Title
Factors associated with Effectiveness of Methadone Maintenance Treatment in Yunnan Province of China

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Factors associated with Effectiveness of Methadone Maintenance Treatment in Yunnan Province of China

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in Epidemiology

by

Songyuan Tang

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ABSTRACT OF THE DISSERTATION

Factors associated with Effectiveness of Methadone Maintenance Treatment

in Yunnan Province of China

by

Songyuan Tang

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2015

Professor Roger Detels, Chair

Background: China introduced the Methadone Maintenance Treatment (MMT) to cope with the rapidly rising number of heroin users and related increases in the prevalence of HIV for a decade. Currently, China's MMT program is the largest single MMT program in the world. However, relatively low retention rate of MMT has been a concern for China's MMT program ever since the first pilot was initiated. The objectives of the prospective cohort study are: 1) To document the retention rate of MMT program and identify the factors associated with retention

of MMT in Yunnan. 2) To examined effect of MMT for 204 drug users who entered methadone maintenance between baseline and 6-month follow-up.

Methods: Anonymous in-depth interviews were conducted with 13 clients of MMT clinics, 18 dropouts from MMT, 8 officers and 19 services providers of MMT program. The perceived facilitators and barrier associated with retention of MMT from the perspectives of clients and service providers were documented. Meanwhile, a prospective cohort study was employed in this study. 523 clients from the four selected MMT clinics from four city/prefectures of Yunnan Province were recruited into the cohort, beginning on January 2014 and followed up until September 2014. In total, 523 clients completed questionnaire interview at baseline and 204 clients who still remained in MMT clinics were interviewed at six-month follow up. Additionally, to evaluate the effects of MMT program, this study also compared the baseline information and followed up information among the 204 clients who were remaining in the MMT program.

Results: The qualitative study revealed that over ten years, MMT program has already gradually accepted by societies including the department of public security. Fear of arresting in and/or around MMT clinics was not a major barrier for accessing and remaining in. Service providers believed they are able to prescribe appropriate dosage of methadone to clients. However, that methadone dose and dose-adjustment are still problem at the maintenance phase because of poor provider-client communication, misunderstanding and inappropriate perceptions of the MMT treatment goals and side effect. The major individual-level barriers are: 1) Lack of knowledge of MMT treatment goal, side effects and long-term treatment process; 2) fear of addiction of

methadone and opposition to utilize MMT on a long-term basis; 3) low accessibility of comprehensive services such as psychological counseling and side effect diagnosis and treatment; 4) economic burden; 5) concurrent use of heroin and methadone due to temptation of drug user friends and lack of family support, and 6) the drug-related stigma and discrimination in societies. The major structural and institutional barriers are: 1) high turnover rate and shortage of human resources in MMT clinic due to financial difficulties and lack of institutional support; 2) lack of related skills such as communication and counseling skills because of insufficient professional trainings; 3) logistical barriers such as the inflexible service hours, location and transportation and take away dose of methadone is restricted. 4) MMT services diversity and, 5) affordability of MMT. Furthermore, this study showed that individual barriers and structural barriers often interact synergistically and make the situation more complicated and difficult.

The quantitative study found that the cumulative probabilities of retention at 1, 3 and 6months were 80.9%, 47.8% and 39.0%, respectively. The mean survival time was 3.5 months (Se=0.098) and median was 2.9 months. Seven factors were found to significantly predict retention in the MMT clinics. The seven factors were: female gender, in employment, good family relationships and support, currently married, never dropped out of MMT, subjective feeling of adequate dosage, and good provider-client relationship.

With regarding to the effects of MMT, this study found that those clients who remaining in MMT reduced their heroin using and only 3 clients (1.5%) reported sharing needles in last month at the follow up. The MMT improved the sexual function and the average times of having sex in last month. Meanwhile, the proportion of having commercial (paid) sex also increased. The

physical health status of clients retained in the program was improved significantly. However, the psychological health status underwent no considerable improvement through the 6-month MMT.

Conclusions: Individual and institutional interacted each other, which causes relatively low retention rate of Chinas' MMT program. Currently, the quality of service in MMT is still at the low level. Non-treatment predicting predictors, such as employment status, family relationship and support, provider-client relationship, need to addressed and improved by providing the comprehensive services to clients. Improving the quality of comprehensive services should set up as the first priority of China's MMT program after ten-year rapid scaling up.

Key words: Methadone Maintenance Treatment, Retention, Effectiveness, Quality of services, Yunnan, China, Prospective cohort study, Drug users, HIV/AIDS

The dissertation of Songyuan Tang is approved.

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Chapter I Introduction

1. Epidemiology of HIV/AIDS among the Drug users

The first Chinese AIDS case was reported in 1985, with 17 more cases by 1988 (Zheng, 1999). In 1989 the first drug-related HIV infection was identified in Yunnan Province, and then 146 cases were detected among IDUs in Dehong prefecture of Yunnan Province. Between 1989 and the mid-1990s, HIV spread steadily from Yunnan into neighboring areas and along the major drug trafficking routes, then from injecting drug users (IDUs) to their sexual partners and children (Wu, etc., 2007). Since 1994, HIV/AIDS spread rapidly from drug abusers to the general population. By the end of 2013, there were a reported 437,000 people living with HIV/AIDS (including 263,000 people living with HIV and 174,000 AIDS patients) and a reported 136,000 deaths around the country. (National Health and Family Planning Commission of The People's Republic of China, 2014).

Injecting of drugs and sharing of contaminated needles, and other injecting paraphernalia, have resulted in the transmission of HIV, leading to a high prevalence of HIV and AIDS among injecting drug users (IDUs). Given the above characteristics of drug users in China, it is not difficult to understand that drug users have played a key role in the spread of HIV/AIDS in China.

Since 2005, sexual transmission has been the primary mode of transmission in China. Of the 780,000 people estimated to be living with HIV in 2011, the percentage infected through sexual transmission reached 63.9% and the percentage infected through IDU dropped to around 28.4%

(Ministry of Health of the People's Republic of China, 2012). However, the HIV infection prevalence among drug users (particularly IDUs) is the highest but exhibits significant regional disparities. Bao and Liu systematically reviewed 40 peer-reviewed publications to determine the HIV and hepatitis C virus (HCV) geographical distribution among drug users in China. They reported that of the overall HIV prevalence and HCV prevalence were 12.55% and 66.97% respectively among the IDUs. They also concluded that the large geographical variation of HIV prevalence among drug users was largely based on the route of drug administration. The highest infection prevalence is concentrated in the provinces along the drug smuggling corridor. The HIV prevalence rate among the IDUs ranged from 0% in Anhui and Inner Mongolia to 52.51% in Yunnan Province. Among all the identified drug users, Yunnan Province has the highest prevalence of HIV (47.33%), followed by Xinjiang (39.93%), Guangxi (16.95%), Sichuan (11.97%) and Hunan Province (11.71%). Each of these five provinces can be found in the so-called 'China Channel' of drug smuggling from the 'Golden Triangle' (specifically Myanmar) and the 'Golden Crescent' (specifically Afghanistan) to inner cities and abroad (Bao & Liu, 2009). Based on the data sets from China's national HIV/AIDS care reporting system, Wang et al., also indicated that after two decades of expansion of the HIV epidemic among IDUs in China, it is clear that southwest provinces (Yunnan, Sichuan, Guangxi and Guangdong) and Xinjiang Uygur Autonomous Region in the far northwest still bear a disproportionately large HIV burden relative to the rest of the country (Lan Wang, et al., 2014).

Drug abuse also facilitates HIV transmission in indirect ways. Due to the influence of drugs, drug users are more likely to practice unprotected sex behaviors, and thereby they may transmit or become infected with HIV (Darrow et al., 2005). Drug users may also trade sex for drugs,

which has been observed in both female and male drug users. (Wang & Lin, 2003; Lau, et al., 2005). Lau and his colleagues reported that about 60% of the female respondents were engaged in commercial sex within the 6-month period before admission to the centre. In addition, female IDU needle sharers were more likely to do so, as compared to non-IDUs (71.7% vs. 45.8%). 43.1% of all female respondents admitted that they had exchanged sex for drugs. Over 80% of all female respondents reported that some of their peers had been exchanging sex for drugs. About 40% of the female respondents who had engaged in commercial sex did not always use condoms with their commercial sex partners (Lau, et al., 2005).

Considering the remarkably high prevalence of engaging in unsafe sex behavior among the drug users, especially IDUs, as well as the dramatic increase in the commercial sex industry in China, the intermixed IDU and heterosexual at-risk population may serve as a bridge population, transferring HIV from IDUS to the general population. Therefore, a number of harm reduction strategies among the drug users have been initiated and rapidly scaled up in order to control the spread of HIV/AIDS in recent years (Sullivan & Wu, 2007).

2. MMT in China

The first Methadone Maintenance Treatment program (MMT) was established as a substitution treatment for opioid dependence in New York City in 1964 by Drs. Vincent Dole and Marie Nyswander (Ball, 1991). Since then, MMT has demonstrated efficacy in improving the physical and psychological health of those receiving treatment for opium dependence (Bell, et al., 1997; Metzger, et al., 1993). A number of controlled trials, longitudinal studies and observational studies provide considerable evidence that MMT is associated with reductions in illicit drug use,

injecting-related behavior, criminal behavior, deaths due to overdose, and reduced risk of spread of HIV/AIDS (Ball, 1991; Gottheil, et al., 1993; Gunne, 1981; Newman, 1979; Strain, et al., 1993). The emergence of HIV/AIDS in the 1980s and intravenous drug use contributed significantly to the transmission of HIV. MMT was suggested as the most efficient strategy of harm reduction, and then a number of MMT programs globally were implemented to reduce risk of spread of HIV/AIDS among IDUs.

