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An analysis of factors influencing dropout in methadone maintenance treatment program in Dehong Prefecture of China based on Cox regression and decision tree modelling

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Abstract

Background The high dropout rate among Methadone Maintenance Treatment (MMT) patients poses a significant challenge to drug dependence treatment programs, especially in regions with prevalent drug use and HIV transmission risks. This study aimed to analyze factors of dropout in MMT clinics over an 18-year period in Dehong Prefecture, Yunnan Province, China.

Methods A retrospective cohort study was conducted using data from China's HIV/AIDS Comprehensive Response Information Management System (CRIMS). Participants included individuals who enrolled in MMT between June 2005 and December 2023 and completed baseline surveys. Cox proportional hazards regression identified independent predictors, while decision tree modeling (CART algorithm) captured variable interactions. The decision tree employed Gini impurity minimization, a 70:30 training-test split, and pruning to prioritize factors like treatment duration and urine test results.

Results The study included 9,435 MMT participants, with a male-to-female ratio of 26:1 (9,086 males and 349 females). The median duration of treatment was 12.2 months (ranging from 2.7 to 43.9 months), with a minimum of 1 day and a maximum of 217 months. From 2005 to 2023, the cumulative dropout rate among MMT patients in Dehong Prefecture reached 89.6% (8,458/9,435), with an incidence rate of 34.75 dropouts per 100 person-years over 24,354.98 person-years of follow-up. The Cox proportional hazards regression identified that participants with occupations as farmers (AHR = 1.52, 95% CI: 1.41–1.62) or positive urine test results (AHR = 2.47, 95% CI: 2.35–2.59) exhibited significantly higher dropout risks. Protective factors included enrollment age > 35 years (AHR = 0.86), being married (AHR = 0.81), higher education levels (AHR = 0.94), good family relationships (AHR = 0.30), and methadone doses > 60 ml/day (AHR = 0.60). The decision tree model prioritized treatment duration as the root node, followed

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by urine test results, family relationships, education level, and methadone dosage. Patients with ≤ 12 months of treatment and positive urine tests faced the highest dropout probability (98.9%), while those with > 12 months of treatment but poor family relationships and doses ≤ 60 ml showed intermediate risks (82.3%).

Conclusion Between 2005 and 2023, the dropout rate among MMT patients in Dehong Prefecture was relatively high, driven by modifiable factors (low methadone doses, positive urine tests) and contextual hierarchies (early-phase treatment duration). By integrating Cox regression and decision trees, we advance both epidemiological risk assessment and precision intervention design. Policymakers should prioritize dose optimization and targeted monitoring for high-risk subgroups (e.g., patients ≤ 12 months with concurrent drug use) to improve retention in resource-limited settings.

Keywords Methadone maintenance treatment (MMT), Dropout, Retention, Risk factors, Cox regression, Decision tree model, China

Introduction

Methadone Maintenance Treatment (MMT) is a globally recognized pharmacological intervention for opioid dependence, offering dual benefits in reducing illicit drug use and curbing HIV transmission among people who inject drugs (PWID) [1]. However, the efficacy of MMT program has been persistently undermined by high dropout rates, particularly in regions burdened by intersecting epidemics of drug use and HIV/AIDS [2]. China's Dehong Prefecture exemplifies such a high-risk setting, where the nation's first HIV cluster among PWID was identified in 1989. Since then, Dehong Prefecture has become one of the regions most severely affected by HIV/AIDS across China [3]. Due to its geographical location along the drug trafficking routes of the "Golden Triangle," Dehong Prefecture has faced ongoing drug-related issues, with the widespread prevalence of drug use significantly elevating the risk of HIV transmission. To mitigate these risks, MMT was introduced in Dehong in 2005 to reduce opioid dependency among drug users and decrease HIV high-risk behaviors [4]. However, despite its intended benefits, the MMT dropout remain a critical challenge [5].

MMT dropout refers to the premature discontinuation of methadone treatment before achieving long-term therapeutic benefits. It is typically defined as failure to attend MMT clinics for a specified period (e.g., seven days of consecutive absence) without formal program completion or transition to alternative treatment [6]. The consequences of MMT dropout are severe, including relapse into illicit drug use, severe withdrawal symptoms, increased risks of HIV and HCV transmission, and higher mortality rates. Patients who discontinue MMT are at high risk of returning to heroin or other opioid use [7]. Abrupt cessation of methadone can lead to severe withdrawal symptoms, increasing psychological distress and the likelihood of relapse [8]. Dropped-out individuals often resume injecting drug use, leading to a higher risk of HIV and hepatitis C virus (HCV) infections [9]. Studies have also shown that opioid users who leave MMT prematurely have significantly higher risks of overdose-related deaths [10].

Globally, MMT retention rates vary widely. Most studies indicate that the 6-month dropout rate is approximately 30–50%, while the dropout rate for treatment exceeding one year can reach 50–70% [11]. High-income countries, such as the United States and Canada, exhibit relatively lower dropout rates (around 30–40%), which are attributed to well-established social support systems and long-term treatment policies [12]. In contrast, low- and middle-income countries, including Iran and several Southeast Asian countries, experience higher dropout rates (50–70%) due to limited healthcare resources and social stigma [13]. China initiated its national MMT program in 2004, and by 2022, it had expanded to approximately 650 clinics, providing treatment to nearly 500,000 individuals. However, the one-year retention rate remains at only 40–55% [14]. The western regions, such as Yunnan and Guangxi, report higher dropout rates (approximately 60%), largely due to severe drug epidemics and a high prevalence of mobile populations [15]. In contrast, eastern metropolitan areas such as Shanghai and Beijing demonstrate lower dropout rates (around 40%), which can be attributed to greater healthcare accessibility and stronger social support networks [16]. Several challenges contribute to poor compliance and high dropout rates, including socioeconomic factors, methadone dose, treatment accessibility, and stigma associated with drug dependence [7]. Socioeconomic and demographic factors such as younger age, male gender, unstable employment, and lower education levels increase the likelihood of dropout [10]. Treatment-related factors, including insufficient methadone dosage, side effects, and fear of methadone dependence, further deter long-term adherence [8]. Structural and policy barriers such as long travel distances to MMT clinics, stigma, legal concerns, and limited psychosocial support services contribute to treatment discontinuation [17, 18].

