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ORIGINAL RESEARCH

Factors Influencing Adherence to All-Oral Short-Course Treatment for DR-TB and Establishment of a Predictive Model

Jie Huang[1,2,*], Qing-Dong Zhu[2,*], Zhi-Feng Li[2], Kan Xie[2], Jian-Ning Deng[2], Qiu-Ying Ma[2], Han-Zhen Su[2], Ting-Ting Lu[2], Xing-Fa Lu[2], Yan-Ling Hu[1], Zhou-Hua Xie[2]

[1]Faculty of Data Science, City University of Macau, Macau, 999878, People's Republic of China; [2]HIV/AIDS Clinical Treatment Center of Guangxi (Nanning) and The Fourth People's Hospital of Nanning, Nanning, 530000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yan-Ling Hu, Faculty of Data Science, City University of Macau, Macau, 999878, People's Republic of China, Email ylhupost@163.com; Zhou-Hua Xie, HIV/AIDS Clinical Treatment Center of Guangxi (Nanning) and The Fourth People's Hospital of Nanning, Nanning, 530000, People's Republic of China, Email xiezhouhua6711@163.com

Objective: To explore factors influencing adherence to all-oral short-course treatment for drug-resistant tuberculosis (DR-TB) and establish a predictive model.

Methods: The study is retrospective and single-center. 241 TB patients treated at our hospital from January 2022 to December 2024 were retrospectively selected. Using a random number table method in a 7:3 ratio, patients were divided into a modeling group (n=169) and a validation group (n=72). The modeling group patients were categorized into groups of good adherence (n=89) and poor adherence (n=80). Univariate and binary Logistics regression analyses were used to identify influencing factors. A predictive model was constructed using SPSS, and R language was utilized to assess the model's application value through receiver operating characteristic (ROC) curves, calibration curves, and decision curve analysis (DCA).

Results: Binary logistic regression analysis showed that family monthly income, level of education, history of previous confirmed TB, and family-supervised drug administration were influencing factors for adherence to short-course treatment for DR-TB ($P<0.05$). The combined predictive model expression was Logit(P) = −1.394 + (0.421*family monthly income) + (0.344*level of education) + (0.310*history of previous confirmed TB) + (0.452*family-supervised drug administration). The model demonstrated good consistency between predicted risks and actual risks, with calibration curves showing a slope close to 1 in both the modeling group and validation group. ROC analysis indicated an area under the curve of 0.88 in the modeling group. For the validation group, the AUC was 0.85. The DCA curve illustrated a clear net benefit, indicating good clinical utility of the model.

Conclusion: Family monthly income, level of education, history of previous confirmed TB, and family-supervised drug administration are factors influencing adherence to short-course treatment for DR-TB. The model established based on these factors holds significant value in predictive applications.

Keywords: drug-resistant tuberculosis, all, oral short, course treatment, adherence, DR-TB, TB

Introduction

Tuberculosis (TB) remains a significant threat in the global infectious disease landscape, posing a serious challenge to public health security. According to the World Health Organization report in 2022, there were 10.6 million new cases of tuberculosis globally in 2021, with 450,000 cases of rifampicin-resistant and multidrug-resistant tuberculosis, highlighting the focus on tuberculosis prevention and control.[1] A study conducted in Iran[2] reported approximately 9000 new cases of tuberculosis in 2022, with a high proportion of previously treated patients at 33.7%. Such factors as comorbid diabetes, inadequate treatment adherence, and limited diagnostic capabilities further exacerbate the risk of drug-resistant tuberculosis transmission.[3] China, as the third highest burden country for tuberculosis globally, estimated 780,000 new

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cases in 2021, with 33,000 cases of MDR/RR-TB. The transmission patterns and distribution characteristics of drug-resistant mutations vary by region, presenting complexities in understanding the national-level transmission dynamics.