After countless political and medical debates, eight MMT clinic trial sites in five pilot provinces were initiated in March, 2004 in China. Clinic coverage and the number of people receiving treatments has rapidly increased year by year. By the end of 2012, there were a total of 756 MMT clinics across 28 Chinese provinces (including districts and cities). The total number of drug addicts who had received treatment was 384,000, and 208,000 people were currently receiving treatment (China Narcotics Control Report 2013, Narcotics Control Bureau of the Ministry of Public Security, 2013, at HTTP://WWW.MPS.GOV.CN). The rapid scaling up of MMT programs in China has reduced drug use and spread of HIV infection among IDUs. However, this rapid progress has also brought many special challenges in terms of initiation, implementation, and evaluation of MMT for policy makers, program managers, program staff and researchers at both the national and local levels. For example, high dropout rates and low retention rates are still a major problem in most MMT clinics; also there is a large variation in the numbers of patients in individual MMT clinics (Yin, et al., 2010; J. Li, et al., 2013). A number of systematic evaluations on the effectiveness of MMT programs have already been conducted in China (Ruan, et al., 2005; Peng, et al., 2007; Zhang, et al., 2008). However, these evaluation studies only addressed either the associated factors with implementation of MMT

programs at the individual or institutional levels. To address these problems, this study will evaluate the effectiveness of MMT programs and describe the associated factors from both the individual and institutional levels. The situation of the rapid scaling up will be addressed throughout the study.

3. Objective of the Study

Since the 8 pilot MMT clinics in 5 pilot provinces were initiated in March 2004 in China, the MMT program has rapidly scaled up. As described above, the MMT program is still facing a number of challenges in terms of initiation, implementation and evaluation. The overall objective of this proposed study is to evaluate the effectiveness of the MMT program in China. For reasons of practicality, we decided to restrict the on-site data collection to four MMT clinics in Yunnan Province that is one of 5 pilot provinces with the most serious injection drug abuse and HIV/AIDS problems. To achieve the overall goal, more specific objectives have been addressed:

1) To document the retention rate of drug users in the MMT program;

2) To document the reduction of drug use during the MMT program;

3) To identify the patient baseline individual characters and structural factors associated with patients' retention and reduction of drug use in the MMT clinics;

4) To explore the reasons for drug users leaving the MMT program;

5) To explore the addiction status and the relapse of injection drug use after leaving MMT program among drug users who leave the MMT program;

6) To investigate characteristics of drug users who remain in the MMT program;

and 7) To investigate the associated structural factors of MMT clinics and staff in MMT program.

4. Study Site

The study was conducted in Yunnan provinces. Yunnan Province is located in the most southwestern part of China, it is one of the most remote and poorest provinces in China. At the end of 2014, the population in Yunnan was 46.65 million and the population natural growth rate was 12.37 per 1000 per year. Yunnan is noted for a very high level of ethnic diversity. There are 51 ethnic groups in Yunnan, about one third of the population is ethnic minorities, while two thirds are the majority, Han. More than 70% of the people are agricultural labors. Administratively, there are 16 prefectures, under which there are 129 counties (Yunnan Statistics Bureau, 2014).

Yunnan is one of the most HIV/AIDS affected provinces in China. By the end of 2014, Yunnan had recorded 79,915 cases of HIV infection among whom 29,625 had progressed to AIDS. Since Yunnan province is situated along the drug trafficking routes channeling heroin into China from Southeast Asia's opium-producing ''Golden Triangle'' region, drug use is still one of the major risk factors for the HIV/AIDS epidemic. In those prefectures which are along the drug trafficking routes, such as Dehong, Dali, Chuxiong, Wenshang, Lincang, Hongheand the municipality of Kunming have higher prevalence of HIV/AIDS, making up around 70% of all reported cases in Yunnan by the end of 2014 (Yunnan Bureau of HIV/AIDS Prevention and Control, 2014). Furthermore, HIV/AIDS disproportionately impacts ethnic minorities, especially drug users. Surveillance data show that among IDUs, the Jingpo, Dai, and Yi minorities have the highest prevalence rates (after controlling for different levels of education across ethnicities.). Heroin injections in these populations are thought to be associated with these communities' long exposure to heroin through their proximity to the Golden Triangle region. This exposure,

coupled with limited access to health care and lower public health awareness, has fueled the spread of HIV within these subpopulations.

Given the serious drug use and HIV/AIDS epidemic in Yunnan, Yunnan was selected as one of the 5 pilot provinces for MMT programs. The first MMT clinic was set up in Gejiu city of Honghe prefecture in April 14th, 2004. As of June of 2014, Yunnan province had 68 MMT clinics and 92 methadone-dispensaries treating accumulatively more than 41,800 patients. 20,178 patients were in the program in 2014 (China CDC, 2014).

Kunming City, Dali prefecture, Honghe prefecture and Dehong Prefecture were selected as the study sites for this study. The reasons for selecting these four city/prefectures are: 1) these city/prefectures have the greatest concentration of heroin addicts in Yunnan Province. 2) HIV/AIDS prevalence among the IDUs is quite high in these city/prefectures. 3) These city/prefectures are representative of Yunnan in terms of social-economic situation. Kunming city is the capital of Yunnan, it represents the high economic development area of Yunnan. Dali and Dehong prefectures represent the average level of Yunnan. Honghe prefecture is at the low development level of Yunnan. Dali, Dehong and Honghe prefecture have a high level of ethnic diversity. 4) The four city/prefectures initiated their MMT clinics in 2004 and 2005. There are 13, 7, 12 and 8 MMT clinics in Kunming, Dali, Dehong and Honghe respectively by the end of 2013. The number of MMT clinics in the four city/prefectures account for around 60% (40/68) of MMT clinics in Yunnan. Therefore, a study of MMT program effectiveness in these four city/prefectures should provide an overview of the situation in Yunnan.

According to the selected protocol, one clinic was selected in each of the four selected city/prefectures. The basic characteristics of the 4 selected MMT clinics are given in the table 1-1.

Table 1-1 the basic characteristics of the 4 selected MMT clinics

	Kunming	Dehong	Dali	Honghe
Duration of operation	9 years	9 years	7 years	9 years
Current client number	640	430	550	440
Retention Rate (reported)	74.5%	70.0%	81.5%	79.0%
Affiliation	YIDA	CDC	CDC	CDC
Operating hours	8	8+	8	8+
Number of Staff	7	6	5	7
Services provide				
Psychological counseling	Y	Y	Y	Y
HIV/AIDS-related education	Y	Y	Y	Y
Group counseling	N	N	N	N
Counseling to family members	N	N	N	N
Employment Skills training and consultation	N	N	N	N
Payments for MMT (YUAN/DAY)	10	0	0	10
Subjective Assessment*	Good	Average	Average	Poor

* Note: We invited three officers of Yunnan MMT program to rank the four selected clinics subjectively. The criteria of assessment include: human resources, quality of services and retention rate. They categorized the four clinics into three groups (i.e. good, average and poor) through the full discussion.

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Chapter II Research Article 1

Service Providers and Clients' Perceived Factors Associated with Retention of Methadone Maintenance Treatment in Yunnan, China:

A Qualitative Study

ABSTRACT

Background: China introduced the Methadone Maintenance Treatment (MMT) to cope with the rapidly rising number of heroin users and related increases in the prevalence of HIV for a decade. Relatively low retention rate of MMT has been a concern for China's MMT program ever since the first pilot was initiated. The objective of this study was to explore the perceived facilitators and barrier associated with retention of MMT from the perspectives of clients and service providers at the new phase of MMT program in Yunnan, China.

Methods: Anonymous in-depth interviews were conducted with 13 clients of MMT clinics, 18 dropouts from MMT, meanwhile, 8 officers and 19 services providers of MMT program completed in-depth interview in Yunnan, China. Qualitative data were code and analyzed using ATLAS.ti.

Results: Over ten years, MMT program has already gradually accepted by societies including the

department of public security. Fear of arresting in and/or around MMT clinics was not a major barrier for accessing and remaining in. Service providers believed they are able to prescribe appropriate dosage of methadone to clients. However, that methadone dose and dose-adjustment are still problem at the maintenance phase because of poor provider-client communication, misunderstanding and inappropriate perceptions of the MMT treatment goals and side effect. The major individual-level barriers are: 1) Lack of knowledge of MMT treatment goal, side effects and long-term treatment process; 2) fear of addiction of methadone and opposition to utilize MMT on a long-term basis; 3) low accessibility of comprehensive services such as psychological counseling and side effect diagnosis and treatment; 4) economic burden; 5) concurrent use of heroin and methadone due to temptation of drug user friends and lack of family support, and 6) the drug-related stigma and discrimination in societies. The major structural and institutional barriers are: 1) high turnover rate and shortage of human resources in MMT clinic due to financial difficulties and lack of institutional support; 2) lack of related skills such as communication and counseling skills because of insufficient professional trainings; 3) logistical barriers such as the inflexible service hours, location and transportation and take away dose of methadone is restricted. 4) MMT services diversity and, 5) affordability of MMT. Furthermore, this study showed that individual barriers and structural barriers often interact synergistically and make the situation more complicated and difficult.

