UCLA

UCLA Previously Published Works

Title

Retention and its predictors among methadone maintenance treatment clients in China: a six-year cohort study.

Permalink

<https://escholarship.org/uc/item/8v95x5dn>

Authors

Cao, Xiaobin
Wu, Zunyou
Rou, Keming
[et al.](#)

Publication Date

2014-12-01

DOI

10.1016/j.drugalcdep.2014.09.776

Peer reviewed

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Retention and its predictors among methadone maintenance treatment clients in China: A six-year cohort study

Xiaobin Cao^a, Zunyou Wu^{a,*}, Keming Rou^a, Li Li^b, Chunqing Lin^b, Changhe Wang^a, Wei Luo^a, Lin Pang^a, Wenyuan Yin^a, Jianhua Li^c, the National Working Group on Methadone Maintenance Treatment Program^d

^a National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China

^b Semel Institute Center for Community Health, University of California, Los Angeles, CA, USA

^c Yunnan Institute of Drug Abuse, Kunming, Yunnan, China

^d Under the governance of the National Health and Family Planning Commission, Ministry of Public Security and China Food and Drug Administration, Beijing, China

ARTICLE INFO

Article history:

Received 10 June 2014

Received in revised form 9 September 2014

Accepted 20 September 2014

Available online xxx

Keywords:

Methadone maintenance treatment

Retention

Risk factor

Cohort study

ABSTRACT

Background: To investigate factors associated with retention among the first cohort of drug users attending methadone maintenance treatment (MMT) clinics in China.

Methods: A six-year cohort of 1511 drug users was enrolled in the first 8 MMT clinics in China in 2004 and followed between March, 2004 and December, 2010. Six-year retention rates were calculated and compared by methadone dosage, clinic location, and length of follow-up. Factors associated with retention were evaluated using Cox proportional hazard regression models.

Results: The overall retention rate over 6-year was 35.7%. Highest drop-out occurred within the first 12 months of treatment. The retention rates for the 6-year by low (≤ 30 mg/day), medium (31–60 mg/day), and high (> 60 mg/day) methadone dosage groups were 20.8%, 34.8% and 53.2%, respectively ($p < 0.001$). The highest 6-year retention rate among eight clinics was 43.8%, while the lowest one was 17.7% ($p < 0.001$). The results from Cox proportional hazard models indicate that clients having > 30 mg daily methadone dosage ($p < 0.001$), having relatives receiving MMT ($p = 0.027$), and having $> 10\%$ urine morphine positive result ($p < 0.001$) were more likely to be retained in MMT over the six-year period. It has also found that drug injection ($p = 0.005$) and needle sharing ($p < 0.0001$) were significantly associated with better retention.

Conclusions: Health workers should adjust individuals' methadone dosages as a method to prevent early treatment termination. Further studies are needed to explore the impact of severity of opiate addiction on long-term retention of MMT clients. Careful assessment of drug users upon MMT enrollment may be helpful for providing additional care to clients.

© 2014 Published by Elsevier Ireland Ltd.

1. Introduction

In the last two decades, the number of registered drug users in China has increased rapidly from 70,000 in 1990 to 2.47 million in 2013 (Wu et al., 2007; Qian et al., 2006; National Narcotic Control Commission, 2014). The actual number of drug users, however, is thought to be approximately 3.5 million (Qian et al., 2006). Since the first case of HIV infection in China was identified in 1985, needle-sharing behavior among drug users (DUs) has been a major

driver of the epidemic in China. By the end of 2011, approximately 780,000 people were estimated to be living with HIV/AIDS nationwide, with 28.4% of infections attributed to injecting drug use and HIV prevalence among drug users as high as 50% in some regions (China Ministry of Health et al., 2011).

To curb the spread of HIV among drug users, China's national, community-based methadone maintenance treatment (MMT) program was initiated in 2004 as a small pilot project and has since expanded nationwide (Pang et al., 2007). At the end of December 2012, the program encompassed 755 clinics in 28 provinces and had served more than 380,000 DUs, cumulatively (Cao et al., 2012). This rapid scale-up of China's national MMT program has resulted in reduced drug use and criminality, and improved quality of life

* Corresponding author. Tel.: +86 10 5890 0901; fax: +86 10 5890 0900.
E-mail addresses: wuzunyou@chinaaids.cn, wuzy@263.net (Z. Wu).

and employment rates that have benefited both drug users themselves and their communities (Yin et al., 2010). Nonetheless, many challenges remain including low overall program coverage, low retention rates, and high concurrent drug use rates (Cao and Wu, 2011; Li et al., 2012).

