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## Correlates of methadone client retention: A prospective cohort study in Guizhou province, China

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### Abstract

**Background**—Methadone client retention levels and treatment doses of patients vary widely in methadone clinics across China. Because methadone clinics have been available in China only recently, this study explored the relationship between methadone dosage and client retention in methadone maintenance programmes in Guizhou province.

**Methods**—The study used a prospective cohort study design. Injecting and non-injecting heroin-using clients who had been treated for no more than two and half months in one of eight methadone maintenance treatment clinics in Guizhou province were recruited into the cohort, beginning on 3 June 2006 and followed up until 1 June 2007. A total of 1003 participants were enrolled. Face-to-face interviews were conducted to collect baseline information, and clients' daily doses were recorded.

**Results**—The 14-month retention rate was 56.2%. Controlling for other covariates in the multivariate Cox model, a higher methadone dose was found to predict higher client retention. Retention was also associated with intention to remain in treatment for life and the clinic attended.

**Conclusion**—Clients need to receive an adequate methadone dose to assure continued retention. Patients who expect to be treated for life have higher retention rates than patients who anticipate only short-term treatment. Key factors associated with successful clinics in China need to be elucidated.

### Keywords

Methadone maintenance; Methadone dose; Methadone client retention; Heroin

### Introduction

Drug use re-emerged as a problem in China in the 1980s. Since then, drug use has spread from the southwest border into inland China (Liu, Lian, & Zhao, 2006). The number of drug users in China has increased rapidly since 1990. In 1990, there were 70,000 registered drug users in China. By the end of 2005, the number had reached 1.16 million, among whom

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81.1% were heroin drug users and 79% were 17–35 years old (Liu et al., 2006; Wu, Sullivan, Wang, Rotheram-Borus, & Detels, 2007). Kulsudjarit estimated that there may actually be 3.5 million drug users in China (Kulsudjarit, 2004).

Drug use is closely associated with the HIV epidemic in China. In 1989, the first epidemic of HIV infection among drug users was identified in China. By the end of October 2007, there were 223,501 cumulative reported HIV/AIDS cases, among whom 62,838 were AIDS patients and 22,205 were deaths. It was estimated that there were actually 700,000 people living with HIV/AIDS in China in 2007. Among people living with HIV/AIDS, 38.1% were infected through injection drug use. Among the estimated number of new HIV cases in 2007, 42.0% were associated with injection drug use. Thus, needle-sharing is one of the major transmission routes of HIV in China (State Council AIDS Working Committee Office & UN Theme Group on AIDS in China, 2007). An important intervention strategy for preventing the spread of HIV nationwide, methadone maintenance treatment (MMT) programmes, was implemented jointly by the Chinese Ministry of Health, the Ministry of Public Security, and the State of Food and Drug Administration, beginning in 2004. From March to June 2004, the first eight MMT clinics opened in five provinces (Guangxi, Guizhou, Sichuan, Yunnan, and Zhejiang) (Pang et al., 2007; Sullivan & Wu, 2007). By the end of 2006, there were 320 methadone clinics operating in 22 provinces. By the end of March 2007, 51,854 heroin drug users had been treated in MMT clinics, and 35,888 clients were currently being treated. Over 500 MMT clinics were operating in China by the end of 2007.

This study investigated the success (measured in terms of client retention) of eight clinics in Guizhou and the relationship between the methadone dose and the retention rate, using a prospective cohort study design.

## Methods

### Study design

This study used a prospective cohort design. Injecting and non-injecting heroin users who had been treated at one of the eight study MMT clinics for no more than two and half months were recruited into the cohort, beginning on 3 June 2006. The last client was recruited on 28 February 2007. A total of 1003 clients were recruited and followed up through the end of the study on 1 June 2007.