Conclusions: Individual and institutional interacted each other, which causes relatively low retention rate of Chinas' MMT program. Currently, the quality of service in MMT is still at the low level. Improving the quality of comprehensive services should set up as the first priority of China's MMT program after ten-year rapid scaling up.

Key words: Methadone Maintenance Treatment, Yunnan, China, retention, qualitative, drug users, HIV/AIDS

1. Introduction

Methadone Maintenance Treatment (MMT) is one of the effective treatments for opiate addiction (WHO, 2004). Numerous studies provided clear evidence that MMT could help prevent the speared of HIV by reducing injecting drug user's engagement in HIV risk behaviors, particularly needle-use and sexual risks (Ball et al, 1988; Kleber, 2008; Ruan, et al, 2005; Sorensen, et al. 2000; Sullivan, et al, 2014). In acknowledgment of this evidence, in 2004 the Chinese government introduced MMT in response to the rapidly rising number of heroin users and related increases in the prevalence of HIV (Sullivan & Wu, 2007). Eight pilot MMT clinics were established in five pilot provinces: Guangxi, Guizhou, Sichuan, Yunnan and Zhejiang. After one year pilot program, the effectiveness of MMT has been documented. Reduction in heroin use, drug-related crime and increase in employment and healthy family relationship among those who received MMT are proved in eight pilot MMT clinics (Pang et al., 2007). Therefore, the MMT program was scaled up rapidly. As of August 2014, there were a total of 765 MMT clinics spread across 28 Chinese provinces (including districts and cities). The total number of drug addicts who had received treatment was 410,000, and 210,000 people were currently receiving treatment (WHO, 2014). The MMT program in China is believed to have made a considerable impact on drug use and HIV infection among drug users in the country (Yin, et al., 2010). Dr Bernhard Schwartländer, WHO Representative in China, commended that "the rapid nationwide scale-up of China's MMT program is the cornerstone of the response to the HIV epidemic among IDUs."(WHO, 2014). However, there remain a wide range of challenges and gaps that need to be addressed to achieve the overall goal of universal access (Yin, et al., 2010). Among these challenges and gaps, relatively low retention rate of MMT has been a concern for China's MMT program ever since the first pilot was initiated. Sullivan and her colleagues conducted a study to

examined nation-wide data from China to assess client outcomes after 6-months of methadone treatment. They reported that in total 107,740 clients enrolled, and only 55,214 (51%) clients at 512 clinics were still actively in treatment 6 months after enrolment (Sullivan, et al., 2014). A number of studies have been conducted to explore the major factors associated with high dropout rate of MMT in China. Low dosage, poor quality of services, lack of additional services provide to clients, ambiguous goal of MMT, low accessibility to reach the majority of drug users due to political, financial, logistical and administrative reasons, poor provider-client interaction and relationship, as well as lack of supports from community and family to help clients establish new social networks and discourage socialization with their drug-using friends (Liu, et al., 2008; Li, et al., Lin, et al., 2011a; Lin, et al., 2011b; Sullivan, et al. 2014; Wu, et al., 2012; Cao, et al. 2014.).

Yunnan province, one of the most remote and poorest provinces in China, had a population of over 46 million and one third of the population is ethnic minorities (Yunnan Statistics Bureau, 2014). Yunnan is one of the most HIV/AIDS affected provinces in China. By the end of 2014, Yunnan had recorded 79,915 cases of HIV infection among whom 29,625 had progressed to AIDS. Since Yunnan province is situated along the drug trafficking routes channeling heroin into China from Southeast Asia's opium-producing ''Golden Triangle'' region, drug use is still one of the major risk factors for the HIV/AIDS epidemic. Given the serious drug use and HIV/AIDS epidemic in Yunnan, Yunnan was selected as one of the 5 pilot provinces for MMT programs. The first MMT clinic was set up in Gejiu city of Honghe prefecture in April 14th, 2004. As of June of 2014, Yunnan province had 68 MMT clinics and 92 methadone-dispensaries treating

accumulatively more than 41,800 patients. 20,178 patients were in the program in 2014 (China CDC, 2014).

Several studies have already been conducted to determinate facilitators and barriers associated with retention of MMT in Yunnan (Wu, et al., 2012; Che, et al. 2010; Jiang, et al., 2014.). However, these previous studies were carried out during the period from 2007 to 2010, while this period also was referred as "Rapid expansion phase"(Yin, et al., 2010.). From 2010 to present, Yunnan's MMT program went into the slowdown phase. This phase also was referred as "the improving quality of care stage" because improving the quality of care was set as the first priority of China's MMT program. (Yunnan Bureau of HIV/AIDS Prevention and Control, 2014). As of December 2008, 67 MMT clinics had been established in Yunnan, however only one new MMT clinic was approved since 2010 (China CDC, 2014). Therefore, the aim of our study was to explore the perceived facilitators and barrier associated with retention of MMT from the perspectives of clients and service providers at the new phase of MMT program in Yunnan.

2. Methods

In-depth interviews with officers/managers of MMT programs, current clients and health staff members in the MMT clinics were carried out to obtain subjective information about the situation and status of clients and MMT clinics in Yunnan. In addition, Clients who have left the MMT program were contacted by MMT staff, who invited them for qualitative interviews to determine the reasons why they left the program and their current addiction status and relapse of injection drug use after leaving the MMT program.

2.1 In-depth interviews of officers of MMT programs and managers of MMT clinics

Four officers of MMT programs at the city/prefecture levels and 5 managers of the MMT programs in the four selected MMT clinics underwent in-depth interviews. Information about the following were collected:

1) Methadone treatment policies and regulations

2) Treatment location and facilities

3) General situation of MMT clinic and working procedures, such as how was initial dosage and maintenance dosage, medical services provided and how they deal with side effects etc.

4) Training received by MMT staff

5) Perceptions of provider-client relationships

6) The difficulties, suggestions and comments about the function of their MMT program

7) Perceived reasons for drop outs

8) Monitoring and evaluation of MMT program

9) Very general work history and professional background and training information.

2.2 In-depth interviews of staff members in MMT clinics

The study team also personally interviewed 19 staff members of the four MMT clinics. The general information in terms of MMT program, such as methadone treatment policies, working procedures, provider-patient relationship, professional trainings, as well as the difficulties and challenges of the MMT program, was explored by interviews.

2.3 In-depth interviews of clients of MMT clinics

Through the posting flyers, 13 MMT clients were recruited and interviewed. The following information were collected through the interviews:

1) Basic demographic background.

2) History of drug use, detoxification and Concurrent use of heroin (change-use-change) since entering MMT.

3) Experience with MMT.

4) Perceptions of MMT services, doctor-client and staff-client relationships, and perceived stigma/discrimination.

5) The barriers, difficulties, suggestions and comments about MMT programs, as well as operation of their MMT clinic.

6) Family and social support

2.4 In-depth interviews of MMT dropouts

Within the six-month period between baseline and follow-up (March to September 2014), the study team conducted 18 in-depth interviews of MMT dropouts from the four selected MMT clinics. As the same, basic demographic background, history of drug use, detoxification and experience with MMT, perceptions of MMC service, doctor/staff-client relationships and perceived stigma were collected. Most important, the study team focused on collecting the information in terms of the reasons for leaving the MMT program and factors that would encourage resuming MMT.

All the interviews were held in a private office in the MMT clinic or a quiet location of participants' choice, and completed within two hours. The interviews were audio-recorded with

the permission of the participants. The study team also took notes if participants unwilling to be audio-recorded.

Officers, managers, and staff members of the MMT clinics who completed an interview were given a small gift, such as stationary or a box of candy to thank them for their time (worth app. 40 yuan; $6 US). The participant is currently attending MMT, they were given a phone card worth 40 Yuan for completing the interview, to compensate them. Drop-out participants were reimbursed for their travel expenses (40 Yuan; app $6 US) to and from the interview appointment (at the MMT clinic or to a location of their choice). In addition, each was given a small gift, such as a box of candy or toiletries, to thank them for their time (app. 40 Yuan/$6 US).

Assistants transcribed field notes and audio files word-by-word immediately following the interviews. ATLAS.ti v5.0 software in Chinese (http://www.atlasti.com/zh-hans/) was used in the qualitative data analysis process. All the transcripts were be recorded and analyzed in Chinese, only selected quotations were translated into English in the final dissertation. A set of basic rules for transcription was developed to ensure that they are followed consistently. The study investigator reviewed several transcriptions of the interview to develop a preliminary codebook. Then the preliminary codebook was revised as more data are collected. In this way, the codes that were grounded from the data will be developed. The codes were used to retrieve and organize the data segments into categories. After all the transcriptions have been coded, a matrix was developed to display identified categories by groups of respondents. The answers to each question were summed up in several main points. Once the matrix of codes and

corresponding quotations were built, themes shown in the matrix were summarized and examined by making comparisons and contrasts to facilitate interpretation and conclusion of the data. Typical and informative answers were quoted in the final report.