Worldwide, studies consistently indicate that increasing length of treatment is correlated with improved treatment outcomes including decreased concurrent drug use and HIV transmission (Ward et al., 1999; Metzger et al., 1993, 2010). Furthermore, predictors of longer retention times are known to be socio-demographics, drug use history, dosage, treatment models, and client-provider interaction (Ball and Ross, 1991; Simpson et al., 1997; Kelly et al., 2010; Ward et al., 1998; Lin et al., 2010).

In China, several previous studies on the effectiveness of the national MMT program have suggested that barriers and facilitators to client retention may be unique to China's social, political, and cultural context (Li et al., 2012; Lin et al., 2010). However, no nationwide study of factors associated with MMT retention has been conducted in China, yet a better understanding of these factors is crucial for the future enhancement of China's MMT program so that outcomes for China's drug users can be improved. More importantly, the results of a national cohort study from China would add to the existing literature, given that previous studies came from English-speaking countries which may differ in terms of culture and political context. Thus, the primary aim of this study was to identify various predictors of treatment retention over a six-year period. We sought to test the hypothesis that while rapid scale-up of China's MMT program, there were crucial factors being associated with MMT clients' retention in China's social, political, and cultural context.

2. Methods

2.1. Study design and participants

The China national MMT program is a prospective, observational open cohort of treatment of opioid users. This study is a secondary analysis of existing government MMT data. A subset of fixed cohort MMT clients enrolled in the first eight MMT clinics in China – one in Yunnan, one in Guangxi, two in Sichuan, two in Guizhou, and two in Zhejiang – between 23 March, 2004 and 31 December, 2004, were selected and followed up to 30 June, 2010. The study was conducted in the first eight MMT clinics. These clinics were located in areas selected due to their high prevalence of injecting drug use and HIV infection relative to the rest of the country (State Council AIDS Working Committee Office, UN Theme Group on HIV/AIDS in China, 2004). Details of program administration have been described in China's MMT protocol (China Ministry of Health et al., 2006).

When the national MMT program began in China, all DUs were required to meet the following MMT program enrollment eligibility criteria, which had been described in papers published (Cao et al., 2013; Pang et al., 2007; Wu et al., 2007): (1) have failed several times at attempts to discontinue heroin use, (2) have served at least two times in a compulsory detoxification center, (3) be 20 years old or older, (4) be registered as a local resident in the area in which the clinic is located, and (5) be of full capacity for civil duties, meaning able to take responsibility for himself or herself. HIV-positive DUs were only required to meet the latter two criteria. A total of 1511 MMT clients were included in our study. A flow diagram depicting the development of our study population is shown in Fig. 1.

2.2. Sources of data

Information collected in China's National MMT Information Management System from baseline surveys completed by MMT clients within one month after enrollment as well as from on-site follow-up interviews were used in this study. The details of this data system as well as the methods used for collecting baseline and follow-up data from MMT clients have been described previously (Yin et al., 2010; Mao et al., 2010). The retention of study participants was assessed from 23 March, 2004 to 30 June, 2010, and verified retrospectively in 2010.

2.3. Outcomes

The primary outcome measure in this study was retention. Clients, who were still on methadone at the end of the study period (June, 2010) were considered retained over the six-year period. Clients no longer on methadone at the end of the study were defined as having dropped out of the treatment. Retention duration was calculated from the date of first methadone treatment to the date of the last

methadone treatment or the study end date, whichever occurred first. Methadone exposure was measured as mean daily methadone dosage, which was calculated as the sum of all doses divided by the total number of days on methadone. According to China's MMT protocol, client was required to take urine morphine test every month after he/she enrolled in the MMT clinic. Proportion of concurrent illicit drug use was calculated as the number of urine morphine positive results divided by the total number of urine morphine tests administered. The statuses of clients after withdrawal from MMT were categorized as addicted, self-reported abstained from heroin, incarcerated, hospitalized, or deceased based on information gathered from interviews with local MMT clinic and Center for Disease Control and Prevention (CDC) staff, family and community members, policemen, and other drug users.