While prior studies have identified the above predictors, critical knowledge gaps persist. First, longitudinal analyses spanning MMT's full implementation timeline (2005–2023) in hyperendemic regions like Dehong are lacking, obscuring temporal trends and evolving barriers. Second, existing research predominantly relies on single-model statistical approaches (e.g., Cox regression), neglecting interactive effects between predictors—a limitation compounded by the absence of machine learning applications in this context. Third, region-specific determinants, including cross-border drug trade dynamics and culturally rooted stigma, remain underexplored despite their profound influence on treatment adherence in Dehong.

This study fills these gaps through a dual analytical framework, utilizing 18 years of programmatic data (2005–2023) from China's HIV/AIDS Comprehensive Response Information Management System (CRIMS) to examine MMT dropout among 9,435 MMT patients in Dehong Prefecture. To address the multifactorial nature of MMT dropout, this study integrates decision tree modeling with Cox regression—a dual approach designed to capture both independent predictors and contextual risk hierarchies. Cox regression quantifies isolated effects of variables like methadone dosage and sociodemographic factors, while decision trees reveal interactions among risk factors that drive discontinuation in specific subgroups. This dual-model approach enhances methodological rigor, strengthens the robustness of our findings, and improves predictive accuracy for tailored risk stratification [19]. By identifying both independent and synergistic risk factors, our findings support the development of personalized interventions to improve MMT retention, particularly in resource-limited settings.

Materials and methods

Study design and data sources

This retrospective cohort study included MMT patients who enrolled in treatment at MMT clinics in Dehong Prefecture, Yunnan Province, China, from 2005 to 2023. Data were retrieved from China's HIV/AIDS Comprehensive Response Information Management System (CRIMS). This module provides data on MMT patients' sociodemographic information, drug use history, and treatment-related information. CRIMS is a unified, real-time, web-based national HIV/AIDS information system launched in 2004 by the National Center for AIDS/STD Control and Prevention (NCAIDS) at the Chinese Centers for Disease Control and Prevention (China CDC) [20].

Participants

MMT patients who enrolled in treatment in Dehong Prefecture and from June 1, 2005, to December 31, 2023, were included. All admitted patients met the enrollment criteria for MMT as outlined in "Community-Based Methadone Maintenance Treatment Protocol for Drug Dependence in China" [5]. The inclusion criteria were: (a) age ≥ 15 years at enrollment and (b) completion of baseline surveys upon enrollment. Participants who were enrolled after December 31, 2023, or with incomplete or unclear data records, were excluded. Waiver of informed consent was granted because this analysis used existing data collected during the course of routine surveillance under the Infectious Diseases Act in China. This study was approved by the Institutional Review Board of the National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention (X230222728). The data obtained complied with relevant data protection and privacy regulations and individual identifiers were removed.

Study variables

In this study, the response variable was defined as the treatment dropout event (event status: dropout = 1, no dropout = 0) and its corresponding survival time (the time from the start of treatment to dropout or the end of follow-up, with the unit being years). The predictor variables included: (1) demographic characteristics (gender, age, ethnicity, occupation, marital status and educational level); (2) treatment-related factors (average daily methadone dose, most recent urine test result); and (3) Behavioral and psychosocial variables (history of drug injection, perceived relationship with family).

According to the Community-Based Methadone Maintenance Treatment Protocol for Drug Dependence in China [6], individuals who fail to participate in maintenance treatment for seven consecutive days or more without a valid reason are considered to have dropped out. In this study, **(1) Number of active MMT patients**: defined as individuals who received methadone treatment at MMT clinics in December of each year; **(2) Average number of active MMT patients**: calculated as the total number of individuals receiving methadone treatment at MMT clinics in December of each year divided by the number of active MMT clinics that year; **(3) Dropout**: failure to participate in maintenance treatment for seven consecutive days or more before December 31, 2023. The starting point of the study was the date when patients received their first treatment at local MMT clinic upon initial enrollment in 2005, and the endpoint was December 31, 2023. If a participant dropped out and later re-enrolled, only their treatment data of the initial enrollment were included in the analysis; **(4) Censored event**: participants who had not dropped out at the end of follow-up, including those who died, were lost to follow-up, or remained in treatment without dropout.

Statistical analysis

For the baseline characteristics of MMT patients, the Shapiro-Wilk test indicated that continuous variables such as age, treatment duration, and average daily dose did not follow a normal distribution. Therefore, they are presented as medians with interquartile ranges (IQR), while categorical variables are expressed as frequencies and proportions. Pearson $\chi2$ tests were used to compare categorical variables. The number of days in MMT clinics from first admission until the patient quit treatment or until the end of follow-up (18 years) was taken for calculating cumulative retention in treatment using survival analyses with log-rank. Kaplan-Meier (K-M) curves were plotted using GraphPad Prism 10.1.2. All analyses were performed using SPSS (version 24, IBM Inc., Armonk, NY, USA). Hypothesis testing was two-sided, with an alpha level of 0.05 indicating statistical significance. The analysis employed two complementary methodologies. Cox regression provides precise risk estimates and statistical significance for each factor, and decision trees effectively capture interactions and identify key predictors. We combine the two approaches to enhance model robustness and informs targeted intervention strategies for improving MMT retention. Model performance was assessed using receiver operating characteristic (ROC) curves, generated with MedCalc 23.0.2 software, and DeLong's test was conducted to compare predictive accuracy between the decision tree and Cox regression models.