Traditional epidemiological researches, limited to single-center or provincial data, struggle to reveal the nationwide patterns of transmission.[4,5] The treatment dilemma of drug-resistant tuberculosis (DR-TB) is not only rooted in the resistance of the pathogens themselves but also closely tied to treatment regimen adherence. Traditional long-term treatment regimens containing injectable drugs (18–24 months) have high rates of treatment interruption (30–50%) due to injection pain and high hospitalization requirements, directly hindering the improvement of cure rates.[6,7] In 2022, the WHO recommended all-oral short-course regimens (6–9 months) for the first time. This regimen, centered around bedaquiline, pretomanid, and linezolid, optimizes pharmacokinetics, reduces adverse reactions, and increases treatment success rates to over 80%, significantly lowering economic costs, marking a revolutionary breakthrough in the treatment model for drug-resistant tuberculosis.[8,9] However, the effectiveness of oral regimens heavily relies on patients' consistent adherence throughout the treatment course. Inadequate adherence has made the treatment of DR-TB complex and multifactorial challenge.[10]

Previously, we conducted a related study focusing on multidrug-resistant tuberculosis (MDR-TB) in the Nanning area.[11] Through retrospective analysis of specimens, we identified independent factors affecting multidrug resistance and built a predictive model to provide a basis for precise prevention and control, mainly by carrying out a cross-sectional epidemiological survey. However, we did not further explore related treatments. The factors influencing adherence to the fully oral short-course treatment for drug-resistant tuberculosis remain to be investigated. This study differs from the previous one in focus and objectives.

This study aims to integrate clinical indicators and construct a predictive model for predicting the compliance of short-course treatment for drug-resistant tuberculosis (DR-TB). The goal is to develop a predictive model that can be seamlessly embedded into daily clinical screening processes, enhancing its translational application value. At the treatment initiation stage, medical staff can quickly collect patient information through electronic medical record systems or mobile tools, and input it into the model to generate a compliance risk score immediately. For high-risk patients, they can be prioritized into an intensive supervision plan, and intervention plans can be customized based on patient preferences. For low-risk patients, conventional management is adopted, thereby optimizing resource allocation, achieving precise stratified management of DR-TB treatment, providing a scientific basis for formulating personalized supervision strategies, and ultimately promoting precise intervention in the treatment of drug-resistant tuberculosis.

Research Objects and Research Methods

Research Objects

Following research conventions, the sample size should typically be 5 to 20 times the number of variables. This study involves 13 variables, and 20% is reserved for handling missing data, deletion, etc. Therefore, the theoretical sample size should be between 60 and 260. In this study, 241 cases were selected and enrolled, meeting the basic requirements.241 TB patients treated at our hospital from January 2022 to December 2024 were selected retrospectively. Inclusion criteria: (1) Diagnosis of drug-resistant tuberculosis in accordance with established criteria;[12] all patients were undergoing short-course treatment for DR-TB. (2) Age >18 years. (3). Exclusion criteria: (1) Patients with visual or auditory impairments or communication barriers. (2) Patients with other malignant tumors. (3) Patients with psychiatric or cognitive disorders.

Research Methods

Grouping

Patients were divided into a modeling group (n=169) and a validation group (n=72) using a random number table method in a 7:3 ratio. Patients in the modeling group were further categorized based on treatment adherence into a group with good adherence (n=89) and a group with poor adherence (n=80). Criteria for assessment:[13] Based on previous experimental observations, patients were classified as having good adherence if they met the following criteria: a completion rate of doses ≥87.2%, missed days of medication ≤5 days, and completion of the treatment course. Patients failing to meet any of these criteria were classified as having poor adherence.

General Data Collection

General patient information including gender, age, height, weight, and occupation was collected using an electronic medical record system.

Statistical Analysis

The experimental data collected were analyzed using SPSS 27.0 (International Business Machines Corporation, Armonk, New York, USA). The Shapiro–Wilk test was employed for normality testing. Quantitative data conforming to a normal distribution were presented as $\bar{X} \pm S$. Independent sample *t*-tests were used for comparisons, and *F*-test was used for multiple group comparisons. Count data were presented as frequencies or rates, with comparisons conducted using χ^2 test or Fisher's exact test. Factors that are significant in the single-factor analysis are evaluated using the variance inflation factor (VIF), and factors without collinearity are selected for inclusion in the binary logistic regression analysis as influencing factors and a predictive model was constructed using SPSS. Receiver operating characteristic (ROC) curves, calibration curves, and decision curve analysis (DCA) were performed using the R language to assess the model's application value. A significance level of $P<0.05$ was considered statistically significant for differences.This study employs multiple imputation methods to handle missing data (with a missing rate of less than 5%).