2.4. Statistical analysis

First, we descriptively analyzed the distribution of socio-demographics, drug use history on enrollment and characteristics of methadone treatment, using numbers and percentages to describe categorical variables, and using mean, median, and standard deviation (SD) to describe quantitative variables. Second, univariate analysis was conducted before proceeding to more complicated models. Chi-square tests were used to compare retention at different clinics. For all categorical variables, Kaplan–Meier curves were created and log-rank tests were used to look at whether or not to include predictors in the final model. For continuous variables, they were categorized and then Kaplan–Meier curves and log-rank tests were used to find potential candidates for the final model. Third, Cox Proportional Hazards (Cox PH) regression models were built to assess predictors of retention. Variables which met the proportional hazard assumption of the Cox PH model and had a *p*-value of less than 0.25 in univariate analysis were included in the final multivariate Cox PH models. We treated retention at the end of the six-year period as the dependent variable and others as predictor variables. Dummy variables were created for categorical variables selected in the model. Hazard Ratios (HRs) and their 95% confidence intervals (CIs) were reported, all *p*-values were two-tailed and a *p*-value of less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed using SAS software (version 9.2, SAS Institute, USA).

2.5. Ethical approval

This study was a secondary data analysis using existing Chinese government MMT program data. All MMT clients signed an informed consent upon enrollment to participate in MMT program saying that their data, after removing their personal identifications, could be used in epidemiological studies such as this. Therefore, no additional study-specific consent for this current study was sought. This study protocol was reviewed and approved by the Institutional Review Board of the National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention.

3. Results

3.1. MMT patient characteristics

As shown in Fig. 1, a total of 1511 drug users met the eligibility criteria and were recruited and followed in this study. In our study population, 77.1% (1165) were male, 77.4% (1170) had no more than nine years education, 77.8% (1176) were unemployed, 56.1% (848) were unmarried, 67.2% (1015) were injecting drug users (IDUs), 60.3% (912) were aged 30 years old or above, and 31.9% (482) reported having close family relationships at baseline. At enrollment, 67% (1,013) were IDUs, and 48.7% (736) had shared needles and syringes with others. About one-third (30.6%, 337) did not have any contact with other drug users, whereas 46.6% (605) had at least 30 contacts with drug users in the past 30 days. The mean age of onset of drug use was 23.8 years (SD = 5.7), mean length of drug use was 8.6 years (SD = 3.3), mean travel distance between the clinic and home was 5.5 km (SD = 8.4), mean daily dosage was 48.6 mg (SD = 32.4), and mean proportion of positive urine morphine tests was 26.5% (SD = 29.9). There were 13.2% (199) clients who had at least one relative on methadone treatment.

3.2. Overall retention rate

The median duration of treatment over the study period was 50.9 months, with the longest at 75.8 months and shortest at 3 days. The retention rates at the end of 2004, 2005, 2006, 2007,

* Continuous: Did not miss more than 30 consecutive days during the follow-up period.
** Non-continuous: Missing more than 30 consecutive days during the follow-up period.

Fig. 1. Overall retention rate of 1511 subjects over six-year follow-up period.

2008 and 2009 were 75.0%, 42.5%, 33.2%, 30.8%, 32.1% and 31.4%, respectively. By the end of the study period in June 2010, 35.7% (539) clients were still receiving methadone treatment, 54.1% (818) had dropped out and 10.2% (154) had died during the follow-up period.

3.3. Comparison of retention rates between MMT clinics

Table 1 presents the average daily dosage and retention rates among the eight MMT clinics over the six-year follow-up period. At the end of 2004, the retention varied between 40.0% and 88.9% ($p < 0.01$). At the end of the follow-up period, the range in retention rates had narrowed, with the highest rate at 43.8% and the lowest rate at 17.7% ($p < 0.01$).