Cox proportional hazards regression

It is a semi-parametric model which assessed the association between predictors and time-to-dropout, accommodating right-censored data (e.g., patients remaining in treatment at follow-up end). Variables were selected through a two-step process, and in Univariate analysis, all covariates with $p < 0.20$ in log-rank tests were retained; and for multivariate analysis, backward elimination (likelihood ratio test, $p < 0.05$) identified independent predictors, adjusting for age and sex as relevant confounders [21]. Hazard ratios (HRs) with 95% confidence intervals quantified effect sizes.

Decision tree modeling

It is a non-parametric approach that predicts outcomes by recursively partitioning data based on predictor variables. It selects the most informative variables at each split, optimizing homogeneity in the resulting subgroups. In this study, the Classification and Regression Tree (CART) algorithm was applied to analyze MMT dropout risk, using a 70% training set for model construction and a 30% test set for validation. The key steps included: (1) Splitting Criterion: The model employed Gini impurity minimization to identify optimal thresholds for partitioning (e.g., treatment duration ≤ 12 months), ensuring homogeneity within each node. (2) Variable Importance: Predictors were ranked based on their frequency and depth of splits in the tree, with higher-ranked variables contributing more to classification. (3) Pruning and Validation: To prevent overfitting, cross-validation was performed, retaining only nodes that enhanced predictive accuracy.

Results

Changes in the number of active MMT patients in Dehong Prefecture from 2005 to 2023

From 2005 to 2023, the total number of active MMT patients increased from 253 in 2005 to a peak of 2679 in 2013, representing a significant growth over eight years. After 2013, the total number of active MMT patients began to decline, reaching 853 by the end of 2023. The average number of patients per clinic rose from 11 in 2005 to a peak of 237 in 2007, then gradually declined each year, reaching 25 by 2023. This trend showed a shift from high average patient numbers per clinic to a more dispersed distribution as the MMT program expanded and more clinics were established (Fig. 1).

Comparison of dropout in MMT patients with different characteristics

A total of 9,435 participants were included in this study. From 2005 to 2023, the cumulative dropout rate among MMT patients in Dehong Prefecture reached 89.6% (8,458/9,435), with an incidence rate of 34.75 dropouts per 100 person-years over 24,354.98 person-years of follow-up. The median age at enrollment was 35.11 years (IQR: 28.90–42.71), with men accounting for 96.3% (9,086/9,435) and Han ethnicity for 37.6% (3,547/9,435). The majority were farmers (71.5%, 6,706/9,374), and 58.7% (5,540/9,435) were married. Educational level was primarily elementary school or below, accounting for 52.9% (4,994/9,435). Among the participants, 32.7% (3,089/9,435) had injected drugs, 35.5% (3,275/9,229) had a positive result on their most recent urine test, and 57.8% (5,056/8,741) reported having an average relationship with their family. The median average daily dose was 46.53 ml (31.22–65.19), with 70.0% (6,607/9,435) taking a daily dose of ≤ 60 ml. The $\chi2$ test compared dropout rates in MMT patients across different characteristic and significant factors associated with higher dropout rates included being male, younger than 35, of Han ethnicity, a farmer or unemployed, single or divorced/widowed, with lower education, a positive urine test result, poorer family relationships, shorter treatment duration (≤ 12 months), and an average daily dose of ≤ 60 ml (see Table 1). The median retention duration was 12.23 years (IQR: 2.67, 43.93). The cumulative dropout rate at 1, 5, 10 and 15 years were 45.5%,77.1%,90.0% and 94.7%,

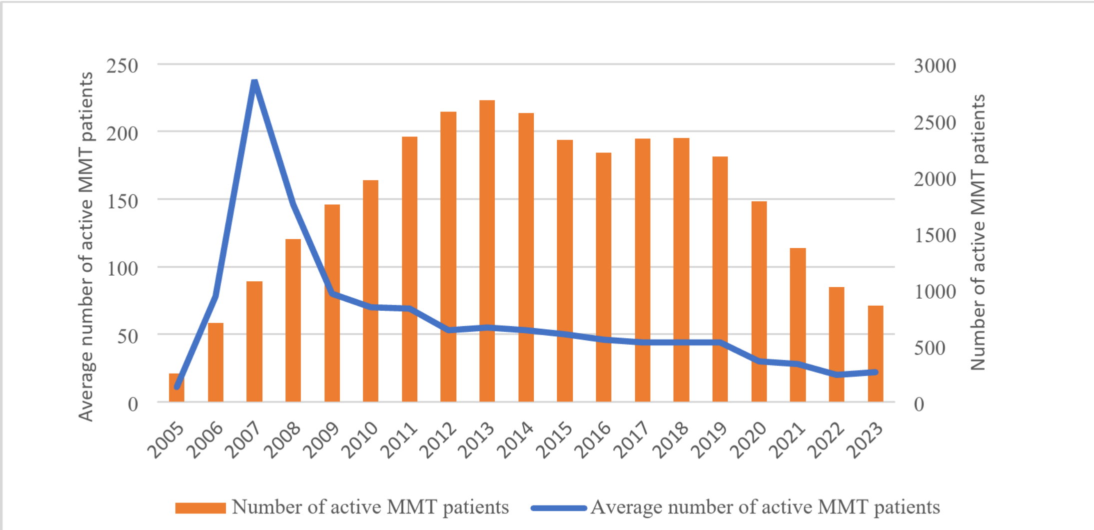

Fig. 1 Trends in average and total number of active MMT patients in Dehong Prefecture 2005 to 2023 in from Dehong Prefecture, Yunnan Province, 2005–2023

respectively. Figure 2 depicts the cumulative retention rates for study sample. Cumulative retention in treatment decreased over time and over 50% of patients dropped out of treatment in the first 20 months. Kaplan-Meier curves were generated comparing dropout trends across groups based on age groups, average daily dose and most recent urine test result (see Fig. 2).