### Study sites

Eight methadone clinics were selected in Guizhou, which has one of the highest rates of injection drug use in China. These clinics were located in six cities/counties of Guizhou province, and included the Shengeryi hospital methadone clinic in Guiyang City, the Yuneryi hospital methadone clinic in Guiyang City (clinic 1), the Guiyang Jianyu hospital methadone clinic in Guiyang City, the Honghuagang district methadone clinic in Zunyi City, the Panxian People's Hospital methadone clinic in Pan County; the Duyun methadone clinic in Duyun City, the Xixiuqu methadone clinic in Anshun City, and the Tongren methadone clinic in Tongren City.

### Subject selection

Inclusion criteria for recruitment into the study were: (1) being either an injecting or non-injecting heroin user who was willing to participate in the MMT programme; (2) already having been treated for no more than two and half months in the MMT clinic; and (3) not having been transferred from another clinic. Exclusion criteria for recruitment into the study

were: (1) having been treated for more than two and half months in the clinic; (2) planning to transfer to another MMT clinic in the near future; and (3) never having used heroin.

The study was approved by the Institutional Review Boards of UCLA and the National Center for AIDS/STD Control and Prevention, Chinese Centers for Disease Control and Prevention.

### Data collection procedures

The questionnaire was adapted from the fifth version of the Addiction Severity Index (ASI) (McLellan, Cacciola, Alterman, Rikoon, & Carise, 2006). The principal investigator translated the ASI into Chinese, and additional questions were added. Signed informed consent was obtained from each participant. Face-to-face interviews were conducted by investigators and trained interviewers from the local Centers for Disease Control and Prevention.

Clients' treatment dose information was abstracted from the Methadone Clinic Data Management System, a database that records clients' daily doses, using SAS 9.13 software (SAS Institute, Cary, NC).

### Data analysis

Survival (retention) analysis with potential predictors was performed to search for associations between predictors and retention (Allison, 1995). Because face-to-face interviews were conducted, single variables had few missing values. Therefore, our analyses ignored the missing values.

Client retention in the MMT programme was the outcome variable. Retention was defined in this study as a client still taking methadone during the month prior to the study being completed. A client confirmed by the MMT clinic to have not taken any methadone in the past month was considered to have dropped out. If a client was transferred to another MMT clinic but had still taken methadone in the past month, he/she was considered to still be in the MMT programme.

Methadone dosage, age, gender, education, ethnicity, religion, marital status, chronic disease history, drug use history, methods of drug use, local residency, family support, employment, treatment goals, clinic operation times, clinic locations, and clinic fees were the variables explored in the analyses. Dummy variables were created for categorical variables in multivariate analysis.

The retention time (in months) was calculated as the last date a client took methadone, minus the first date he/she took methadone. If a client was still in the programme when the study was completed, retention time was calculated as the completion date of the study minus the first date he/she was treated in the MMT clinic.

A participant's time-weighted average methadone dose was calculated using the following formula:

$$\text{time-weighted average dose} = \frac{\sum(\text{dose in ml} \times \text{no. of days at that dose})}{\sum(\text{no. of days receiving each dose})}$$

The Kaplan–Meier (product-limits) method was used to calculate the retention rate, and log-rank tests were used for univariate analysis for categorical variables. The Cox model was used to conduct univariate analysis for continuous variables and multivariate analysis. If a

predictor had a  $p$ -value of  $\leq 0.3$  or less in univariate analysis, it was included in the multivariate Cox model.

## Results

### Retention rates of study subjects

The retention rate was 93.5% for the first month, 88.5% for the second month, 57.4% for the 12th month, and 56.2% for the 14th month. Fig. 1 shows the retention rates of the 1003 participants. The average retention was 10.2 months for all participants. The retention time was similar among injecting and non-injecting clients; therefore, they have been combined in the analysis.