3.4. Socio-demographic and treatment characteristics

Table 2 presents correlations between socio-demographic, drug use history and MMT treatment characteristics and retention over the six-year period. Clients reporting close or average family relationships, drug injection, needle sharing and contact with drug users in the month prior to MMT enrollment were significantly associated with retention ($p < 0.01$). Gender, age, employment status, marital status, living situation, education level, age at first drug use and length of drug use were not significant predictors of

retention over six-year period ($p > 0.05$). Receiving higher mean daily dosages was strongly correlated with retention in treatment (20.8% for ≤ 30 mg/day vs 34.8% for 31–60 mg/day vs 53.2% for > 60 mg/day, $p < 0.0001$). Clients living less than 5 km away from their prescribing MMT clinic were more likely to stay in treatment over the six-year period than clients living more than 5 km away (38.7% vs 31.4%). Clients with relatives who were also engaged in MMT were associated with a higher retention rate than clients who did not have relatives in MMT (53.8% vs 32.9%).

3.5. Multivariate Cox PH models

Table 3 summarizes the multivariate Cox PH models examining predictors of retention. After adjusting for gender, living situation, income, education, family relationships, injecting behavior, needles sharing behavior, length of drug use, and travelling distance between clinic and home, the multivariate analysis found that clients who received 31–60 mg/day ($HR = 0.57$, $p < 0.0001$), > 60 mg/day dosages ($HR = 0.38$, $p < 0.0001$), had relatives concurrently receiving MMT ($HR = 0.72$, $p = 0.0270$), and had higher proportions ($> 10\%$) of positive urine morphine tests results ($HR = 0.55$, $p < 0.0001$; $HR = 0.63$, $p < 0.0001$) were associated with higher probabilities of retention over the six-year period. Frequent contact with current drug users was found not to be a significant predictor of retention ($p > 0.05$).

Table 1
Comparison of retention rates by methadone clinics in December 2004 and June 2010.

Clinic	Mean dosage $\pm$ SD (mg/day)	Overall number of subject <i>N</i>	December 2004			June 2010		
			Retained <i>N</i>	Retention rate (%)	<i>p</i> -Value ^a	Retained <i>N</i>	Retention rate (%)	<i>p</i> -Value ^a
1	47.8 $\pm$ 25.2	345	208	60.3	<0.01	151	43.8	<0.01
2	56.7 $\pm$ 34.6	280	205	73.2		111	39.6	
3	43.5 $\pm$ 23.6	221	195	88.2		39	17.7	
4	42.0 $\pm$ 14.9	81	72	88.9		21	25.9	
5	46.2 $\pm$ 21.5	195	169	86.7		78	40.0	
6	39.2 $\pm$ 22.0	126	88	69.8		34	27.0	
7	50.5 $\pm$ 31.3	203	172	84.7		85	41.9	
8	57.3 $\pm$ 32.4	60	24	40.0		20	33.3	
Overall	48.6 $\pm$ 32.4		1133	75.0	–	539	35.7	–

SD: standard deviation.

^a *p*-Values determined using chi-square tests.

4. Discussion

Treatment retention is one of the key factors to consider when assessing MMT program effectiveness. China began its community-based MMT program in 2004. And an assessment of long-term retention rates and other key features is critical to plan the future development of the MMT program. To address this need, the present study investigated MMT retention in eight community-based MMT clinics over a six-year period and identified factors that were associated with client retention.

4.1. Main findings

For this study population, the median duration of retention was 50.9 months and 35.7% of clients were retained in the community-based MMT program at the end of the study period. The drop-out rates reached a peak at 1.5 years after enrollment and subsequently decreased with the length of treatment, which suggested that the counseling and additional services at the initial stage of MMT is most important for subsequent retention. According to China's national MMT protocol, MMT providers are required to provide 2–3 counselling services per week within the first two weeks after enrollment and then one counselling service per week during the first 3 months after enrollment. Subsequently, counselling and additional services will be provided by MMT providers as of needs of MMT clients.

Compared with studies reported from other countries, our results indicate a higher long-term retention rate. Past research suggests that this may be due to the family-oriented nature of traditional Chinese culture; family support is associated with a higher quality of life for MMT clients (Lin et al., 2011). In Australia, the overall retention of a 12-month follow-up study was 65% at three months, 51% at six months, and 38% at one year (Bell and Mutch, 2006).