Risk factors of dropout in MMT program

Cox proportional hazards regression analysis

As of December 31, 2023, there were 977 censored cases, including 19 deaths, 0 lost to follow-up, and 958 who remained in treatment without dropout. The median treatment duration was 12.23 (2.67–43.93) months. Using treatment duration (months) as the time variable and dropout status (No = 0, Yes = 1) as the dependent variable, a univariate analysis was conducted using the Cox regression model. The analysis indicated that dropout rates varied significantly by gender, ethnicity, occupation, marital status, education level, history of drug injection, perceived relationship with family, average daily dose, age at enrollment, and most recent urine test result. The factors with statistical significance in the univariate analysis were then included in a multivariate Cox regression model. The results showed that patients with the occupation of farmer (HR = 1.52, 95% CI: 1.41–1.62) or other occupations (HR = 1.50, 95% CI: 1.36–1.64), and those with a positive result in the most recent urine test (HR = 2.47, 95% CI: 2.35–2.59) had a higher risk of dropout. In contrast, being married (HR = 0.81, 95% CI: 0.76–0.85), having an education level of middle school or above (HR = 0.94, 95% CI: 0.89–0.99), perceiving a good (HR = 0.30, 95% CI: 0.28–0.33) or average (HR = 0.35, 95% CI: 0.32–0.38) relationship with family, an average daily dose > 60 ml (HR = 0.60, 95% CI: 0.57–0.64), and age over 35 at enrollment (HR = 0.86, 95% CI: 0.82–0.90) were associated with a lower risk of dropout (see Table 2).

Decision tree modelling analysis of factors influencing dropout

A decision tree model was constructed with dropout status as the dependent variable. Five statistically significant variables were included in the decision tree model: treatment duration, most recent urine test result, perceived family relationship, education level, and average daily dose. The first split in the decision tree was based on treatment duration, with those receiving treatment for ≤ 12 months having a higher probability of dropout. For those with treatment duration > 12 months, a positive urine test result further increased the dropout likelihood. If the urine test result was negative, dropout risk increased for participants with average or poor family relationships, elementary or lower education, and a daily methadone dose ≤ 60 ml (see Fig. 3).

Comparison of the decision tree model and cox regression model

The ROC curves were plotted to compare the predictive performance of the Cox proportional hazards regression model and the decision tree model for MMT dropout factors. As shown in Fig. 4, the area under the ROC curve (AUC) for the decision tree model was 0.84 (95% CI: 0.83–0.85), with a sensitivity of 67.31% and specificity of 97.03%, indicating strong predictive accuracy. In contrast, the Cox proportional hazards model had an AUC of 0.77 (95% CI: 0.77–0.78), with a sensitivity of 63.10% and specificity of 81.13%. The decision tree model demonstrated higher overall predictive power, as reflected

Table 1 Comparison of dropout in MMT patients with different characteristics ($n=9435$)

Variables	Total ($N=9435$)	Retention ($n=977$)	Dropout ($n=8458$)	χ2	*P*-value
Sex				21.436	<0.001
Male	9086(96.3%)	915(93.7%)	8171(96.6%)		
Female	349(3.7%%)	62(6.3%)	287(3.4%)		
Age at enrollment (years)				70.083	<0.001
Median (IQR)	35.11 (28.90, 42.71)	38.62 (31.62,47.84)	34.76 (28.68,42.13)		
≤35	5075(53.8%)	402(41.1%)	4673(55.2%)		
>35	4360(46.2%)	575(58.9%)	3785(44.8%)		
Ethnicity				19.136	<0.001
Han	3547(37.6%)	430(44%)	3117(36.9%)		
Other	5888(62.4%)	547(56%)	5341(63.1%)		
Occupation *				10.074	<0.001
Farmer	1796(19.2%)	664(68.0%)	6042(72.0%)		
Others	6706(71.5%)	89(9.1%)	783(9.3%)		
Unemployed	872(9.3%)	224(22.9%)	1572(18.7%)		
Marital status				27.669	<0.001
Single	2781(29.5%)	217(22.2%)	2564(30.3%)		
Married	5540(58.7%)	633(64.8%)	4907(58%)		
Divorced or widowed	1114(11.8%)	127(13%)	987(11.7%)		
Education level				14.439	<0.001
Elementary or below	4994(52.9%)	461(47.2%)	4533(53.6%)		
Middle school or above	4441(47.1%)	516(52.8%)	3925(46.4%)		
History of drug injection				1.306	0.253
Yes	3089(32.7%)	304(31.1%)	2785(32.9%)		
No	6346(67.3%)	673(68.9%)	5673(67.1%)		
Most recent urine test result *				570.226	<0.001
Positive	3275(35.5%)	9(0.9%)	3266(39.6%)		
Negative	5954(64.5%)	968(99.1%)	4986(60.4%)		
Perceived relationship with family *				185.073	<0.001
Good	3030(34.7%)	508(52.1%)	2522(32.5%)		
Average	5056(57.8%)	460(47.2%)	4596(59.2%)		
Poor	655(7.5%)	7(0.7%)	648(8.3%)		
Treatment duration (months)				1008.788	<0.001
Median (IQR)	12.23 (2.67, 43.93)	90.53 (55.60,138.10)	9.23 (2.20,31.28)		
≤12	4751(50.4%)	22(2.3%)	4729(55.9%)		
>12	4684(49.6%)	955(97.7%)	3729(44.1%)		
Average daily dose (ml)				96.454	<0.001
Median (IQR)	46.53 (31.22,65.19)	55.75 (39.59,77.67)	45.50 (30.33, 63.64)		
≤60	6607(70.0%)	551(56.4%)	6056(71.6%)		
>60	2828(30.0%)	426(43.6%)	2402(28.4%)		

Asterisk indicates missing values

in a higher AUC and specificity, making it a more effective model for predicting dropout in MMT patients. The Youden index also favored the decision tree model (0.64) over the Cox model (0.44), further supporting its superior performance in distinguishing between dropout and retention groups (see Table 3).