### Demographic characteristics (Table 1) and univariate analysis (Table 2)

Of the 1003 participants, 26.0% were females, and the average age was 33.3 years. The mean methadone dose for all participants was 38.0 mg/day. For 79.4% of participants, the time-weighted average dose was lower than 50 mg/day. Half (49.6%) of the participants had never married. Most were Han Chinese (the major ethnic group), and only 8.1% practiced any religion. Full-time employment was held by 35.8% of subjects. Almost all (94.2%) were local residents. Most (88.7%) intended to eventually quit using methadone. Clinic locations and operation times were perceived as convenient by most. Almost all clients' families (94.0%) supported treatment in MMT clinics. Half (52.3%) lived in their parents' homes, 11% reported a chronic disease, and 52.5% were injection drug users (IDUs). The majority (71.8%) had been previously placed in a detoxification programme. Univariate analysis indicated that only clinic attended, practicing a religion, intending to remain in treatment for life, methadone dosage, and years of education were significantly correlated with retention ( $p < 0.05$ ).

### Multivariate analysis results

Clients were recruited from eight clinics. Therefore, seven dummy variables were created for clinic variables. The Yuneryi methadone clinic was coded as the reference clinic (clinic 1). Never being married was coded as the reference group for marital status. Multivariate analyses controlling for covariates in Table 1 indicated that time-weighted average dose (in increments of 1 mg of methadone) (HR = 0.99,  $p = 0.0034$ ); attending the Panxian clinic (HR = 1.845,  $p = 0.0002$ ), Zunyi clinic (HR = 0.566,  $p = 0.0013$ ), or Anshun clinic (HR = 0.491,  $p = 0.0157$ ); not previously being in a detoxification programme (HR = 1.306,  $p = 0.0412$ ); and intending to be treated for life (HR = 0.657,  $p = 0.0259$ ) were the factors that influenced retention of clients.

We dichotomized dosages using cut points of daily methadone doses at 40, 45, 50, 55, 60, and 65 mg, and correlated them with retention rates. Table 3 shows hazard ratios,  $p$ -values, and retention rates at the different cut points. Retention rates increased with increasing dosage of methadone to a maximum of 65 mg. There were too few participants with doses higher than 65 mg to calculate retention rates above that level.

## Discussion

Retention is key for a successful MMT programme. Thus, retention has been accepted as an indicator of programme success (Ward, Mattick, & Hall, 1998). Several studies have found that the longer duration in a MMT programme, the more likely the client will remain crime-free and reduce his/her use of heroin (NIDA, 1995). Grella, Hser, Joshi, & Anglin (1999) found there was a strong positive relationship between methadone treatment retention and abstinence at follow-up amongst younger adults.

Many studies have found that methadone dose is an important factor that can influence retention in methadone treatment. A meta-analysis of randomized, controlled, double-blind clinical trials found that a dose of 50 mg/day was associated with higher retention rates (Farre, Mas, Moreno, & Camí, 2002). Ward et al. (1998) concluded that an adequate methadone dose, on average, should be above 60 mg to be effective. A randomized trial by Strain & Stitzer (1999) found that high-dose methadone treatment resulted in longer retention in MMT (Strain & Stitzer, 1999). Other studies also that found higher methadone doses were associated with higher retention rates (Booth, Corsi, & Mikulich-Gilbertson, 2004; D'Ippoliti, Davoli, Perucci, Pasqualini, & Bargagli, 1998; Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003; Strain & Stitzer, 1999). The objective of the present study was to confirm this relationship among Chinese drug users, and to identify other correlates of retention.

In this study, considering time-weighted average dosage as a continuous variable, the hazard ratio (HR) of the average dose was 0.99 ( $p = 0.0034$ ), which indicates that a 1-mg incremental increase in methadone dose reduced the hazard of dropping out by 1% after controlling for other covariates. A methadone dose of <45 mg was not associated with retention. Increasing doses above 45 mg were significantly associated with increasingly smaller HRs for dropping out. The results suggest that higher doses can achieve better retention rates, and that there is a positive dose–response relationship between methadone dose and client retention.

The National Institutes of Health (NIH) expert panel recommended a daily methadone dose of at least 60 mg as a best practice for successful methadone maintenance (Brady et al., 2005). The General Accounting Office reviewed 24 methadone maintenance clinics, based on 5600 active clients, and concluded that the minimally effective dose was 50 mg (Blaney & Craig, 1999). According to the results of this study, we recommend a minimum daily dose of 65 mg as a best practice for Chinese methadone clinics, but we were unable to evaluate doses above 65 mg. Programme participants, however, should be started on lower doses that are gradually increased to assure that clients sensitive to methadone do not receive overdoses.