The results also noted wide variations in long-term retention rates between the eight study sites. Retention rates may be correlated with one or more of the following program factors: (a) clinic location; (b) clinic organizational structure; (c) characteristics of the staff and the work environment; and (d) service quality. Further research is needed to explore potential impact of program factors on client retention, which was beyond the scope of this study.

This study observed that clients who had relatives on methadone treatment were associated with a higher retention rate. The factors contributing to this trend remain unclear. Past research proposes that in Chinese culture, family ties have greater influence on individuals' drug use behaviors than in Western cultures. Support between relatives who are concurrently engaged in MMT may result in mutual assistance in the form of reminders, financial assistance, and emotional encouragement to remain in

treatment. Relatives may also discourage concurrent drug use. However, there is also potential that concurrent engagement with another family member(s) may prompt negative social influences and effects. We suggest future research focusing on households with multiple MMT clients and providing such households with targeted educational programs.

High daily dosages of methadone (>60 mg) was another important predictor of long-term retention. Many randomized controlled trials and observational studies have clearly demonstrated that higher daily dosages resulted in less illicit opioid use, fewer crimes, and longer duration of treatment (Gowing et al., 2011; Kerr et al., 2005; Peles et al., 2006; Liu et al., 2009). A recent review observed that while the majority of clients require at least 60 mg per day, a dosage of 80–100 mg or greater is even more strongly correlated with positive outcomes (Joseph et al., 2000). We found that an increase of 30 mg in daily dosages reduces the risk of dropout by almost 30%. It was emphasized that this study not only added to the existing evidence from a geographical perspective but also because it concurred with existing evidence of higher methadone doses positively correlating with long-term retention.

It should be noted that the average daily dosage in this study was only 48.6 mg, lower than the dosage recommended by the China National MMT guideline (China Ministry of Health et al., 2006). Clients may have been reluctant to accept higher dosages due to increased side effects, unwillingness to terminate all drug use, social pressure from other drug users or dissatisfaction with clinic services. In order to improve client retention and to produce better positive outcomes, including less illicit drug use, fewer criminals related to drug and better social function recovery, it is crucial for MMT clients to be on sufficient daily dosages of methadone. We recommend increasing methadone dosages based on clients' individual needs in order to promote treatment efficacy and retention.

Another interesting finding of this study is a correlation between needle sharing, frequently concurrent illicit drug use and higher retention in retreatment, which is contradictory to the existing literature (Wong et al., 2003). Possible reasons for this phenomenon might be that the longer drug users addicted to opiates, the more likely they had needle sharing behaviors and frequently concurrent illicit drug use during methadone treatment, which means that they might have higher severity rating of addiction. Drug users with higher severity rating of addiction are less likely to be abstinent from heroin and tended to have higher motivation to enroll in MMT and as well as remain in treatment. Further studies are needed to explore the impact of severity of opiate addiction on long-term retention of MMT clients.

4.2. Strengths and weaknesses

Our study had several strengths. First, this is the first prospective cohort study with a large sample size and a six-year follow-up

Table 2

Comparison of retention rates by demographics, drug use history, and MMT treatment characteristics of clients at time of initial MMT enrollment.