Discussion

This study provides critical insights into the multifactorial determinants of high dropout rates in MMT programs within Dehong Prefecture, a region emblematic of China's long-standing challenges in combating opioid dependence and HIV transmission. Although the MMT program has been implemented in Dehong since 2005, our study is the first to comprehensively report the longitudinal factors of dropout of individuals who attend the MMT clinics for treatment from 2005 to 2023. We found that the number of active MMT patients in Dehong Prefecture declined annually since 2013, a trend that was consistent with the national pattern [22]. The continuous decrease in the number of active MMT patients after 2013 may have been related to intensified anti-drug efforts, the impact of the COVID-19 pandemic, and concerns about identity exposure. The dropout rate among

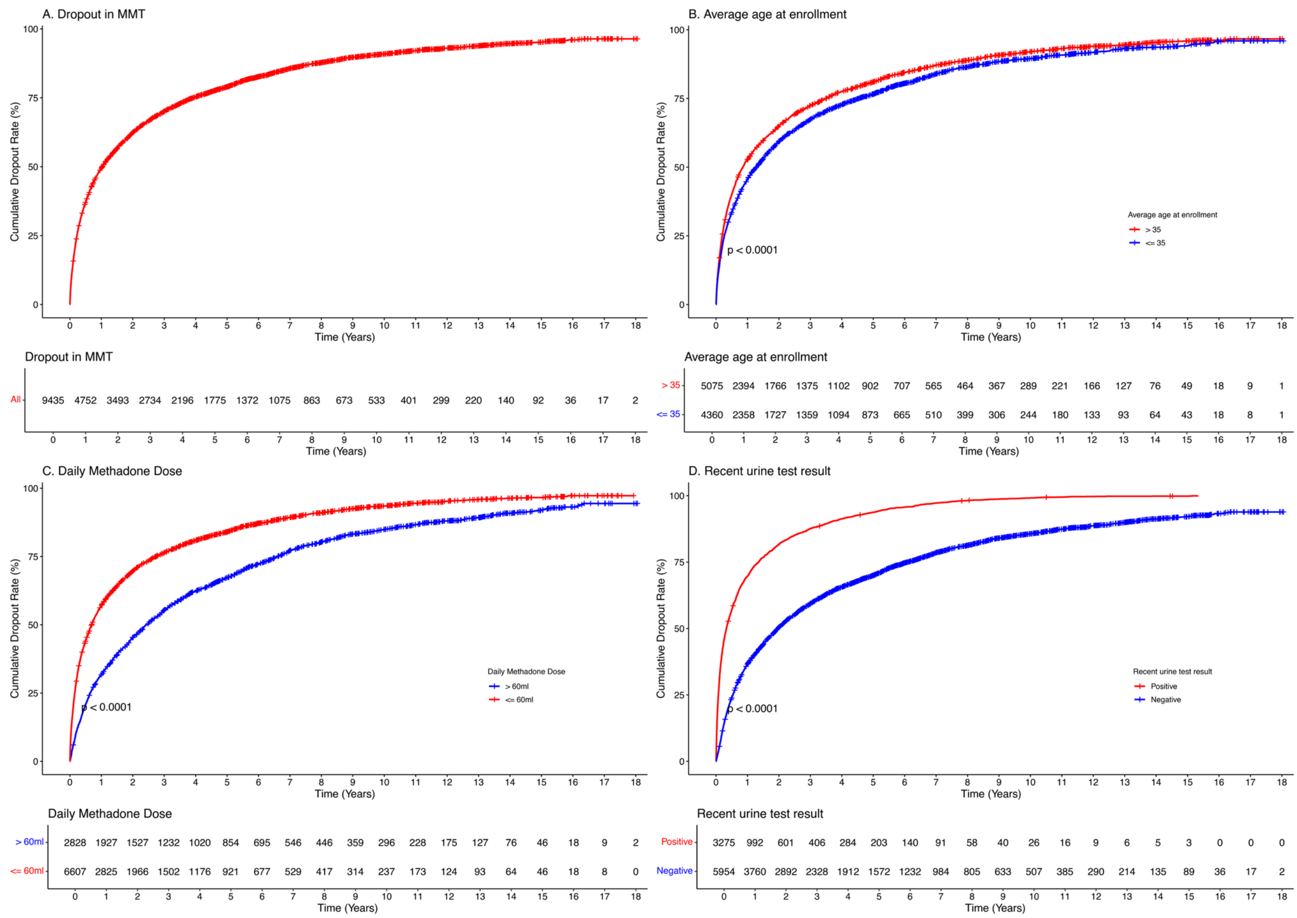

Fig. 2 **a** K-M curve of cumulative retention rate in study samples. **b** The cumulative dropout rate for MMT patients with different age groups. **c** The cumulative dropout rate for MMT patients with different methadone doses. **d** The cumulative dropout rate for patients with different urine test results

MMT patients in Dehong Prefecture was 89.6%, higher than that in Hubei Province (86.75%) [21], Hangzhou (65.71%) [10], and Yunnan Province as a whole (61.0%) [23], indicating that the high dropout rate remained a significant challenge for MMT programs in Dehong. We identified both traditional and modifiable risk factors while demonstrating the methodological synergy of combining Cox proportional hazards regression with decision tree modeling. Key findings indicate that low methadone dosage, positive urine tests, poor family relationships, farmers, and younger age were significant predictors of MMT dropout, as identified by the Cox model, while the decision tree model further prioritized treatment duration as the primary determinant, revealing that early-phase patients (≤ 12 months) with concurrent drug use faced the highest dropout risk.