Results

Comparison of General Data Between Patients in Modeling Group and Validation Group

Comparison of general data between patients in the modeling group and validation group showed no statistically significant differences ($P>0.05$); see Table 1 for details.

Univariate Analysis of Factors Influencing Adherence to Short-Course Treatment for DR-TB

In the modeling group, comparisons of monthly income, education level, history of previous confirmed TB, and family-supervised drug administration between patients in the group with good adherence and the group with poor adherence showed statistically significant differences ($P<0.05$); see Table 2 for details.

Table 1 Comparison of General Data Between Patients in Modeling Group and Validation Group

Baseline Data		Modeling Group (n=169)	Validation Group (n=72)	t/χ^2 Value	*P* value
Gender	Male	142(84.02)	55(76.39)	1.461	0.227
	Female	29(17.16)	17(23.61)		
Age (years)		52.48±15.92	49.18±15.35	1.489	0.138
Height (cm)		164.09±7.39	161.53±20.03	1.449	0.149
Weight (kg)		54.06±11.60	50.92±11.59	1.924	0.056
BMI (kg/m^2)		19.95±3.72	19.02±3.78	1.768	0.078
Monthly Income (RMB)	<5000	61(36.09)	22(30.56)	0.686	0.408
	≥5000	108(63.91)	50(69.44)		
Education Level	High School or Below	132(78.11)	60(83.33)	0.852	0.357
	High School and Above	37(21.8)	12(16.67)		
History of Previous Confirmed TB	Yes	97(57.40)	46(63.89)	0.882	0.348
	No	72(42.60)	26(36.11)		

(*Continued*)

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Table 1 (Continued).

Baseline Data		Modeling Group (n=169)	Validation Group (n=72)	t/χ^2 Value	*P* value
Diabetes	Yes	62(36.69)	23(31.94)	0.497	0.481
	No	107(63.31)	49(68.06)		
Fever	Yes	35(20.71)	13(18.06)	0.224	0.637
	No	134(79.29)	59(81.94)		
Cough	Yes	150(88.76)	64(88.89)	0.001	0.976
	No	19(11.24)	8(11.11)		
Cavity	Yes	108(63.91)	47(65.28)	0.041	0.839
	No	61(36.09)	25(34.72)		
Family-Supervised Drug Administration	Yes	124(73.37)	55(76.39)	0.240	0.624
	No	45(26.63)	17(23.61)		

Table 2 Univariate Analysis of Factors Influencing Adherence to Short-Course Treatment for DR-TB

Baseline Data		Good Adherence Group (n=89)	Poor Adherence Group (n=80)	t/χ^2 Value	*P* value
Gender	Male	76(85.39)	64(80.00)	0.862	0.353
	Female	13(14.61)	16(20.00)		
Age (years)		53.08±13.41	49.48±17.54	1.507	0.134
Height (cm)		163.39±8.12	164.88±6.45	1.311	0.192
Weight (kg)		53.74±10.28	54.42±12.99	0.379	0.705
BMI (kg/m^2)		20.08±3.28	19.78±4.25	0.516	0.606
Monthly Income (RMB)	<5000	22(24.72)	39(48.75)	10.548	0.001
	≥5000	67(75.28)	41(51.25)		
Education Level	High School or Below	63(70.79)	69(86.25)	5.891	0.015
	High School and Above	26(29.21)	11(13.75)		
History of Previous Confirmed TB	Yes	58(65.17)	39(48.75)	4.644	0.031
	No	31(34.83)	41(51.25)		
Diabetes	Yes	32(35.96)	30(37.50)	0.043	0.835
	No	57(64.04)	50(62.50)		
Fever	Yes	19(21.35)	16(20.00)	0.047	0.829
	No	70(78.65)	64(80.00)		
Cough	Yes	78(87.64)	72(90.00)	0.235	0.628
	No	11(12.36)	8(10.00)		
Cavity	Yes	57(64.04)	51(63.75)	0.002	0.968
	No	32(35.96)	29(36.25)		
Family-Supervised Drug Administration	Yes	72(80.90)	52(65.00)	5.451	0.020
	No	17(19.10)	28(35.00)		