3. Results

The study team recruited 13 clients of MMT clinics and conducted in-depth interviews. Within the six-month period between baseline and follow-up (March to September 2014), the study team conducted 18 in-depth interviews of MMT dropouts from the four selected MMT clinics. Meanwhile, 4 officers of MMT programs at the city/prefecture levels and 5 managers of the MMT programs in the four selected MMT clinics completed in-depth interviews. The study team also personally interviewed 19 staff members of the four MMT clinics. For the demographic characteristics of the interviewees please see table 2-1.

3.1 Police approval of MMT enrollment is a barrier to initiating and maintaining MMT

Both the providers and clients complained that the police intervention in MMT enrollment served as a big deterrent for initiating and maintaining MMT. One of the MMT program officers introduced the MMT application procedure to the PI:

"*Drug users (some clinics even required to have local residency) apply for MMT, take a physical examination, submit relevant application documents to MMT clinics, MMT clinics submit all documents to drug control offices in local public security departments for approval, and then applicants accepted into MMT."* Almost all the interviewed managers complained that: "*without the approval from public security department, we are not allowed to enroll the drug users in MMT program*", "*They (policemen) are the real leaders of the MMT program.* "

Get an approval from local police departments means drug user will be registered formally in a real-time drug user monitoring system. However, all the MMT clients and dropouts who were interviewed stated that no one wants to be registered in the monitoring system because they will become targets of the police and will get irregular mandatory testing by public security department. Below are some examples given by interviewees:

"*One day my girlfriend and I went back to her parents' home by train. As you know, I need to show national ID card for purchasing the ticket. At begin, everything was okay, I thought that I was lucky this time. But the terrible thing was happened when we got down from train and walk out of the train station. I saw that there were three policemen standing at the exit of the train station. They stopped me and brought me to do the urine testing in the local police station, I realized that they located me through "the drug users system" when I showed the ID card. The worst thing is that my girlfriend's family saw this and was much scared because they do not know I was a drug user. After that trip, my girlfriend had to broken with me. (Male, 38 years old, high school gradate, unmarried, currently using MMT)*"

"I heard that your profile have never erased from the system although you had already get rid of the drug. (Male, 27 years old, college graduated, clinic staff from a MMT clinic) "

"Easing travel restrictions for registered people who use drugs—to reduce the extent of police monitoring and 'supervision', which includes random urine testing." One manager of the MMT clinic suggested that.

3.2 Financial difficulties and economic burden

The grant from central and local government to subsidize the MMT clinics at varying degrees for the operations includes: staff salary, utilities, room rent and the fee for methadone. Clients pay 2~10 RMB Yuan per day to partially cover the expenditure of methadone's transportation and storage. However, many of the officers, managers and service providers complained that the financial support were not sufficient to cover the operation expenditures, and the financial difficulties have became even worse with the increasing of CPI (Consumer Price Index). As a consequence, the comprehensive services for clients and the opportunities for service providers cannot be implemented. On the other hand, some of clients also stated that payment for MMT (10 RMB Yuan per day) is unaffordable without the financial support from their families. For those clients who are living far from the clinics, the daily transportation fees are also a financial burden. To solve this problem, some of the local governments, such as Dali, Chuxiong and Wenshang, offered partial reimbursement to patients for their daily payment through involving the MMT program into the New Collective Medical Scheme (NCMS).

"The grant from upper level (central and local governments) is only enough to cover the staff salary and the utilities. I planed to hire one more contract nurse since three years ago, but no money; I planed to organize a mental health education lecture for the clients, but no money; I had many ideas and plan to improve quality of our services but they cannot be implemented because of financial difficulties. It disturbed me a lot, I sometimes feel disappoint and think of quit from the clinic (Male, 33 years old, college graduated, manager of MMT clinic in Kunming).

"I do not have income. 300 Yuan per month is a big sum of money to me. Peoples do not trust drug users, they do not employ a person who have a drug abuse history. You've never understood how difficult to find a job. " (Male, 44 years old, junior high school gradate, married, currently using MMT)

"We do not need to pay money for the pink drinking (methadone), it is free, New Collective Medical Scheme cover the payment since year 2012. However, I have to spend 10 Yuan for taking bus every day. My home is too far from here (MMT clinic). My old mom gives me money for this, she has to work at this kind of age, and she is too poor." (Male, 39 years old, junior high school gradate, unmarried, currently using MMT)

3.3 The different understanding of length of MMT between service providers and clients

Service providers believed that methadone maintenance is a corrective but not a curative treatment for heroin addiction, it need administered over a prolonged period of time (can be indefinite). All interviewed service providers encourage clients to stay in methadone program as long as they can. However, about 70% of the interviewed clients complained that it is impossible to adhere to the MMT and visit the clinic every day. Moreover some of the clients fear of the serious side effect due to long-term methadone treatment. Clients' family members also do not understand why MMT need so long time treatment, as well as worried about the long-term side effect. The inappropriate perception of methadone is one of the reasons for dropping out of MMT.

"I knew MMT is like the treatment for high blood pressure, the patient need to take the medicine for long time, even for lifetime. So I told my patients that intense mental preparation (long-term treatment) is a critical success factor of MMT. But it is easier said than done! Many patients complained that they lost heart and cannot insisted anymore. I think the logistical barriers also make this long-term treatment even tougher." (Male, 43 years old, college graduated, clinic staff from a MMT clinic.)

"I think it (MMT) must damage my liver and kidney. Drinking it every day, the poison will accumulate in my body. A major function of liver is detoxication, so it (methadone) is harmful to liver. I have already take the methadone for more than 2 years, I need to reduce the intake of methadone, then cut out it." (Female, 33 years old, junior high school gradate, married, currently using MMT)

"My wife complained to me that it (MMT) just likes eating, you have to eat everyday. When is the end?" (Male, 42 years old, high school gradate, married, currently using MMT)

"My dad asked me 'drinking it everyday, what is difference with using heroin?'"(Male, 42 years old, high school gradate, married, currently using MMT)

3.4 Logistical barriers still influenced the accessibility and retention of MMT, but there are some positive changes from bottom to up.

Clients have to attend MMT clinics on a daily basis because the take away dose of methadone is not accessible in Yunnan. Furthermore, MMT is a long-term maintenance therapy that increases

the logistical difficulties for many MMT clients. New clients complained daily commute time to the clinic is too long. Long commute times were often cited as a reason associated with the low treatment retention.

"It took me around 10 minutes to go to the clinic before I move to the current place. But I have to spend at least two hours to go and back from the clinic now. It takes another half hour for drinking methadone (clinic staff need to fill the form, prescribing and recoding the dose). I spent whole morning for MMT everyday, so I have no chance to find a job. " (Male, 44 years old, senior high school gradate, married, currently using MMT)

"I am pregnant for 6 months now. I still can come to clinic for drinking methadone now although my body is becoming heavier and heavier. Now I am most worried about how can I get methadone when I give birth in hospital. I have talked this problem with doctor here; she (doctor) just said that she would report my case to their leader but no response yet so far. My friend had the same experience couple years ago, her husband had to seek drug (heroin) instead of methadone when she was in hospital for delivery."

We asked the doctor about how to deal with this problem, the doctor answered that "*I cannot tell you more about what to do but we will try to solve the problem in a 'smart' way. As you knew, prescribed methadone is not allowed to bring out the clinic according to the national regulations*. "

Both service providers and some of clients stated that the issue in terms of only being able to

access methadone doses at designated clinics must be addressed. The managers and service providers of MMT program had started to develop strategies to challenge and change the strict regulation. An officer of MMT program at provincial level shared a true story with us:

" A national level workshop was held in Kunming years ago. The objective of the workshop was about harm reduction and drug policy advocacy. Participants had very intense discussion on the strict regulation of access to methadone and taking home doses of methadone in the first day of the workshop. 7 methadone clients were invited to participate in the workshop and they would continuously participate the discussion in second day. An expert made a suggestion- sending methadone doses to the workshop venue so that the 7 clients can participate in the workshop and did not have to waste time and money to travel to the MMT clinic for their dosage. The manager of the clinic was silent. Finally, with the help of Yunnan Institute of Drug Abuse, the local MMT clinic agreed to send methadone doses to the workshop venue. Every participant was very exciting. I still remembered the facilitator's conclusion: This gave us all one more reason to hope that the controls over access to methadone would gradually ease in the future. I believe the regulations will be change soon."

3.5 Stigma and discrimination

Very few interviewed clients stated that there are stigma or discrimination from service providers at the MMT clinics. However, many of interviewed clients mentioned that stigma and discrimination from society are very serious because peoples knew the "patient" in MMT clinic was a drug abuser. The same stigmatization is also from employers and coworkers. The

identification of drug addict would result in losing the job. Two drug abusers shared their experiences with us:

"Nobody respect drug abuser, they call us 'ghost' or 'No.4 guy'. One day, I went to the store next to the clinic to buy cigarettes. The shopkeeper did not hand pick the note I paid, but let me directly put the money in a box. I could feel his fear of being infected by me; he thought I am an AIDS patient. "" (Male, 41 years old, junior high school gradate, married, currently using MMT)

"My co-workers happened to see I drank methadone here. He realized that I was drug user. I begged him not to tell other person, and he promised. But soon I was fired. I do not hate him or our boss. If I were he, I would do the same thing. I would not employ a drug addict. (Male, 42 years old, collage graduated, single, currently using MMT)

3.6 Side effect and fear of addiction

The service providers and clients have different perception of the side effects. Many service providers interviewed in the study believed that side effects of methadone are rare and most of them are slight. Physical discomfort caused by side effects is normal, and the patient supposed should be able to overcome and do not need to give a treatment. However, Users believed that methadone is also a kind of drug. It will certainly lead to a variety of side effects. The most common side effects what they reported were fatigue, night sweating, tachycardia, dizziness, headache and anorexia. These symptoms are sometimes very serious, intolerable. When they turn to doctors, often was told it was normal, no need for any treatment. They had to buy the

medicines in pharmacy to reduce their discomfort and symptoms. Few users also reported that their liver function is abnormal. Side effects were cited as one of the reasons for dropping out of the MMT, however, no one mentioned the side effects is a reason of making them dropout from MMT (We interviewed 18 dropouts).