*Not* having previously been in a detoxification programme and the clinic currently attended were predictors of client retention. The retention of drug users expecting long-term treatment may reflect a greater desire to get off drugs and a greater trust in the effectiveness of methadone treatment. Clients previously in a detoxification programme constitute individuals who have failed previous attempts to get off drugs.

A limitation of this study was that clients voluntarily participated in the study, and might not represent all clients treated in methadone clinics. Clients who dropped out before the initiation of the study were not included. The drop-out rate in the first 1 or 2 months is probably high. Therefore, our observed retention rates are probably higher than would be observed for all clients entering the MMT programme. Although no assumptions are made about the nature or shape of the hazard function of the Cox proportional hazard model, we must assume that the ratio of the hazard functions for independent variables does not depend on time, and that there is a log–linear relationship between the independent variables and the underlying hazard function (Hill & Lewicki, 2007; Hosmer & Lemeshow, 1999).

This study indicates that after 14 months of treatment, 44% of patients had dropped out, which underscores the need to review the MMT programme and to identify factors associated with successful clinics. Although a 100% success rate is unlikely with any treatment, a retention rate of 50% or less and the wide variation between clinics in retaining clients underscores the need to identify factors associated with retention in successful

clinics. This will be the objective of a new study. In conclusion, China has made an impressive commitment to MMT programmes, with considerable success. Further analyses for the key differences between successful and unsuccessful clinics will lead to even greater success.

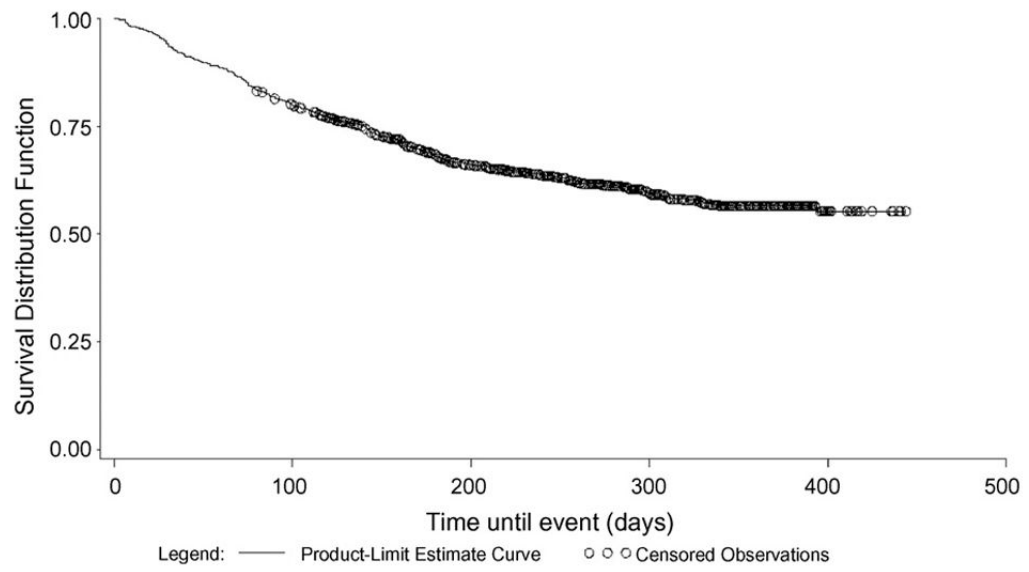
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**Fig. 1.** Kaplan–Meier analysis retention rates of the 1003 participants.



**Table 1**

Demographic information and univariate analysis for retention rates.