Binary Logistics Regression Analysis of Factors Influencing Adherence to Short-Course Treatment for DR-TB

The significant variables identified in the univariate analysis were used as independent variables and assigned values for analysis, as shown in Table 3. Treatment adherence was considered the dependent variable (poor adherence = 1, good

Table 3 Variable Assignment

Factor	Assignment
Monthly Income	≥5000=0, <5000=1
Education Level	High School and Above=0, High School or Below=1
History of Previous Confirmed TB	Yes=0, No=1
Family-Supervised Drug Administration	Yes=0, No=1

Table 4 Binary Logistics Regression Analysis of Factors Influencing Adherence to Short-Course Treatment for DR-TB

Variable	B	SE	Wald	P	Exp(B)	95% CI
Constant	−1.394	6.752	0.043	<0.001	0.248	–
Monthly Income	0.421	0.158	7.089	<0.001	1.523	1.117~2.076
Education Level	0.344	0.143	5.797	<0.001	1.411	1.066~1.867
History of Previous Confirmed TB	0.310	0.122	6.474	<0.001	1.364	1.074~1.732
Family-Supervised Drug Administration	0.452	0.149	9.217	<0.001	1.572	1.174~2.105

adherence = 0) for analysis. The results of the binary Logistics regression analysis indicated that monthly income, education level, history of previous confirmed TB, and family-supervised drug administration are factors influencing adherence to short-course treatment for DR-TB (P<0.05), as shown in Table 4.

Establishment of a Prediction Model

Based on the results of the Logistics regression analysis, variables including monthly income, education level, history of previous confirmed TB, and family-supervised drug administration were incorporated into the constructed prediction model. The expression for the joint detection factor model is given as Logit(P) = −1.394 + (0.421 * Monthly Income) + (0.344 * Education Level) + (0.310 * History of Previous Confirmed TB) + (0.452 * Family-Supervised Drug Administration). See nomogram in Figure 1. The calibration curve slopes in both the modeling group and validation group closely align with a straight line, indicating good consistency between the predicted risk and actual risk of the model, as shown in Figure 2.