The in-depth interviews show that both MMT clients and service providers understand long-term use of methadone may result in methadone addiction. However, the two groups had different perceptions of methadone addiction and methadone's withdrawal symptoms. Service providers perceived that compared to heroin addiction, methadone addiction is considered the lesser of two evils. The side effects and consequences associated with methadone addiction are much less severe and less dangerous. Meanwhile, methadone's withdrawal symptoms are very unpleasant, however they are not as extreme as heroin's. The service staff of MMT clinic has very little knowledge and skills of dealing with methadone's withdrawal symptoms because majority of withdrawal cases happened in jail, voluntary detoxification centers or home (self-prescribed strategies).

"Yes. Long-term use of methadone may cause drug dependence. If client does not timely take the methadone, she/he will have uncomfortable symptoms, such as fatigue, irritability, anxiety, aches and discomfort and so on, but the symptoms are not serious and bearable." (Male, 43 years old, college graduated, clinic staff from a MMT clinic in Kunming.)

"Although methadone will produce certain drug dependence, this dependence is mainly dependent on individual health status and tolerance. Withdrawing from the methadone does not

make significant psychological dependence problems."(Male, 48 years old, college diploma, clinic staff from a MMT clinic.)

"Here is methadone clinic, so I have not seen the patient with methadone withdrawal symptoms. I learned some very simple theoretical knowledge from the guidebook and training course. There is no opportunity to practice."(Female, 27 years old, nurse school diploma, clinic staff from a MMT clinic.)

Most of the clients of MMT treatment believed that Methadone is very addictive and if the addict does not take a dose of methadone timely, the addict will experience very painful and insufferable withdrawals. We interviewed 18 dropouts of MMT program, only one dropouts from MMT treatment reported that he had ever experienced methadone addiction and withdrawing. His withdrawal symptoms were as same as those associated with the use of heroin.

"I have had methadone withdrawal symptoms and experiences. It was a very bad process, which last at least one month. The worst part was appearing at the beginning of the fourth week after withdrawing. Bones acutely painful! The spirit was high tension! Sleepless! Indescribable discomfort. I felt methadone's withdrawal symptoms were as extreme as heroin's."(Male, 23 years old, unmarried, dropouts of MMT.)

3.7 Provider-client relationship

A number of studies have reported that provider-client's relationship could be positively associated with MMT treatment outcomes. This study respectively interviewed service providers

and clients to understand about how they perceived the provider-patient relationship in MMT clinics. Most of the service providers and clients felt that the provider-client's relationship was reasonable in the MMT clinics where they work or use. Unlike patients in hospital or community health center, MMT clients come to clinics everyday for taking the methadone. The providers also interact simply with clients. As a consequence the brief and procedural nature of the provider-client interaction in MMT clinics may become a barrier to set up a sound provider-client's relationship, thereby affecting the MMT outcomes, even cause clients' dropping out. The following were partial statements from the in-depth interviews.

"I think it is a good doctor-patient relationship in our clinic. Clients come to clinic for treatment, we almost meet each other everyday. But there is also a problem. There are only very simple exchange and conversation between us, like asking him / her how was feeling today and so on. So we are not actually close." (Female, 43 years old, university, clinic staff from a MMT clinic.)

"I have had MMT treatment at the clinic for more than 2 years. I knew every doctors and nurses here, they are all very busy but nice. I dropped out from the treatment (MMT) half year ago and this is my second time. They treated me well. "(Male, 41 years old, junior high school, currently using MMT)

"They are too busy, like robots. So we have almost no chance to talk. There are five doctors (service providers) here, I only knew two of them. I come here everyday, drinking drugs and left, without much communication."(Male, 47 years old, high school, currently using MMT)

Several clients complained that some service providers are not patient. When clients stated the symptoms of side effect to the providers, some of them are unwilling to listen what the client talking, just answer them briefly. Two current MMT clients (from different clinics) stated that the service providers treated them unfair because they were suspected using heroin as their urine morphine tests were positive.

"I used heroin during the MMT treatment and my urine test was positive. The male doctor blamed me that 'if you do not want to participate in this treatment just leave. There are a lot of people on the waiting list.' After that, he rarely talks to me. I am afraid I will be kick out from the clinic."(Male, 45 years old, high school, currently using MMT)

"She intentionally let me waiting for long time for taking methadone, because I used heroin several times during the MMT treatment. I was so resentful and helpless, then I stopped the treatment."(Female, 29 years old, junior high school, dropout of MMT)

The leading officer of the MMT program in Yunnan province indicated that the provider-client interaction and relationship become a most important determinant to retention of MMT and other outcomes of MMT in Yunnan. He stated that:

"China's MMT program has expanded from 8 clinics to 765 clinics cumulatively in 10 years. As the same as the whole China, the number of MMT clinics has scaled up from 1 clinic to 68 clinics in 10 years, severing more than 40,000 opiate users cumulatively since the first clinic opened in April 2004. The low retention of MMT is the biggest problem of MMT program in both

pilot phase and present stage. At the beginning phase, from 2004 to 2006, Yunnan has 29 MMT clinics and served around 3000 clients. Inappropriately low dosage was the leading cause of the low retention rate at that time. Through 10 years program implementation, service providers has mastered the skills in terms of methadone dosage, compliance and retention. So I believed that the dosage is no longer a leading cause of the high dropout rates in MMT, but the root cause was thought to be that the not good provider-client interaction and relationship. We need more effective training on this. " (Male, 57 years old, MD, officer of MMT program)

3.8 Methadone dosage: the service providers and clients' perceptions

Appropriated methadone dosage was cited as a determinant of the MMT retention in a number of studies. The MMT services staff stated that there is no dose limit on prescriptions now, so they are able to prescribe appropriated methadone dosage to clients based on observations of clients' physical and psychological situations, or abstinence symptoms now. However, the dosage could not exceed 50mg per day before 2007 according to the National MMT practice rules. Service providers believed that the high dropout rate was associated with low dosage methadone prescription at that time.

"I normally prescribe a starting dose of up to 30mg or 40mg, as you know, by government regulation, the first dose of methadone cannot exceed 40 mg. I will add 5 mg or 10 mg everyday for control the abstinence symptoms. I will stop increasing the dosage if client feels good. Normally the methadone induction process lasts for 15days to 20 days, some of them will last for more than one month. I got the relevant knowledge from training courses given by YIDA (Yunnan Institute for Drug Abuse), and accumulated the experiences from the routine practices.

I have already worked in this field for ten years." (Female, 41 years old, medical collage graduated, doctor in MMT clinic)

"I prescribe the methadone dosage according to the clients feeling. If client feels comfortable and without obvious abstinence symptoms, and she/he does not have the feeling like 'high' or 'floating'; that indicated the dosage is appropriated. The appropriate dosage is on the individual basis, 10 ml may be sufficient for someone, but someone may need 150ml. (Male, 39 years old, medical collage graduated, doctor in MMT clinic)

In the interviews, some of the service providers indicated that the clients often do not tell them the real history of drug abusing, so that the prescription of the methadone dosage is interfered. The service providers suggested that clinic need a professional staff, such as social worker, to collect the reliable information about the drug abusing.

"They (clients) do not tell me the truth (using the drug). I can understand why they lied to me. One of my clients came to my MMT clinic accompanied with his wife. When I asked about the information of drug abuse before he came to me, he told me that he just used the heroin by nasal method without injection, and just used one time per day. A few days ago, I recognized that he lied to me because of his wife's pressure. I knew many of the clients here still used heroin during their treatment, but they told me nothing. Given this situation, I seldom reduce the dosage although my clients want to reduce. "(Male, 43 years old, medical university graduated, doctor in MMT clinic)

"The clients lied to me, because it is kind of self-protection. They had various stories to tell you, you had to very careful. "(Female, 33 years old, medical university graduated, doctor in MMT clinic)

Around two thirds of interviewed clients thought the dosage was enough, and the doctor will change (increase) the dosage when they asked for. Some of the clients still complained that the dosage prescribed by service providers is not sufficient to control their abstinence symptoms. Some of the clients would negotiate with providers to reduce the dosage if they used heroin when they were treating in MMT clinic.

"The doctor here is nice, he will change the dosage if you ask. For my experience, the doctor here is willing to increase the dosage as your request. But he won't decease the dosage easily, he will observed you and make decision. Yes, increasing dosage is easier." (Male, 47 years old, high school graduated, current client in MMT.)

"The female doctor only gave me 30 ml (mg) methadone per day. I could not bear it (abstinence symptoms) so I had to find 'drug' to save myself, then I left the treatment. (Male, 33 years old, high school graduated, dropouts from MMT.)