Characteristics	Retained <i>N</i>	Withdrawn <i>N</i>	Retention rate (%)	<i>p</i> -Value [*]
Demographics				
Age (years)				
≤30	218	381	36.4	0.7700
≥31	321	591	35.2	
Gender				
Male	412	753	35.4	0.2370
Female	127	219	36.7	
Employment status				
Unemployed	116	219	34.6	0.9580
Employed	423	753	36.0	
Marital status				
Single	297	551	35.0	0.3258
Married	187	305	38.0	
Divorced	55	116	32.2	
Living situation				
With family/friends	468	872	35.0	0.1492
Alone	71	227	41.5	
Education level				
≤Junior high	1170	404	766	0.0861
≥High school	341	135	206	
Family relationships				
Close or average	463	765	36.7	<0.0001
Estranged	76	207	26.9	
Drug use history				
Age at first drug use (years)				
≤25	374	647	36.6	0.2830
>25	165	325	33.7	
Length of drug use (years)				
≤6	134	256	34.4	0.1250
7–12	335	609	35.5	
>12	70	107	39.6	
Injection behavior [†]				
No	344	671	33.9	0.0050
Yes	195	301	39.3	
Needle sharing behavior [†]				
No	229	507	31.1	<0.0001
Yes	310	465	40.0	
Contact with drug users ^{‡,§}				
None	182	215	45.8	0.0002
1–30	223	382	36.9	
>30	94	201	32.9	
MMT treatment experience				
Dosage (mg/day)				
≤30	57	217	20.8	<0.0001
31–60	334	625	34.8	
>60	148	130	53.2	
Illicit drug use during treatment (%)				
≤10	238	554	30.0	<0.0001
11–20	91	101	47.4	
>20	210	317	39.9	
Distance between clinic and home (km)				
<5	343	544	38.7	0.0010
≥5	196	428	31.4	
Relatives who were MMT clients				
No	432	880	32.9	<0.0001
Yes	107	92	53.8	
Overall	539	972	35.7	–

^{*} *p*-Values were calculated using log-rank tests.[†] Injection behavior, needle sharing behavior, and contact with drug users variables are limited to within the previous 1 month.[‡] Contact with drug users is measured by the number of times the client has been in contact with known, current drug users in the previous 1 month.[§] Data for contact with drug user variable are missing for 214 clients.^{||} Illicit drug use during treatment was calculated by expressing the number of positive urine morphine test results divided by the total number of tests administered as a percentage.

period on predictors of long-term retention in China. Large sample sizes result in effect estimates with narrow confidence intervals. The prospective follow-up design used in this study enabled us to avoid temporal ambiguity, which a common challenge in cross-sectional and case-control studies. Another important strength of this study is the use of China's MMT Information Management System. The misclassification of "exposures" and "outcomes" are minimized which has enabled us to link and trace the

comprehensive treatment dynamics of each client, including daily dosage, reason and date of dropout, and length of treatment. Furthermore, collecting urine morphine test results in real-time from this system also discourages underreporting of concurrent illicit drug use during the MMT.

There were a few limitations in this study with regards to reliability and validity. This study was not a randomized controlled trial, and its conclusions must be viewed with reservations.

Table 3

Results from multivariate Cox proportional hazards models indicating factors associated with retention in MMT over the six-year follow-up period.

Characteristics	Retained <i>N</i> ^a	Adjusted HR (CI) ^b	<i>p</i> -Value ^c
Contact with drug users			
None	182	1.00	
1–30	223	0.93 (0.76, 1.45)	0.5080
>30	94	1.14 (0.90, 1.45)	0.2630
Dosage (mg/day)			
≤30	56	1.00	
31–60	335	0.57 (0.47, 0.71)	<0.0001
>60	148	0.38 (0.29, 0.51)	<0.0001
Illicit drug use during treatment (%)			
≤10	238	1.00	
11–20	91	0.55 (0.42, 0.73)	<0.0001
>20	210	0.63 (0.52, 0.76)	<0.0001
Relatives who were MMT clients			
No	432	1.00	
Yes	107	0.72 (0.54, 0.96)	0.0270

HR: hazard ratio, CI: 95% confidence interval.

^a Numbers of clients retained at the end of the six-year follow-up period. Only complete cases were included in the multivariate model.^b Hazard ratios, confidence intervals, and *p*-values were calculated using a multivariate Cox proportional hazards ratio model adjusting for factors including gender, living situation, income, education, family relationships, injecting behavior, needle sharing behavior, length of drug use, and distance between clinic and home.

Although we adjusted for known potential confounding factors, other unidentified confounding factors may exist. For instance, being arrested by policemen and detention in compulsory rehabilitation were one of the most causes of drop-out, which have not been adjusted for in this study. Information bias may have skewed the results, i.e., drug users who felt uncomfortable providing accurate information on sensitive questions such as needle and syringe sharing behaviors. Recall bias regarding events that occurred many years ago, such as the age at first drug use, may also be an influencing factor. Finally, it is possible that socio-demographics and drug use history characteristics of the study subjects were different from drug users residing in other parts of China. We suggest caution in interpreting these results and generalizing the findings.