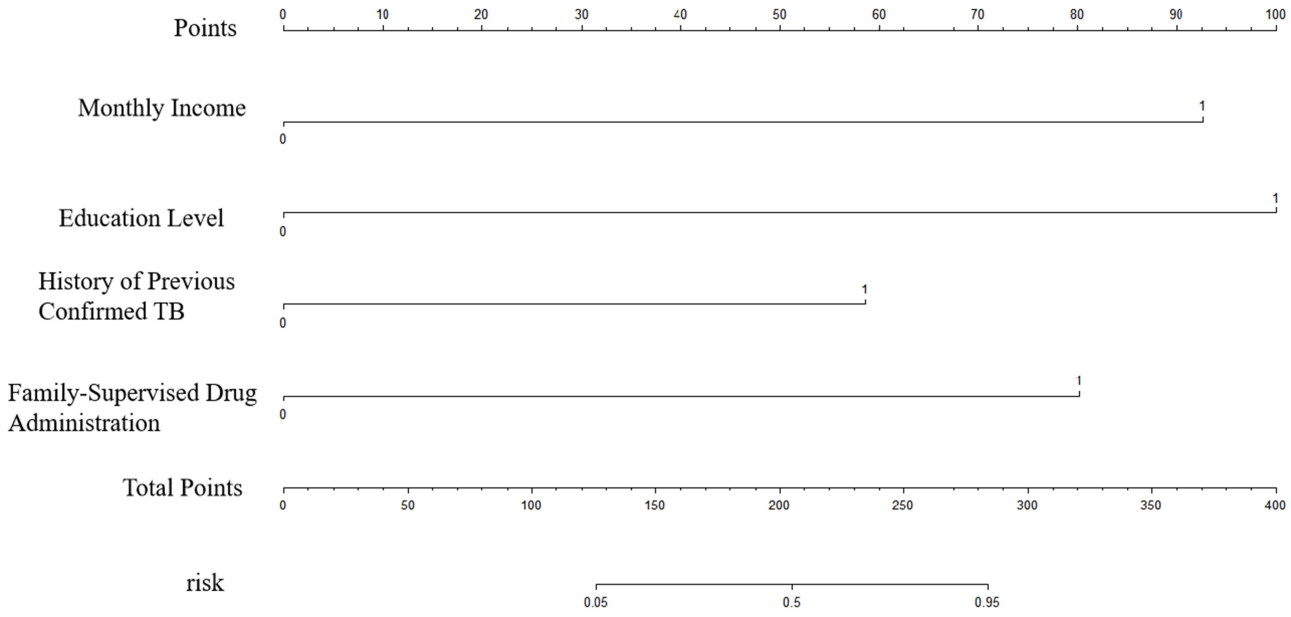

Figure 1 Nomogram.

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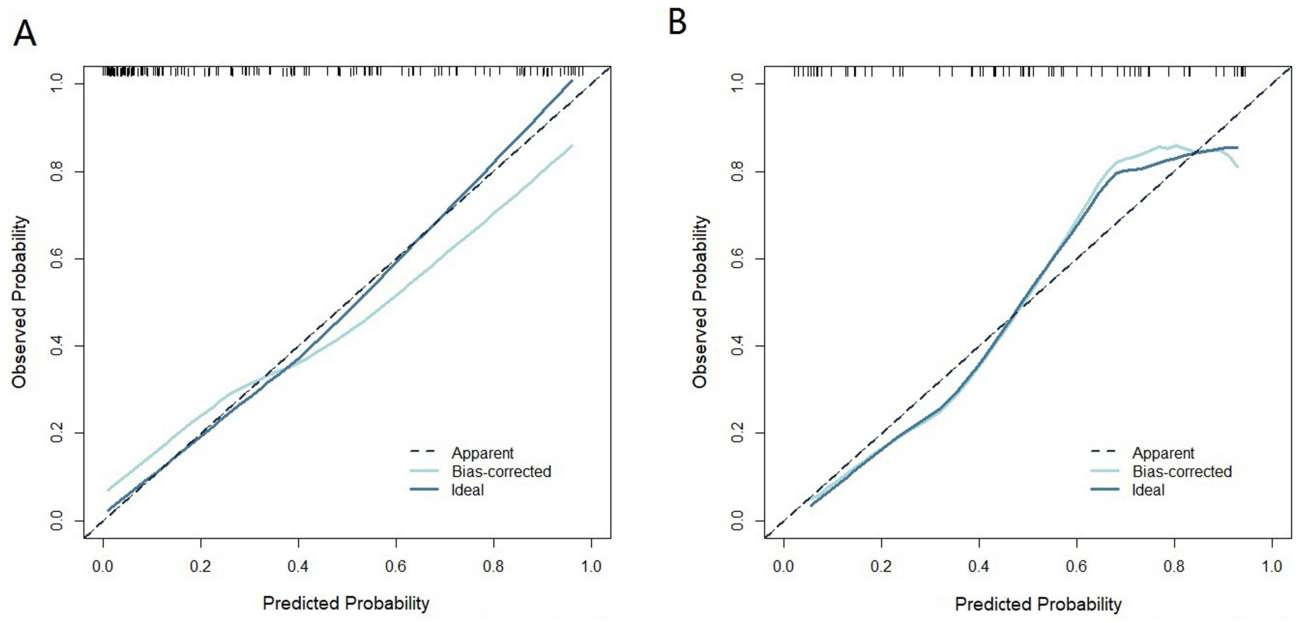

Figure 2 Calibration Curve. (**A**) stands for calibration curve for the modeling group; (**B**) stands for calibration curve for the validation group.

ROC Curve

The ROC analysis results indicated that the AUC of the predictive model in the modeling group was 0.88, with a standard error of 0.024 (95% CI: 0.813~0.914) and a Youden index of 0.68. At this threshold, the sensitivity was 88.54%, and the specificity was 79.85%. In the validation group, the AUC of the model was 0.85, with a standard error of 0.036 (95% CI: 0.768~0.894) and a Youden index of 0.65. At this threshold, the sensitivity was 72.54%, and the specificity was 92.16%. See Figure 3 for details.