Interviews showed that some clients felt ashamed if they take high dose of methadone, because they perceived that methadone is another kind of drug with lower negative impact. Furthermore, they also believed that the higher dose methadone intake the more serious side effects, and more difficult to successfully leave MMT treatment in the future.

"At the beginning of the treatment, doctor gave me 40 ml and increased the dosage everyday. The maximum dose I have ever drunk is 80 ml. My dose is 35 ml (mg) now. I will reduce my dose to 20 ml in the end of this year (2014). My friend told me if I could decrease (dose) to 20 ml that means I will be able to come off from methadone. " (Male, 42 years old, college graduated, current client in MMT.)

"My dose is 120 ml, it is too high, isn't it? I knew such high dose is not good for me, but I cannot reduce it. I tried to decrease it to 100ml but cannot bear. The old saying- medicine always has toxicity, methadone's toxicity is higher than common medicine. I am afraid such high dose will kill me." (Male, 48 years old, high school graduated, current client in MMT.)

3.9 Lack of professional training for service providers and Lack of comprehensive services for clients

The national MMT program has been expending dramatically for last decade. There were 765 MMT clinics in China by the end of 2013. This great increase brought couples problems such as inappropriately low methadone doses, low retention rate, lack of comprehensive services and little professional training for service provider especially local providers at county level. To meet the enormous demand for trained providers, China's National MMT Program redeveloped and conducted numbers of training programs for individual providers and their trainers since 2008. Due to limited financial support and lack of training resources, the professional training for service providers are still insufficient. Additionally, the clients' needs and demands towards the comprehensive services have been increasing with the development of the MMT program. These increasing requested more trained professional providers. All the interviewed service providers

stated that they need more professional trainings to refresh their knowledge and to solve the new-coming questions they faced during providing the treatment in MMT clinics. The most needed trainings include: counseling skills, motivational interviewing skills, management of poly-drug abuse (especially using club drug) , sexual and reproductive health needs among female patients and management of severe side effect.

"I am working in this clinic for more than 10 years, but I just attend one training course in Kunming couple years ago. There are many problems that I am not able to cope with. For example, I do not know how to explain why the long-term treatment is needed in MMT? In fact, I knew the pharmacology of methadone; I just do not know how to explain this in common words making the client understand. "(Male,44 years old, associated college graduate, doctor in MMT clinic).

"More and more clients use the club drug, such as ecstasy, amphetamines, dissociative anesthetic ketamine and depressants. I know nothing about these new drugs beside the terms. I want to know the protocols of dosage adjustment if the clients used the heroin and other club drug together. I really worried about overdose problem when I prescribed methadone to those clients use both heroin and club drugs. "(Male, 33 years old, college graduate, doctor in MMT clinic).

Given the financial difficulties and insufficient professional training, it is not difficult to understand why almost of all the interviewed clients complained about the lack of comprehensive services such as psychological counseling, sexual and reproductive health

education. Some of the clients stated that the vocational training and employment counseling are urgent needed.

"No. I've never attended any counseling and health education seminars. The clinic only gave me a small booklet about MMT and HIV prevention. I do not want to and cannot read it. It was too boring and difficult to me. I want to chat with doctors but they do not want to talk with me. (Male, 41 years old, junior high not graduate, divorced, currently client in MMT).

"I have some reproductive health problems. I do not believe doctor here can help me. They only know prescribing methadone. Additionally they are all male. Nurses are female, but they know nothing." (Female, 33 years old, junior high school gradate, married, currently using MMT) .

3.10 High turnover rate among service providers: low income, heavy workload, and concerned personal safety

All the interviewed officers of MMT program and manager of MMT clinic stated the high turnover rate among service providers in MMT clinic is a big challenge, which directly influences provision and outcome of methadone treatment. With regard to the major reasons of the unstable human resources, the heavy workload, low income and concerned personal safety are most frequently mentioned by respondents.

Service providers' income consists of salary and bonus. In fact the bonus is a major part of

income, which almost accounts for a half of income. The MMT clinic fully depended on the government subsidy, but the subsidy only cover the salary and utilities. In another word, the service providers only have salary but no bonus. So the service providers in MMT clinics get a considerably lower income than those who work in other hospitals. Because MMT clinics are not allowed to collect money from clients, so the only way to solve this problem is increase the government input.

"My income is too low compared to the doctor who work in the clinic. I got 2500 Yuan RMB per month. One of my former classmate in medical college, he is also working in a clinic affiliated to CDC, he receives at least 6000 yuan per month. I plan to turn over to other clinic because my income is too low to survival." (Male, 33 years old, college graduate, doctor in MMT clinic).

"I have not gotten my bonus since GF project left. GF means Global Fund. We can get 500 to 1000 yuan per month from GF project, but GF project was completed."(Male, 43 years old, vocational school graduated, doctor in MMT clinic).

The MMT clinics are open every day to provide the methadone treatment to the clients. Due to the financial difficulties, there are only 3~5 staff members in a clinic. Therefore, the service providers have to bear a heavy workload. According to the administrative regulation, a clinic must provide services to more than 200 clients. On average, a doctor writes about 50 prescriptions per day. Besides the treatment service, providers are also responsible for filling medical records, conducting psychological counseling and health education and preparing and

submitting the monthly, quarterly and annually reports. Sometimes, doctors have to deal with some unexpected events, such as negotiating with the local residents to explain the clinic is safety and not bring any problems to the community.

"One word can describe my work status- 'Give too much, get too little'. I work 10 hours a day, 7 days a week, 52 weeks a year. In addition to provide methadone treatment, I have to write a report to HIV/AIDS office of CDC monthly. In the end of year, annual report and planning have to be submitted. I am a doctor not a secretary, I hate to write those types of reports. According to a new policy, I am eligible to retire next year. I will immediately submit my retirement on my birthday (50 years old). (Female, 49 years old, nurse school graduated, doctor in MMT clinic).

The officers and managers of MMT program indicated that concern of personal safety is also a factor associate to the high turnover rate among health providers in MMT clinics.

"Our city has 13 MMT clinics, around half of clinics have providers left because of concerning personal safety. For instance, a doctor, who just graduated from medical university, handed in his resignation last month. Personal safety concerning is a major reason of his resignation, his parents also do not support he continually work here."(Male, 51 years old, college graduated, manager of MMT program).

The interviews of clinic staff showed that half of the respondents had been threatened or cursed by clients, but very few respondents believed that the clients would actually hurt them. Service

providers mentioned that the clients in MMT clinic are different from other hospitals or clinics. They are often very sensitive and irritable, but vulnerable and weak, the smart way to deal with the clients is do not take offense when the clients lost patience.

"I learned a psychological term, 'instant gratification', in a training workshop. Clients have this problem, if their need was not met immediately, they will be easy to get angry, shout at you and even attack you. For example, one day my computer crashed when I was prescribing. I let him wait for a moment because I need to restart the computer. The client immediately shout at me 'your computer does not crash but your fool brain crashed, do you need I restart your brain?' I just kept silent and pretended not to have heard anything. After a short while he calm down and say sorry to me."(Female, 49 years old, nurse school graduated, doctor in MMT clinic).

3.11 Major reasons to be treated in and dropout of MMT

All the current clients and even the dropouts stated reason to use methadone was to get rid of heroin. Some of them also mentioned that using heroin has already destroyed their life and healthy, they want to change the life. When they were questioned if they plan to use MMT for lifetime, almost all the respondents gave the negative answers. They wish to quit MMT after a period of time, but do not want to take methadone for lifetime.

The reasons of dropping out of MMT are various and complicated. However, the interviews showed that very few dropouts left MMT because a single reason, there were a number of reasons together caused the drug users giving up the treatment. Some respondents stated using

methadone couldn't give the feeling of using heroin. Some respondents also mentioned they used heroin again because of friends tempting. Two respondents stated that taking methadone on daily basis make them giving up. Nobody dropped out of MMT because of being caught by policeman. Service providers also recognized that the department of public security has been changing the strategy of drug control now, the cooperation between department of public security and health bureau has already been set up. In general, the MMT has already accepted by more and more individuals, organizations and societies with the implementing and developing of MMT program in China.

"Methadone did not work for me, it could not control my withdrawal symptoms. I thought it maybe because I used heroin too long. I used the drug for the first time when I was 16 years old. My older cousin took me going to market in Mujie (a small town in Myanmar). He won a lot of money in casino, and invited his friends and me smoking No.4 (heroin) for celebrating, then I started to use heroin. I do not think I can get rid of heroin in my life, I totally depend on it."(Male, 35 years old, married, elementary school graduated, dropouts from MMT)

"I was in MMT program for only 1 month and 10 days. Yes, 1 month and 10 days, I still can remember it. Doctor treated me very well, I drank 60 ml (mg) per day and my withdrawal symptoms are not so serious and almost disappeared. I really believed that I never again touch drug at that time. However, I used heroin in my friend's birthday party. I do not want to say more. I just could not control myself, especially when I saw my friends injected and enjoyed No.4 (heroin). "(Male, 32 years old, unmarried, high school graduated, dropouts from MMT).

"I am a mason so I moved every frequently. I used to drink methadone for 3 weeks, but I had to work in Mengsai (a small town in Myanmar) for quite a while, I cannot come to clinic everyday so I had to give up the treatment. ", "Yes, I used heroin again. As you know, 'little four' (heroin) is 'cabbage price' (very cheap) in Mengsai" (Male, 38 years old, unmarried, junior high school graduated, dropouts from MMT).

