will enhance real-time risk stratification and support timely clinical decision-making without requiring additional data collection. Future directions include conducting external validation across diverse populations and healthcare settings to assess the model's generalizability. Additionally, prospective studies are recommended to evaluate the model's real-world impact on clinical outcomes. These steps aim to address potential biases and gaps identified in the current study, ensuring the model's robustness and applicability in broader contexts.

Ethics approval

Approval for this study was granted by the University of Phayao Human Ethics Committee under the reference number UP-HEC 1.2/093/66. The data used for analysis were anonymized to protect patient identities, and access to the dataset was restricted and secured with coded authorization.

Acknowledgments

We would like to express our gratitude to the Phichit Provincial Public Health Office for providing the necessary support and data. Additionally, this research was partially supported by the University of Phayao and the Thailand Science Research and Innovation Fund (Fundamental Fund 2025, Grant No. 5017/2567).

Competing interests

All the authors declare that there are no conflicts of interest.

Funding

This study received no other external funding.

Underlying data

Derived data supporting the findings of this study are available from <https://doi.org/10.6084/m9.figshare.28457165.v1>.

Declaration of artificial intelligence use

This study used artificial intelligence (AI) tools and methodologies in manuscript writing support. AI-based language models, ChatGPT and Quillbot, were employed for language refinement (improving grammar, sentence structure, and readability of the manuscript). We confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

How to cite

Saisudjarit P, Saokaew S, Duangjai A, *et al.* Development and validation of clinical prediction score for mortality in tuberculosis patients. *Narra J* 2025; 5 (2): e1701 - <http://doi.org/10.52225/narra.v5i2.1701>.

References

1. World Health Organization. Global tuberculosis report 2019. Available from: <https://www.who.int/publications/i/item/9789241565714>. Accessed: 10 June 2022.
2. Bureau of Tuberculosis. National tuberculosis control programme guideline, Thailand, 2018. Available from: <https://www.tbthailand.org/download/Manual/NTP2018.pdf>. Accessed: 24 June 2022.
3. Oursler KK, Moore RD, Bishai WR, *et al.* Survival of patients with pulmonary tuberculosis: Clinical and molecular epidemiologic factors. *Clin Infect Dis* 2002;34(6):752-759.
4. Sterling TR, Zhao Z, Khan A, *et al.* Mortality in a large tuberculosis treatment trial: Modifiable and non-modifiable risk factors. *Int J Tuberc Lung Dis* 2006;10(5):542-549.
5. Lefebvre N, Falzon D. Risk factors for death among tuberculosis case: Analysis of European surveillance data. *Eur Respir J* 2008;31(6):1256-1260.
6. Amnuaiphon W, Anuwatnonthakate A, Nuyongphak P, *et al.* Factor associated with death among HIV-uninfected TB patients in Thailand, 2004–2006. *Trop Med Int Health* 2009;14(11):1338-1346.
7. Horne DJ, Hubbard R, Narita M, *et al.* Factors associated with mortality in patients with tuberculosis. *BMC Infect Dis* 2010;10:258-265.
8. Song JH, Yoon SY, Park TY, *et al.* The clinical impact of drug-induced hepatotoxicity on anti-tuberculosis therapy: A case control study. *Respir Res* 2019;20(1):283.
9. Abbara A, Chitty S, Roe JK, *et al.* Drug-induced liver injury from antituberculous treatment: A retrospective study from a large TB centre in the UK. *BMC Infect Dis* 2017;17(1):231.
10. World Health Organization. Implementing the stop TB strategy: A handbook for national tuberculosis control program. Geneva: World Health Organization; 2008.
11. Joseph VR. Optimal ratio for data splitting. *Stat Anal Data Min* 2022;15:531-538.