Clinical Benefit Analysis of Predictive Model

A decision curve analysis (DCA) curve is plotted to evaluate the clinical utility of the model in predicting therapeutic efficacy. The "net benefit" metric aims to balance the relationship between the benefits of accurate treatment for high-risk

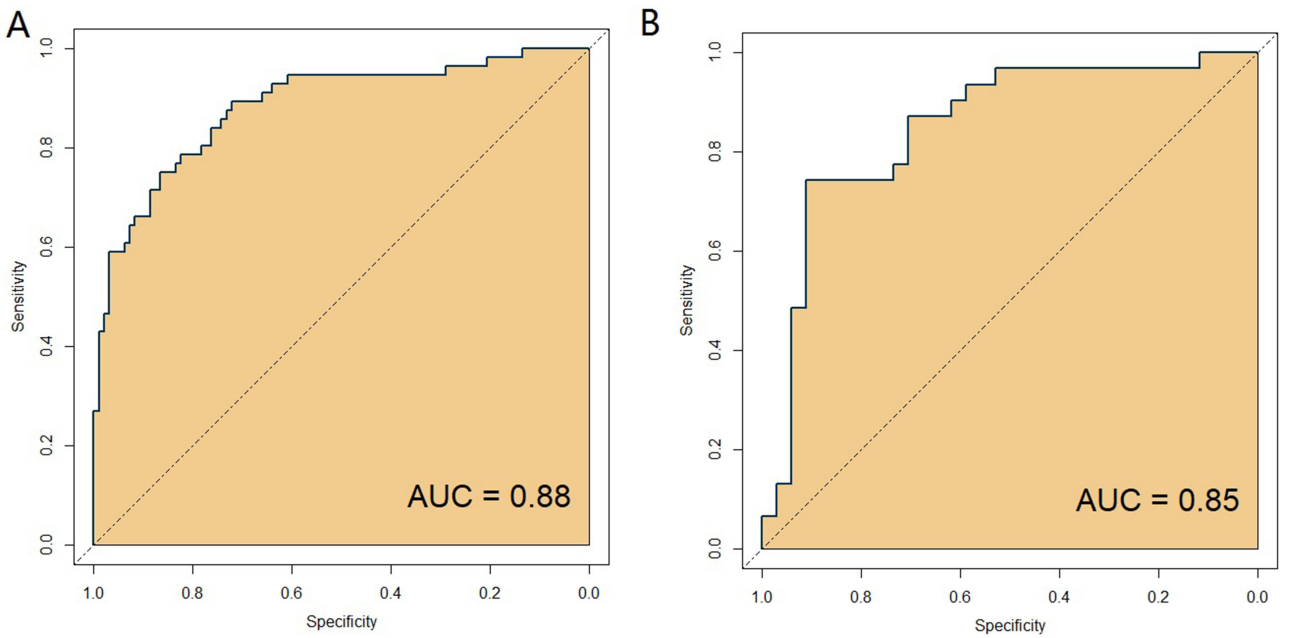

Figure 3 ROC Curve. (**A**) stands for ROC curve for the modeling group; (**B**) stands for ROC curve for the validation group.

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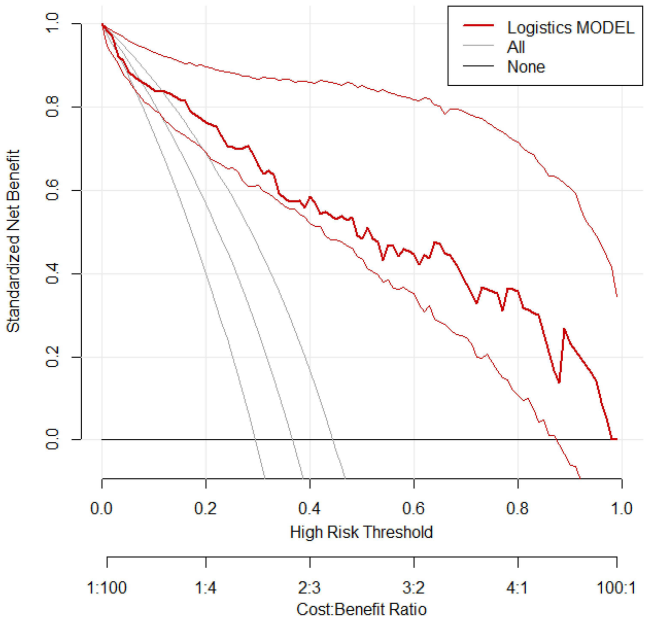