5. Conclusion

To develop a more effective community-based MMT program, studies should continuously monitor and evaluate MMT programs to identify factors related to improved patient care and health outcomes. Studies such as this one can provide policymakers and other researchers with valuable information in designing future interventions and in improving the current MMT program for greater efficacy.

Role of funding sources

This study was funded by the Chinese National Methadone Maintenance Treatment Program (Grant # 131110001050), by the Fogarty International Center and National Institute on Drug Abuse of the US National Institutes of Health (NIH, Grant # 5U2RTW006918) and by the National Science and Technology Major Research Projects on Prevention and Control of Major Infectious Diseases including AIDS and Hepatitis (Grant # 2008ZX10001-016). Funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Contributors

X. Cao and Z. Wu have contributed in the conceptualization and development of this paper. X. Cao conducted data analysis. X. Cao, Z. Wu, K. Rou and L. Li interpreted results and made many revisions of the manuscript. All authors have contributed

to the revision of the manuscript and given final approval for publication.

Conflict of interest

The authors report no conflict of interest.

Disclaimer

The opinions expressed herein reflect the collective views of the co-authors and do not necessarily represent the official position of the National Center for AIDS/STD Control and Prevention, Chinese Center for Diseases Control and Prevention.

Acknowledgements

We want to thank Jennifer McGoogan, Li-Jung Liang, Dai Wan, Julie Hsieh, Cynthia Shi, and Sam Guo for their contribution and editing an earlier draft of this manuscript.

References

- Ball, J.C., Ross, A., 1991. *The Effectiveness of Methadone Maintenance Treatment: Patients, Programs, Services, and Outcome*. Springer-Verlag, New York, NY.
- Bell, J., Mutch, C., 2006. Treatment retention in adolescent patients treated with methadone or buprenorphine for opioid dependence: a file review. *Drug Alcohol Rev.* 25, 167–171.
- Cao, X.B., Wu, Z.Y., 2011. Methadone maintenance treatment as an HIV prevention strategy: a research update. *Chin. J. STD AIDS* 17, 196–199.
- Cao, X.B., Wu, Z.Y., Li, L., Pang Lin Rou, K.M., Wang, C.H., Luo, W., Yin, W.Y., Li, J.H., McGoogan, J.M., 2013. Mortality among methadone maintenance clients in China: a six-year cohort study. *PLoS One* 8, e82476.
- Cao, X.B., Wu, Z.Y., Pang, L., Rou, K.M., Wang, C.H., Luo, W., Yin, W.Y., Mi, G.D., Li, J.H., 2012. Evaluation on the long-term effectiveness among the first eight methadone maintenance treatment clinics in China. *Chin. J. Epidemiol.* 33, 879–882.
- China Ministry of Health, Ministry of Public Security, The State Food and Drug Administration, 2006. *Implementation Protocol of the Community-based Methadone Maintenance Treatment Program for Opiate Addicts in China*. China Ministry of Health, Beijing, China.
- China Ministry of Health, UNAIDS, WHO, 2011. *2011 Estimates for the HIV/AIDS Epidemic in China*. China Ministry of Health, Beijing, China.
- Gowing, L., Farrell, M.F., Bornemann, R., Sullivan, L.E., Ali, R., 2011. Oral substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database Syst. Rev.* 8, CD004145.
- Joseph, H., Stancliff, S., Langrod, J., 2000. Methadone maintenance treatment (MMT): a review of historical and clinical issues. *Mt. Sinai J. Med.* 67, 347–364.
- Kelly, S.M., O'Grady, K.E., Brown, B.S., Mitchell, S.G., Schwartz, R.P., 2010. The role of patient satisfaction in methadone treatment. *Am. J. Drug Alcohol Abuse* 36, 150–154.