A positive urine test was a strong predictor of dropout, indicating ongoing drug use and poor adherence to MMT. Previous studies confirm that continued illicit drug use during MMT correlates with higher dropout rates due to persistent cravings and external influences [24, 25]. Research from Iran also linked abstinence to improved retention [26]. Given this, urine test results could serve as an early warning signal, warranting intensified interventions such as behavioral counseling and contingency management [26]. Patients receiving low methadone doses (≤ 60 ml/day) were at significantly higher risk of dropout, reinforcing the importance of adequate dosing for treatment retention. Studies in China and U.S. show that higher doses correlate with prolonged retention and reduced relapse rates [27, 28]. Similarly, research in Vietnam found that inadequate methadone dosage contributed to early treatment discontinuation [29]. Insufficient methadone may fail to suppress withdrawal symptoms, increasing dropout likelihood. These findings highlight the necessity of individualized dose adjustments to optimize adherence [30]. Higher education levels were linked to greater MMT retention, likely due to increased health literacy and awareness of treatment benefits. Patients with at least middle school education had lower dropout rates, consistent with studies showing that educational attainment improves understanding of MMT protocols and reduces misconceptions [31]. However, in resource-limited settings, education

Table 2 Univariate and multivariate analysis using Cox proportional hazards regression model ($n=9435$)

Variables	Dropout		Univariate analysis		Multivariate analysis	
	N	**%**	**HR (95%CI)**	***P* value**	**HR (95%CI)**	***P* value**
Sex						
Male	8171	89.9	1.00		1.00	
Female	287	82.2	0.84 (0.744 ~ 0.94)	0.003	0.88 (0.774 ~ 1.00)	0.050
Age at enrollment (years)						
≤35	4673	92.1	1.00		1.000	
>35	3785	86.8	0.87(0.83 ~ 0.91)	< 0.001	0.86(0.82 ~ 0.90)	< 0.001
Ethnicity						
Han	3117	87.9	1.00		1.00	
Others	5341	90.7	1.15 (1.10 ~ 1.20)	< 0.001	1.05 (1.00 ~ 1.11)	0.050
Occupation *						
Unemployed	1572	87.5	1.00		1.00	
Farmer	6042	90.1	1.40 (1.33 ~ 1.49)	< 0.001	1.52 (1.41 ~ 1.62)	< 0.001
Others	783	89.8	1.39 (1.28 ~ 1.52)	< 0.001	1.50 (1.36 ~ 1.64)	< 0.001
Marital status						
Single	2564	92.2	1.00		1.00	
Married	4907	88.6	0.87(0.83 ~ 0.91)	< 0.001	0.81(0.76 ~ 0.85)	< 0.001
Divorced or widowed	987	88.6	0.93(0.86 ~ 0.96)	0.037	0.93(0.85 ~ 1.01)	0.062
Education level						
Elementary or below	4533	90.8	1.00		1.00	
Middle school or above	3925	88.4	0.87(0.83 ~ 0.90)	< 0.001	0.94(0.89 ~ 0.99)	0.026
History of drug injection						
No	5673	89.4	1.00		1.00	
Yes	2785	90.2	0.89 (0.85 ~ 0.93)	< 0.001	0.99 (0.94 ~ 1.04)	0.616
Perceived relationship with family *						
Poor	648	98.9	1.00		1.00	
Good	2522	83.2	0.256 (0.23 ~ 0.28)	< 0.001	0.30(0.28 ~ 0.33)	< 0.001
Average	4596	90.9	0.31 (0.28 ~ 0.33)	< 0.001	0.35 (0.32 ~ 0.38)	< 0.001
Average daily dose (ml)						
≤ 60	6056	91.7	1.00		1.00	
>60	2402	84.9	0.59(0.56 ~ 0.61)	< 0.001	0.60(0.57 ~ 0.64)	< 0.001
Most recent urine test result *						
Negative	4986	83.7	1.00		1.00	
Positive	3266	99.7	2.59(2.47 ~ 2.71)	< 0.001	2.47(2.35 ~ 2.59)	< 0.001

Asterisk indicates missing values

alone may not be enough—strong social support systems are essential for maximizing adherence [32]. Poor family relationships were associated with the highest dropout rates, whereas strong family support improved retention. Prior studies confirm that family engagement enhances motivation and reduces stigma, promoting adherence [33]. Research in Beijing found that family involvement significantly increased one-year retention rates, highlighting the role of social reinforcement [34]. Patients over 35 years old had lower dropout rates, aligning with research showing that older individuals are more treatment-motivated due to accumulated health concerns and life stability [31]. Farmers had a higher risk of dropout, likely due to seasonal labor, long hours, and geographic mobility, disrupting consistent clinic visits. While the Cox model identified occupation as an independent predictor, the decision tree model did not prioritize it, suggesting that occupation's impact depends on interactions with other factors, such as financial constraints and clinic accessibility [35].