Variables	No. of subjects (%)	14-month retention rate (%)	<i>p</i> -Value*
Clinics			
Anshun	60 (6.0%)	70.1	
Zunyi	231 (23.0%)	69.7	
Tongen	127 (12.7%)	64.5	
Shengeryi	116 (11.6%)	57.7	<b>&lt;0.0001</b>
Yuneryi	216 (21.5%)	56.6	
Duyu	102 (10.2%)	56.4	
Jianyu	34 (3.4%)	45.3	
Panxian	117 (11.7%)	23.2	
Gender			
Female	261 (26.0%)	61.4	0.4601
Male	742 (74.0%)	54.7	
Marital status			
Divorced	155 (15.5%)	62.0	
Married	349 (34.9%)	56.9	0.1104
Never married	496 (49.6%)	53.9	
Employment			
Full-time	359 (35.8%)	53.5	
Part-time	296 (29.5%)	56.7	0.8407
Unemployed	348 (34.7%)	57.6	
Ethnicity			
Han	889 (88.6%)	56.4	0.5725
Other	114 (11.4%)	55.9	
Local resident			
No	58 (5.8%)	57.4	0.2680
Yes	945 (94.2%)	56.5	
Practicing a religion			
None	922 (91.9%)	55.1	<b>0.0124</b>
Yes	81 (8.1%)	70.0	
Treatment goal			
Treatment for life	112 (11.3%)	65.9	<b>0.008</b>
Temporary treatment	882 (88.7%)	55.6	
Clinic location			
Convenient	853 (85.2%)	57.4	<b>0.0169</b>
Not convenient	148 (14.8%)	49.9	
Clinic operation times			
Convenient	966 (96.3%)	56.1	0.9177
Not convenient	37 (3.7%)	58.3	
Family support			

Variables	No. of subjects (%)	14-month retention rate (%)	<i>p</i> -Value*
Yes	943 (94.0%)	56.5	0.1519
No	60 (6.0%)	54.0	
Residence			
Own house	337 (33.6%)	56.9	
Parent's house	525 (52.3%)	54.7	0.4902
Rent house	111 (11.1%)	62.3	
Other	30 (30.0%)	49.1	
Treatment fee			
Heavy burden	164 (16.4%)	57.3	0.8582
Not a heavy burden	838 (83.6%)	57.1	
Chronic disease history			
No	892 (89.0%)	56.0	0.3296
Yes	110 (11.0%)	59.2	
Drug use method			
Injection	526 (52.5%)	55.9	0.4698
Non-injection	476 (47.5%)	57.0	
Prior detoxification programme			
No	283 (28.2%)	58.6	0.2346
Yes	720 (71.8%)	55.9	

Statistical significant probability values in bold.

\* *p*-values were calculated by log-rank test of equality of survival rates across variable strata.

**Table 2**

Univariate analysis of retention rates for continuous variables.

	<b>Mean</b>	<b>S.D.</b>	<b>HR</b>	<b><i>p</i>-Value*</b>
Dosage	38.0	16.6	0.986	<b>&lt;0.0001</b>
Years of education	9.4	2.8	0.954	<b>0.0091</b>
Age	33.3	6.1	0.992	0.3178
Years of drug use	8.0	4.0	0.979	0.1005

Statistical significant probability values in bold.

\**p*-values were calculated by univariate Cox model.

Table 3

Hazard ratios and retention rates at different cut points.

Dosage cut points (ml)	Hazard ratio	95% Confidence interval	p-Value *	14-month retention rates (%)		
				<cut point	≥cut point	
0	0.852	0.679	1.068	0.1642	52.2	63.5
45	0.796	0.622	1.019	0.0705	53.2	64.7
50	0.709	0.535	0.945	<b>0.0167</b>	53.6	66.6
55	0.681	0.488	0.950	<b>0.0236</b>	54.6	66.5
60	0.632	0.419	0.952	<b>0.0284</b>	54.7	70.7
65	0.505	0.300	0.845	<b>0.0098</b>	54.7	76.4

Statistical significant probability values in bold.

\* p-values are from multivariate Cox model controlling for clinics, marital status, education, religion, years of heroin use, being a local resident, previous detoxification programmes, clinic locations, and clients' treatment expectations.