- Kerr, T., Marsh, D., Li, K., 2005. Factors associated with methadone maintenance therapy use among a cohort of polysubstance using injection drug users in Vancouver. *Drug Alcohol Depend.* 80, 329–335.
- Li, L., Wu, Z.Y., Cao, X.B., 2012. Provider-client interaction in methadone treatment clinics in China. *J. Drug Issues* 42, 147–155.
- Lin, C.Q., Wu, Z.Y., Detels, R., 2011. Family support, quality of life and concurrent substance use among methadone maintenance therapy clients in China. *Public Health* 125, 269–274.
- Lin, C.Q., Wu, Z.Y., Rou, K.M., Pang, L., Cao, X.B., Shoptaw, S., Detels, R., 2010. Challenges in providing services in methadone maintenance therapy clinics in China: service providers' perceptions. *Int. J. Drug Policy* 21, 173–178.
- Liu, E.W., Liang, T., Shen, L.M., Zhong, H., Wang, B., Wu, Z.Y., Detels, R., 2009. Correlates of methadone client retention: a prospective cohort study in Guizhou province, China. *Int. J. Drug Policy* 20, 304–308.
- Mao, Y.R., Wu, Z.Y., Poundstone, K., Wang, C.H., Qin, Q.Q., Ma, Y., Ma, W., 2010. Development of a unified web-based national HIV/AIDS information system in China. *Int. J. Epidemiol.* 39 (Suppl. 2), ii79–ii89.
- Metzger, D.S., Woody, G.E., McLellan, A.T., O'Brien, C.P., Druley, P., Navaline, H., DePhilippis, D., Stolley, P., Abrutyn, E., 1993. Human immunodeficiency virus seroconversion among intravenous drug users in- and out-of-treatment: an 18-month prospective follow-up. *J. Acquir. Immune Defic. Syndr.* 6, 1049–1056.
- Metzger, D.S., Woody, G.E., O'Brien, C.P., 2010. Drug treatment as HIV prevention: a research update. *J. Acquir. Immune Defic. Syndr.* 55 (Suppl. 1), S32–S36.
- National Narcotic Control Commission, 2014. *Annual Report on Drug Control in China* (2014). National Narcotic Control Commission, Beijing, China.
- Pang, L., Hao, Y., Mi, G.D., Wang, C.H., Luo, W., Rou, K.M., Li, J.H., Wu, Z.Y., 2007. Effectiveness of first eight methadone maintenance treatment clinics in China. *AIDS* 21 (Suppl. 8), S103–S107.
- Peles, E., Schreiber, S., Adelson, M., 2006. High methadone dose significantly reduces cocaine use in methadone maintenance treatment (MMT) patients. *J. Addict. Dis.* 25, 43–50.
- Qian, H.Z., Schumacher, J.E., Chen, H.T., Ruan, Y.H., 2006. Injection drug use and HIV/AIDS in China: review of current situation, prevention and policy implications. *Harm Reduct. J.* 3, 4.
- Simpson, D.D., Joe, G.W., Rowan-Szal, G.A., Greener, J.M., 1997. Drug abuse treatment process components that improve retention. *J. Subst. Abuse Treat.* 14, 565–572.
- State Council AIDS Working Committee Office, UN Theme Group on HIV/AIDS in China, 2004. *A Joint Assessment of HIV/AIDS Prevention, Treatment and Care in China*. State Council AIDS Working Committee Office, Beijing, China.
- Ward, J., Hall, W., Mattick, R.P., 1999. Role of maintenance treatment in opioid dependence. *Lancet* 353, 221–226.
- Ward, J., Mattick, R.P., Hall, W., 1998. *Methadone Maintenance Treatment and Other Opioid Replacement Therapies*. Harwood Academic Publishers, Amsterdam.
- Wong, K.H., Lee, S.S., Lim, W.L., Low, H.K., 2003. Adherence to methadone is associated with a lower level of HIV-related risk behaviors in drug users. *J. Subst. Abuse Treat.* 24, 233–239.
- Wu, Z.Y., Sullivan, S.G., Wang, Y., Rotheram-Borus, M.J., Detels, R., 2007. Evolution of China's response to HIV/AIDS. *Lancet* 369, 679–690.
- Yin, W.Y., Hao, Y., Sun, X.H., Gong, X.L., Li, F., Li, J.H., Rou, K.M., Sullivan, S.G., Wang, C.H., Cao, X.B., Luo, W., Wu, Z.Y., 2010. Scaling up the national methadone maintenance treatment program in China: achievements and challenges. *Int. J. Epidemiol.* 39 (Suppl. 2), ii29–ii37.