This study demonstrates the complementary strengths of Cox regression and decision tree models in analyzing MMT dropout. Cox regression identified low methadone dosage, positive urine tests, poor family relationships, occupation as a farmer, and younger age as independent predictors, providing population-level insights by quantifying their effects through hazard ratios. In contrast, the decision tree model prioritized treatment duration, revealing that early-phase patients (≤ 12 months) with positive urine tests faced the highest dropout risk (98.9%), emphasizing context-dependent interactions. While Cox regression determines the independent contribution of each variable, the decision tree model captures hierarchical relationships and complex interactions,

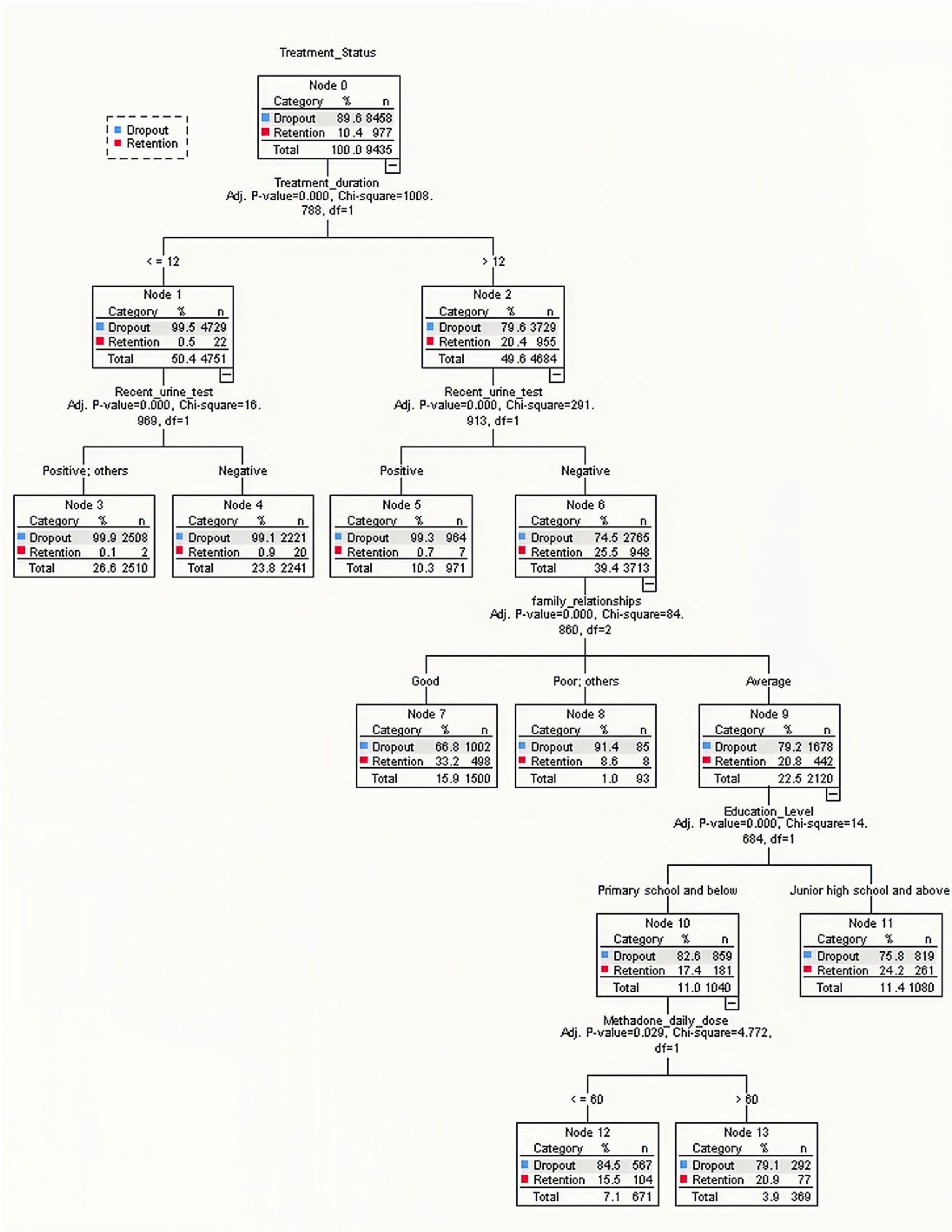

Fig. 3 Decision tree model analysis of factors influencing dropout in MMT

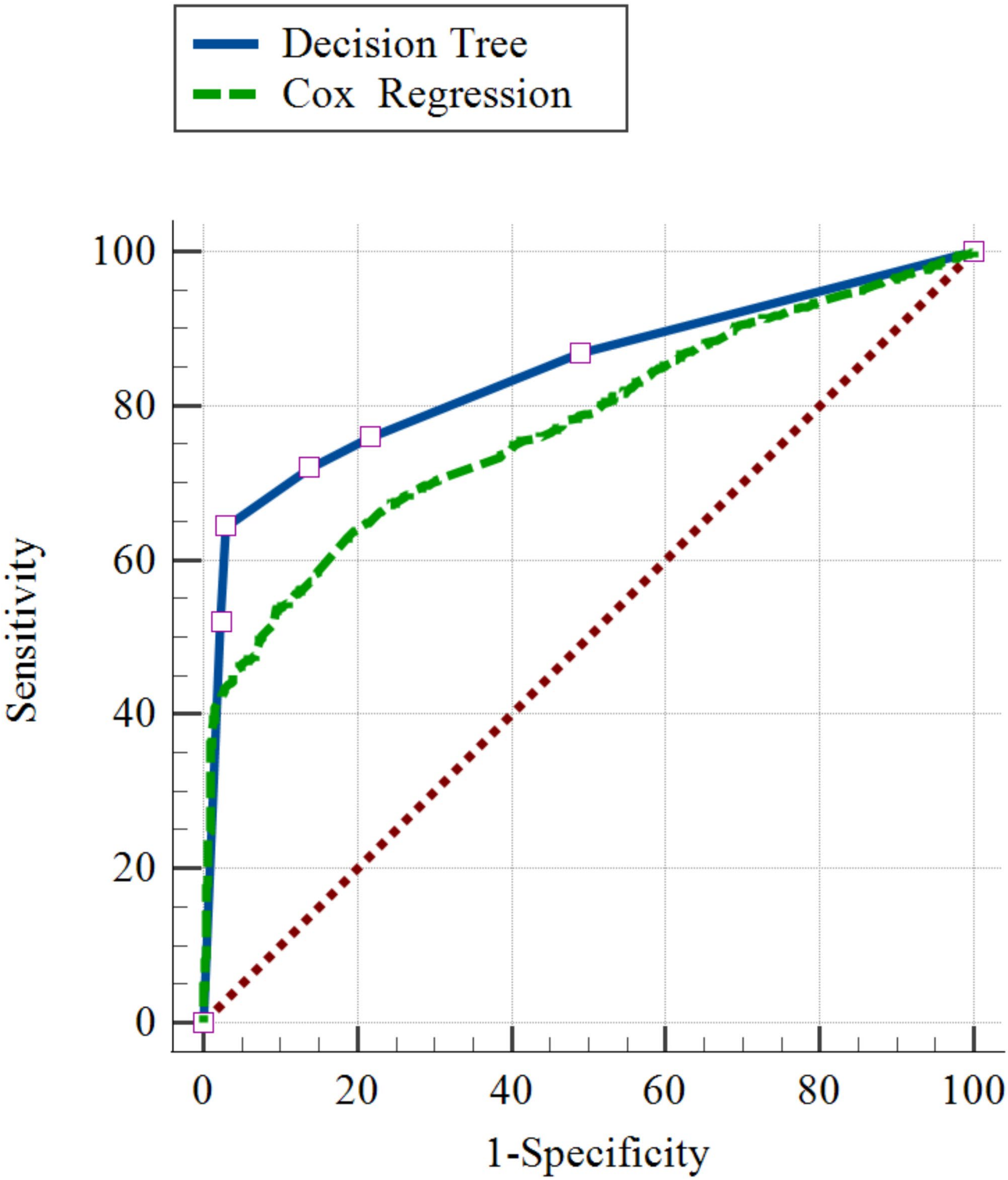

Fig. 4 ROC curves for the cox regression and decision tree models

Table 3 Comparison of the classification effects of the Cox regression and decision tree models

Model	AUC	95%CI	SE	*P*-value	Sensitivity	Specificity	Youden index
Decision tree	0.84	0.83～0.85	0.01	<0.001	67.31	97.03	0.64
Cox regression	0.77	0.77～0.78	0.01	<0.001	63.10	81.13	0.44

offering higher predictive accuracy (AUC = 0.84 vs. 0.77) and better classification of high-risk subgroups. Notably, occupation and age were significant in the Cox model but not in the decision tree, suggesting they influence overall dropout trends rather than direct individual risk. These findings support a dual intervention approach: Cox-informed strategies (e.g., dose optimization, family engagement) for broad retention efforts and decision tree-driven interventions (e.g., intensive monitoring for high-risk early-phase patients) for targeted prevention. By integrating both models, this study provides a comprehensive and precise framework for improving MMT retention strategies, balancing generalized risk assessment with personalized intervention planning.

This study has limitations. First, the research subjects are limited to Dehong Prefecture, which may limit the generalizability of the results. Second, although multiple factors were analyzed, potential influencing factors such as financial status, transportation accessibility, and mental health were not explored in depth, nor were patients who rejoined treatment after interruption were considered. Future research should expand the sample and include more regions and variables to more fully understand the complexity of disengagement.

Moving forward, clinics should enhance early retention efforts with frequent counseling and urine monitoring. Flexible methadone dosing tailored to individual needs, especially for mobile populations, could improve adherence. Strengthening family involvement through workshops or home visits may further support retention. Mobile MMT clinics and digital tools like SMS reminders can enhance accessibility and appointment adherence. Future research should assess mental health outcomes and cost-effectiveness to inform scalable interventions. Integrating insights from Cox regression and decision tree models offers a structured approach to improving MMT retention in high-risk settings.