Additionally, the nearly two third of dropouts admitted that they used heroin again when they quitted from clinic.

"Yes. I do not use any drug now although I used heroin again when I dropped out from MMT."(Male, 42 years old, married, college graduated, dropouts from MMT).

4. Discussion

Since eight pilot MMT clinics were established in 2004, China's program began its rapid expansion in 2006. As of August 2014, there were 765 MMT clinics, including 29 MMT vans, operating in 28 provinces, autonomous regions and municipalities (UNAIDS, 2014). Going details of the development of China's MMT program, we can roughly divided the expansion stage into two substages: the substage of rapid expansion (2006~2009) and the substage of slowdown (2010~ present). In the first substage, the number of the MMT clinics has scaled up from 320 clinics in 2006 to 680 clinics cumulatively serving more than 240,000 clients (Lin, etc. 2011a). With the great expansion, the remarkable successes and benefit were gained, such as reducing consumption of illicit drug use and decrease the prevalence of drug-related disease especially HIV/AIDS. However, the MMT program also recognized that the rapid

implementation brought many challenges for China such as low overall program coverage, low retention rates, uneven service quality, high turnover rate of Service providers, tense provider-clients relationship and need for improved staff capacity. China MMT program therefore changed their development strategy, decelerated the expansion and paid more attentions to the improvement of quality of services. From 2009 to present, the speed of scaling up was significantly slowdown; just 85 new clinics were approved and established within 5 years in whole China.

The slowdown phase also was referred as "the improving quality of care stage" because improving the quality of care was set as the first priority of China's MMT program. (Yunnan Bureau of HIV/AIDS Prevention and Control, 2014). A same trend was observed in Yunnan MMT program. The first MMT clinic was opened in April 2004. As of December 2008, 67 MMT clinics had been established in Yunnan, however only one new MMT clinic was approved since 2010 (China CDC, 2014).

At the new stage of the MMT program in China and Yunnan, some of perceived challenges from the perspectives of clients and service providers have been changed or overcame, and some of them still are major barriers associated with low utilizations and low retention of MMT treatment.

Fear of arresting in and/or around MMT clinics were reported as major barrier for accessing and remaining in MMT by a number of previous studies. However, both service providers and clients did not reported a single case which police waited outside the MMT clinics to arrest the clients

who were concurrently using heroin in this study. Over ten years, MMT program has already gradually accepted by societies including the department of public security. More and more cooperation between the public security department and public health department was established and developed. One of the direct evidence is that information about MMT was reported in the annual report of department of drug control of ministry of public security since 2010.

This study found that police approval of MMT enrollment is still a barrier to initiating and maintaining MMT. Other studies conducted in China also reported the similar findings, MMT clinics need submitted all application documents to local police department for checking and approval (Lu, et al., 2009; Feng & Yu, 2011; Lin et al., 2011a; Mao, et al., 2011). However, in December 2014 the State Ministry of Health and Family Planning commission, Ministry of Public Security and the State Food and Drug Administration jointly issued *"The Regulation for the administration of drug maintenance therapy"* provide a legal basis for completely removing the barrier. In this regulation, the new requirements for entrance into MMT program have been relaxed to encourage greater access. For example, patients are no longer required to have a previous history of internment in a detoxification center. Patients under 18 years old, with the written consent of their guardians, can also apply for MMT. Furthermore, applicant submits the requested documents (a photocopy of ID, drug abuse history and medical examination results report) to MMT clinic for examining and approval, and the MMT clinic will inform the applicant if is eligible to participate in MMT within 5 working days. MMT clinic have full authority of approval and local public security agency no longer intervene the approval process.

Several systematic reviews have shown that retention is associated with on-site dosing and that higher rates of dropout are associated with lower doses of methadone (Bao Y., Liu Z., Epstein D, 2009; Faggiano F, Vigna-Taglianti F, Versino E, 2003; Farre M, Mas A, Torrens M, 2002; Amato L, Davoli M, Perucci AC, 2005.). A number of prospective studies conducted in Yunnan and China also revealed that high doses of methadone were associated with high retention rates (Cao X., etc. 2014; Che Y., etc. 2010; Liu E., 2008). The dosage could not exceed 50mg per day before 2007 according to the National MMT practice rules. At the pilot stage of MMT program, the service providers tended to prescribe lower dosages to clients. A prospective cohort study conducted in 2007 has reported that the average methadone dose was 38.0 mg/day, and 79.4% of participants received lower than 50 mg/day (Liu et al., 2009). With the development of China's program, service providers' capacity was significantly increased because of the professional trainings and experience accumulation. The mean daily methadone dose in 2011 was reported as 58.6 mg- similar to international recommendations of 60-100 mg/day. Interviews in this study showed the same situation: service providers indicated that there is no dose limit on prescriptions now in this study. Additionally, almost of all the interviewed service providers believed they are able to prescribe appropriate dosage of methadone to clients because the MMT program has been implemented for ten-year in Yunnan, meanwhile, two third of the clients felt the dose were enough. Therefore, the clients could receive appropriate dose of methadone at methadone induction phase now. However, this study revealed that methadone dose and dose-adjustment are still problem at the maintenance phase because of poor provider-client communication, misunderstanding and inappropriate perceptions of the MMT treatment goals and side effect. Although there were national guidelines on methadone doses to administer to MMT clients, methadone doses need to be individualized and flexible because there is no single best dose for

all patients and subsequent dose adjustments in maintenance phase has been needed in practice. All these barriers require practical professional trainings for service providers and proper educational programs for clients.

Besides the police intervention and dosage of methadone, this study also confirmed previous research on other associated barriers to MMT retention at individual-level and structural-level. The major individual-level barriers are: 1) Lack of knowledge of MMT treatment goal, side effects and long-term treatment process; 2) fear of addiction of methadone and opposition to utilize MMT on a long-term basis; 3) low accessibility of comprehensive services such as psychological counseling and side effect diagnosis and treatment; 4) economic burden; 5) concurrent use of heroin and methadone due to temptation of drug user friends and lack of family support, and 6) the drug-related stigma and discrimination in societies. The major structural and institutional barriers are: 1) high turnover rate and shortage of human resources in MMT clinic due to financial difficulties and lack of institutional support; 2) lack of related skills such as communication and counseling skills because of insufficient professional trainings; 3) logistical barriers such as the inflexible service hours, location and transportation and take away dose of methadone is restricted. 4) MMT services diversity and, 5) affordability of MMT. Furthermore, this study showed that individual barriers and structural barriers often interact synergistically and make the situation more complicated and difficult. For instance, financial difficulty in MMT clinic (policy barrier) causes insufficient professional trainings, unqualified service providers and low availability and accessibility of comprehensive services for clients. Additionally, the poor quality of services make the client doubted the provider's abilities and qualifications. All these may make the poor provider-client relationship even worse, and finally cause the low enrolment

and high drop out. Therefore, developing of the strategies for coping with these barriers require involving all the stakeholders and beneficiaries.

Several limitations in this study need to be addressed. Firstly, the recruitment approaches restricted the study team from finding some stakeholders and understanding their perceptions of MMT program. For example, we did not interview the drug abusers who are not in MMT clinics because we recruited the interviewees in MMT clinics. The study is therefore able to indirectly explore the reasons why the drug abusers do not want to participate in the MMT program. Similarly, we could not reach those service providers who have already left MMT clinics so that the more critical opinions to MMT program may be missed. Secondly, social desirability bias is a potential limitation of this study. For example, this study asked the current clients about the heroin using during the MMT treatment, the respondents might under-report their drug using behavior to better conform to the societal norm. The social desirability bias also happened in the interviews to service providers. When we asked the questions about provision of psychological counseling to MMT clients, some of respondents over-reported that the clinics provided the comprehensive psychological counseling to MMT clients, but only one provider we interviewed has the certificate of psychiatric consultant and no one clinic has the private psychology consultation room. Thirdly, this study was only conducted in four MMT clinics of Yunnan. Therefore, the findings may not be generalized to other clinics of Yunnan that the epidemic of drug abusing and operation of MMT clinic may very differ from the four selected MMT clinics.

Nevertheless, the findings of this study indicated that retention of MMT program associated with both individual and institutional factors. Moreover, the two categories of factors interacted each

other, which causes relatively low retention rate of Chinas' MMT program. Improving the quality of comprehensive services has already been identified the priority of China's MMT program after ten-year rapid scaling up (Yin, et al., 2010). Based on this qualitative study in service providers and clients in MMT clinics, the suggestions for improving the enrollment and maintenance of MMT program were put as the followings.

1) Effectively allocate the resources in MMT program to increase service providers' payment.
2) Increase training coverage and capacity building for service providers especially the providers at the county level. A number of topics, such as counseling skills, motivational interviewing skills, management of common mental health problems, management of poly-drug abuse, MMT health education for clients and skills needed, management of side effect and overdose, need to be introduced and strengthened through the professional training.
3) Support services, such as MMT health education, psychosocial counseling, motivational enhancement therapy, employment assistance, health screening, need to be improved and provided in MMT clinics.
4) Remove the logistical barriers and increasing the accessibility of MMT services. Extend MMT clinic operating hours, equipping MMT vans for remote area and increasing small MMT extension sites based on community health care center or township hospitals. Meanwhile, conduct a pilot to test the feasibility of takeaway methadone doses, it may increase acceptance and retention of long-term MMT.