Figure 4 DCA Curve.

patients (benefits) and the risks of over-treating low-risk patients (potential risks). In the DCA curve plot, the Y-axis represents the net benefit rate that patients can obtain when guided by this model in clinical decision-making. The red curve in the graph represents the DCA curve drawn based on the model's predicted target population compliance. The black and gray horizontal lines represent two extreme hypothetical scenarios: the black line assumes no patient non-compliance, resulting in a net benefit rate of 0; the gray line assumes all patients would experience non-compliance, leading to a negative diagonal net benefit rate. Comparing the red curve with the black and gray lines, the closer the distance, the lower the clinical utility value of the model, and vice versa. The DCA curve analysis results in this study demonstrate that the model's actual clinical application effects are favorable, with good clinical benefits observed, as shown in Figure 4.

Discussion

This study identified family monthly income, level of education, history of previous confirmed tuberculosis, and family supervision of medication as crucial influencing factors for adherence to short-course treatment for DR-TB. Regarding family monthly income, Lower family monthly income may subject patients to greater financial pressure, making it challenging for them to afford medication costs, examination fees, and work losses due to treatment, thereby affecting their determination and actions in adhering to treatment.[14,15] The confirmation of family monthly income as a contributing factor in this study further underscores the critical role of economic support in the management of DR-TB treatment. This research suggests that in economically underdeveloped regions or for low-income groups, more economic assistance policies and measures are needed to enhance patient treatment adherence. Previous studies by Oh et al[16] have also indicated that economic burden is a factor in interrupting TB treatment, aligning closely with the viewpoint of this study and further substantiating the findings of this research.

The impact of education level on treatment adherence is also notable. Patients with higher levels of education often have a deeper understanding of the disease, clearer comprehension of the importance and necessity of treatment, and are better able to follow medical advice, take medications on time, and attend regular check-ups. Previous research by Santosa et al[17] indicated that inadequate knowledge of tuberculosis is a factor in non-adherence to TB treatment, aligning closely with the viewpoint of this study and further substantiating its findings. Patients with higher education levels have broader sources of health information and stronger capabilities to address potential issues during treatment. In this study, education level as an independent influencing factor suggests that personalized educational programs tailored to patients' education levels should be developed in DR-TB health education to enhance educational effectiveness and patients'

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adherence.[18] The impact of a history of confirmed tuberculosis on treatment adherence in this study is noteworthy. Patients with a history of tuberculosis tend to prioritize treatment due to their understanding of the disease. However, research by Melo et al[19] indicated that in patients showing signs of disease recurrence, despite seemingly good treatment adherence, upon reassessment of treatment abandonment scores, these patients were classified as high risk. Therefore, healthcare professionals should be cautious when dealing with patients with a history of tuberculosis, understanding their medical history and treatment experiences thoroughly, providing targeted psychological counseling and health education to address concerns and boost their treatment confidence.[20] Family supervision of medication also emerged as a significant factor in improving treatment adherence in this study. The family, as the most direct social support system for patients, can encourage and supervise patients to take medication on time, fostering good treatment habits. This aligns with conclusions drawn from various community intervention studies emphasizing the role of family support.[21,22] Current research indicates that exosomal microRNA (miRNA), as a crucial medium for intercellular communication, can influence the course of inflammatory diseases by regulating the activation of inflammatory cells and the release of cytokines. It possesses biomarker potential and offers new strategies for targeted therapy. Currently, related research is accelerating its systematic exploration and clinical translation. In the future, research on exosomal miRNA in the field of Mycobacterium tuberculosis can be strengthened.[23]