Conclusion

This study highlights persistent MMT retention challenges in Dehong Prefecture, China, revealing key dropout predictors through Cox regression and decision tree modeling. The Cox model identified protective factors such as higher methadone doses, marital stability, and strong family support, while positive urine tests and farming occupations increased dropout risk. The decision tree model emphasized treatment duration, identifying early-phase patients with positive urine tests as a high-risk subgroup. These findings support a two-tiered intervention strategy: population-level measures, including dose optimization and family engagement programs, and precision-targeted interventions, such as intensive monitoring for early-phase patients and mobile MMT services for rural populations. Methodologically, this study validates the complementary strengths of Cox regression for risk quantification and decision trees for risk stratification, providing a replicable model for regions facing similar public health challenges.

Abbreviations

HIV	Human immunodeficiency virus
AIDS	Acquired immune deficiency syndrome
IDUs	Injection drug users
OR	Odds ratio
CI	Confidence interval
AOR	Adjusted odds
VCT	Voluntary counseling and testing

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Clinical trial number
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Authors' contributions
Qunbo Zhou, Renhai Tang and Duo Shan designed, drafted, analyzed, and interpreted the results. Yuecheng Yang, Runhua Ye, Jie Gao, Lin Li and Lifen Xiang participated in data collection, data analysis, and critically read the manuscript. Song Duan and Duo Shan participated in designing the methodology, critically read the manuscript, and gave constructive comments for the manuscript. All authors contributed to manuscript preparation, read, and approved the final manuscript. Qunbo Zhou and Renhai Tang contributed equally to the manuscript.

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Data availability
The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The Institutional Review Board of National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention (X230222728) gave ethical approval for this study. Since all data were deidentified and provided in the aggregated form, the informed consent was waived. All methods were performed in accordance with the Declaration of Helsink.

Consent for publication
Not applicable as all data are presented in the aggregate.

Competing interests
The authors declare no competing interests.

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