12. Zhang S, Tong X, Wang L, *et al.* Clinical characteristics and prognostic analysis of patients with pulmonary tuberculosis and type 2 diabetes comorbidity in China: A retrospective analysis. *Front Public Health* 2021;9:710981.
13. Nguyen DT, Graviss EA. Development and validation of a risk score to predict mortality during TB treatment in patients with TB-diabetes comorbidity. *BMC Infect Dis* 2019;19(1):10.
14. Harrell F. Regression coefficients and scoring rules. *J Clin Epidemiol* 1996;49(7):819.
15. Moons KG, Harrell FE, Steyerberg EW. Should scoring rules be based on odds ratios or regression coefficients?. *J Clin Epidemiol* 2002;55(10):1054-1055.
16. Steyerberg EW, Vickers AJ, Cook NR, *et al.* Assessing the performance of prediction models: A framework for some traditional and novel measures. *Epidemiology* 2010;21(1):128-138.
17. Leisenring W, Pepe MS. Regression modelling of diagnostic likelihood ratios for the evaluation of medical diagnostic tests. *Biometrics* 1998;54(2):444-452.
18. Janssens ACJW, Deng Y, Borsboom GJJM, *et al.* A new logistic regression approach for the evaluation of diagnostic test results. *Med Decis Making* 2005;25(2):168-177.
19. Shen X, DeRiemer K, Yuan ZA, *et al.* Deaths among tuberculosis cases in Shanghai, China: Who is at risk?. *BMC Infect Dis* 2009;9:95.
20. Horita N, Miyazawa N, Yoshiyama T, *et al.* Development and validation of a tuberculosis prognostic score for smear-positive in-patients in Japan. *Int J Tuberc Lung Dis* 2013;17:54-60.
21. Bastos HN, Osório NS, Castro AG, *et al.* A prediction rule to stratify mortality risk of patients with pulmonary tuberculosis. *PLoS One* 2016;11(9):e0162797.
22. Alobu I, Oshi SN, Oshi DC, *et al.* Risk factors of treatment default and death among tuberculosis patients in a resource-limited setting. *Asian Pac J Trop Med* 2014;7(12):977-984.
23. Atif M, Sulaiman SAS, Shafie AA, *et al.* Treatment outcome of new smear positive pulmonary tuberculosis patients in Penang, Malaysia. *BMC Infect Dis* 2014;14:399.
24. Nguyen DT, Graviss EA. Development and validation of a prognostic score to predict tuberculosis mortality. *J Infect* 2018;77(4):283-290.
25. Lai YJ, Liu EY, Wang LM, *et al.* Human immunodeficiency virus infection-associated mortality during pulmonary tuberculosis treatment in six provinces of China. *Biomed Environ Sci* 2015;28(6):421-428.
26. Lin CH, Lin CJ, Kuo YW, *et al.* Tuberculosis mortality: Patient characteristics and cause. *BMC Infect Dis* 2014;14:5.
27. Nguyen DT, Jenkins HE, Graviss EA. Prognostic score to predict mortality during TB treatment in TB/HIV co-infected patients. *PloS One* 2018;13(4):e0196022.
28. Nahid P, Jarlsberg LG, Rudoy I, *et al.* Factors associated with mortality in patients with drug-susceptible pulmonary tuberculosis. *BMC Infect Dis* 2011;11:1.
29. Pefura-Yone EW, Balkissou AD, Poka-Mayap V, *et al.* Development and validation of a prognostic score during tuberculosis treatment. *BMC Infect Dis* 2017;17(1):251.
30. Lui G, Wong RY, Li F, *et al.* High mortality in adults hospitalized for active tuberculosis in a low HIV prevalence setting. *PLoS One* 2014;9(3):e92077.
31. Sookya W, Inyaphong J. Factors associated with death during tuberculosis treatment among new patients with pulmonary tuberculosis in Health Region 10th. *Office Dis Prev Control* 10th J 2021;19(2):80-92.
32. Thanwiset T. Factors associated with mortality among patients with tuberculosis at Chaiyaphum hospital. *Chaiyaphum Med J* 2020;40:97-107.
33. Laowittawas W, Sangchart E. Factors related tuberculosis mortality in Khon Kaen province fiscal year 2023. *Res Dev Health Syst J* 2024;17:72-82.