While previous studies have extensively explored the influencing factors of treatment adherence in DR-TB, there remains a notable gap in research focusing on predictive model construction. Most studies have stayed within the realm of analyzing influencing factors, lacking integration of multidimensional variables and model validation. This has rendered existing conclusions challenging to translate into precise intervention tools, impeding the effective identification of high-risk patients and underscoring the urgency of constructing scientifically predictive models to guide individualized management. Therefore, this study, building upon the analysis of influencing factors, developed a predictive model, which exhibited good performance in both the modeling and validation groups. The calibration curve slope approximating a line of 1 indicates good consistency between the model-predicted risk and actual risk, suggesting that the model can accurately predict patients' adherence to short-course treatment for DR-TB. In practical clinical settings, healthcare providers can collect and assess relevant patient information based on the factors included in the model, predict patients' potential treatment adherence in advance, and take targeted intervention measures. Current DOT (Directly Observed Therapy)/VOT (Video-Observed Therapy) strategies primarily rely on direct supervision to ensure DR-TB treatment adherence, yet they often overlook individual patient variations in risk factors. This predictive model complements these strategies by integrating multidimensional variables to identify high-risk patients proactively. By quantifying adherence risk, healthcare providers can tailor interventions, prioritizing intensive support for those predicted to struggle, while reducing unnecessary burden on low-risk patients. This approach enhances resource allocation, improves adherence outcomes, and addresses gaps in current one-size-fits-all supervision frameworks.

ROC analysis results indicate that the model demonstrated high area under the curve values in both the modeling and validation groups, signifying good discriminative ability to distinguish between patients with good and poor adherence. Additionally, based on the Youden index-determined optimal cutoff point, the model achieved desirable levels of sensitivity and specificity, implying that in real-world applications, it can accurately identify high-risk patients with poor adherence, enabling healthcare professionals to focus more efforts and resources on the intervention and management of these patients, thereby enhancing overall treatment outcomes. The DCA curve illustrates that the model yields significant net benefits, further validating its favorable clinical utility. In situations with limited medical resources, this model can assist healthcare providers in balancing the pros and cons during decision-making processes, selecting the most beneficial treatment management strategies for patients. For instance, for patients predicted by the model as high risk for poor adherence, intensified follow-up monitoring, increased psychological support, and financial assistance can be provided to enhance their treatment adherence. Conversely, for patients with good adherence, unnecessary interventions can be appropriately reduced, conserving medical resources.

The study has certain limitations. Firstly, the research sample was only sourced from TB patients admitted to our hospital, potentially limiting the representativeness of the sample and leading to selection bias. Patient characteristics may vary across different regions and levels of hospitals, requiring further validation of the generalizability of the study results. Secondly, in collecting influencing factors, there may be some unconsidered confounding factors, such as

patients' psychological states, other aspects of their social support networks, etc, which could also impact treatment adherence. Additionally, this study is retrospective, potentially introducing information bias during data collection. Addressing the limitations of this study, future researches could expand the sample size and conduct multicenter studies with large samples to enhance the representativeness and generalizability of the findings. Further exploration of factors that may influence adherence to short-course treatment for DR-TB, particularly psychological and social factors like patient anxiety, depression, social discrimination, etc, should be conducted and incorporated into predictive models to continuously improve the accuracy and comprehensiveness of the models. Lastly, prospective studies could be conducted to real-time collect patient treatment information and adherence data, reducing information bias and more accurately evaluating the influencing factors and the application effectiveness of the model. Exploring intervention strategies based on predictive models, verifying the effectiveness and feasibility of personalized interventions for patients with different adherence risks through methods like randomized controlled trials, could provide a more scientific basis for improving the treatment outcomes of DR-TB.

Conclusion

In conclusion, this study investigated the influencing factors of adherence to all-oral short-course treatment for DR-TB and established a predictive model, which holds certain clinical application value but also exhibits limitations. In the future, the model can be embedded into electronic medical record systems in daily clinical practice, automatically calculating compliance risks based on patient data. High-risk groups can be strengthened with follow-up and educational interventions, providing stronger support for improving the management level of DR-TB treatment.

Data Sharing Statement

The data used to support the findings of this study are available from Yan-ling Hu upon request.

Ethics Approval and Consent to Participate

This study is in accordance with the Declaration of Helsinki. The study was approved by the Medical Ethics Committee of HIV/AIDS Clinical Treatment Center of Guangxi (Nanning) and The Fourth People's Hospital of Nanning (【2025】03). The principle of informed consent was followed throughout the experiment, and information about the study was provided to patients or their families, and consent was obtained.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Jie Huang and Qing-Dong Zhu are co-first authors for this study. The authors declare no conflicts of interest in this work.

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