5) Reduce stigmatization and discrimination of drug abuse and MMT treatment from society. Drug dependence is only a health problem and should not be regarded as a criminal act.

Table 2-1 Characteristics of officer, managers, staff members, MMT clients and dropouts

	Officer/ Manager (n=9)	Staff members (n=19)	MMT clients (n=13)	Dropouts (n=18)
Gender				
Men	7	10	11	15
Women	2	9	2	3
Age(range)	44 (32~57)	34(23~55)	39(33~51)	34(29~41)
Education level				
Primary school	0	0	2	5
Junior High school	0	0	8	11
Senior high school/vocational school	1	12	2	2
Collage and university	8	7	1	0
Months in MMT (range)	-	-	22(7~47)	4(1~5)

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Chapter III Research Article 2

Retention and its predictors among methadone maintenance treatment clients: A prospective cohort study in Yunnan Province, China

ABSTRACT

Background: Currently, China's MMT program is the largest single MMT program in the world, However, relatively low retention rate of MMT has been a concern for China's MMT program ever since the first pilot was initiated. The primary objective of the prospective cohort study is to document the retention rate of MMT program and identify the factors associated with retention of MMT in Yunnan, China at the new phase of MMT program in Yunnan, China.

Methods: A prospective cohort study was employed in this study. 523 clients from the four selected MMT clinics from four city/prefectures of Yunnan Province were recruited into the cohort, beginning on January 2014 and followed up until September 2014. In total, 523 clients completed questionnaire interview at baseline and 204 clients who still remained in MMT clinics were interviewed at six-month follow up. Cox regression model was performed to identify factors predicting dropout in the MMT program.

Results: The cumulative probabilities of retention at 1, 3 and 6months were 80.9%, 47.8% and 39.0%, respectively. The mean survival time was 3.5 months (Se=0.098) and median was 2.9 months. Seven factors were found to significantly predict retention in the MMT clinics. The seven factors were: female gender, in employment, good family relationships and support, currently married, never dropped out of MMT, subjective feeling of adequate dosage, and good provider-client relationship.

Conclusions: the retention rate of MMT is relatively low in the four MMT clinics due to the low quality of service. Non-treatment predicting predictors, such as employment status, family relationship and support, provider-client relationship, need to addressed and improved by improving the quality of comprehensive services.

Key words: Methadone Maintenance Treatment, Yunnan, China, retention, prospective cohort study, drug users, HIV/AIDS

1. Introduction

Drug abuse in China has a long history. The first peak of the use and production of the opium in China was in the 1760s with British importation of opium to China. Before the establishment of the People's Republic of China in 1949, approximately 5% of the entire population of mainland China was addicted to opium. Due to a strong national antidrug campaign in 1949, the Chinese government stated that China became "a country free from drug" in the 1950s (Lu, et al., 2008). Since the late 1980s, China has been facing the recurrence of pandemic drug abuse when the Chinese government adopted the open-door policy (Bao, et al., 2009). According to the data from National Narcotic Control Commission (NNCC), the number of registered drug users in China has increased dramatically from 70,000 in 1990 to 2.47 million in 2013 (Qian et al., 2006; National Narcotic Control Commission, 2014). Official statistics indicates that Heroin was still the main abused drug in China, 73.2% of drug users used heroin in China in 2009. Although many new heroin users begin by sniffing (55%) and smoking (8%) the drug, habitual users generally inject heroin presumably for greater efficacy at lower doses and cost (Fang, 2006). One study conducted in Guizhou showed that most registered heroin users shift from sniffing/smoking to injection after about 50 episodes of heroin use (Hu, 2008). Therefore, the proportion of injection users among the drug users is very high in China. Intravenous injection is the most common mean of drug use, with injecting drug users (IDUs) accounting for 59–85% of drug users (Zhuang, et al., 2012). Due to the high prevalence of injection of drugs and sharing of contaminated needles, the HIV prevalence among IDUs is relatively high in China, especially in Yunnan, Guanxi, Guangdong, Sichuan and Xingjiang. According to the data from the national sentinel surveillance system, the prevalence of HIV among IUDs in the five provinces peaked in 1999 at 30.3% (Wang, et al., 2014). As a convenient, safe and effective substitution therapy for

opioid dependence, methadone maintenance treatment (MMT) was introduced in China in 2004 (Pang, et al., 2007). Over ten years development and scaling up, China has built the world's largest methadone maintenance treatment network. As of August 2014, there were 765 MMT clinics, 300 small MMT extension sites and 29 MMT vans, operating in 28 provinces (WHO, 2014). Despite of the great achievements of MMT program in China, many of the challenges and gaps need to be addressed. Relatively low retention rate of MMT has been a concern for China's MMT program ever since the first pilot was initiated. Zhou and Zhuang conducted a systematic review of MMT retention rates in Mainland China during 2004-2012. In nineteen eligible studies, the retention rates ranged from 30.0% at 6 months in Shanghai to 70.3% at 12 months in Xi'an. Zhou and Zhuang concluded that MMT retention rates are heterogeneous and relative lower (Zhou and Zhuang, 2013).

Worldwide, studies consistently indicate that remaining in treatment for an adequate period of time is critical for treatment effectiveness. (Liu, 2009.; Metzger et al., 1993., WHO, 2004.). Therefore, better understanding of factors associated with retention of MMT is critical and benefit to designing and implementation of MMT program in China. The primary objective of our prospective cohort study is to document the retention rate of MMT program and identify the factors associated with retention of MMT in Yunnan, China. The results of this study were helpful to design effective strategies to engage and keep clients in MMT.

2. Methods

There were two major foci of the quantitative data collection for this study. One is to obtain detailed information about a sample of patients at each of the programs that includes the patients'

individual characteristics and experience of the program. The other is to collect comprehensive data about the four MMT clinics that includes the institutional factors, such as management, operation, services provision and utilization of MMT clinics as well as providers-patients relationship. The first foci were addressed by a cohort study, and the second foci were addressed by questionnaire survey for collected from the MMT clinics and existing data review of the MMT clinic.

2.1 Study design

A cohort design was employed to collect the quantitative information for MMT program effectiveness evaluation. The cohort recruitment started on January 1st, 2014. According to the protocol, the study recruited and interviewed (questionnaire) a total of 523 clients from the four selected MMT clinics from January 2014 to March 2014. The follow-up interviews started in July 2014, and were completed in September 2014. In total, 204 clients (39.0%) were interviewed in the follow-up survey. A separate compilation of data from clinical records for each participant at each selected MMT clinic was also collected after follow-up interviews were completed. The figure 3-1 illustrates the follow up study.

2.2 Sample-Size determination

Cox Regression was used to analyze the association between covariates (individual characteristics and institutional factors) and the outcome variable (retention rate) of MMT program. Therefore, the sample size was calculated based on a sample size formula for Cox regression. Using PASS 2008 (Power Analysis and Sample Size) software, the sample size of

this study will be calculated. PASS was developed by NCSS Statistical Software (www.ncss.com). To calculate the desired sample size the following factors were specified.

1) Alpha (significance level): Alpha is the probability of obtaining a false positive on the statistical test. It is the probability of rejecting a true null hypothesis. In this study, Alpha was fixed at 0.05.

2) Beta: Beta is the probability of obtaining a false negative on the statistical test. That is, it is the probability of accepting a false null hypothesis. Power is the probability of rejecting the null hypothesis when it is false. Power is equal to 1-beta. , so specifying power implicitly specifies beta. In this study, Power was fixed at 0.8.

3) Hypothesis test: either one-sided or two-sided test. This study chose a two-sided test.

4) Log hazard ratio: log hazard ratio is the predicted change (base e) in log hazards at one unit change in the predictor variable of interest when the other covariates are held constant, i.e. ln(HR). For calculating the sample size, 1.5, 2, 2.5 and 3 will be tried.

5) Standard deviation: An estimated standard of the predictor variable of interest. The standard deviation of the interest variable was fixed at 0.5 because most variables are dichotomous in this study.

6) R-square: R-squared is achieved when the independent variable of interest is regressed on the other independent variables. This study will fix the R-square=0.75 .

7) Overall event rate: the event rate is the proportion of subjects in whom the event of interest occurs during the duration of the study. For calculating the sample size, 0.2, 0.3, 0.4, 0.5 were tried.

Using the specified parameters, sample sizes are shown in Table 3-1. Considering the budgetary reason and time limit, the investigator decided to recruit 520 patients from the 4 MMT

clinics, average 130 patients per clinic. It meant that a Cox regression of the log hazard ratio on a covariate with a standard deviation of 0.5 based on a sample of 520 observations achieves 80% power at a 0.05 significance level to detect a regression coefficient equal to 0.6930 (i.e. ln(HR=2)=0.6930).

2.3 Inclusion criteria and exclusion criteria

The inclusion criteria for the study population were:

1) Have made several attempts at maintaining abstinence but failed.

2) Have been in the Constraint Detoxification Centre more than twice or have been in a labor re-education program at least once.

3) Be at least 20 years of age.

4) Be a local resident of the area and be able to prove permanent residency.

5) Being of good civil character.

6) had been treated no more than one month in the clinic

Meanwhile, the exclusion criteria for the study population were:

1) Patients with serious medical illnesses and current major psychiatric illness who cannot provide informed consent.

2) Planned move to another methadone clinic in the near future.

2.4 Data collection

523 clients from the four MMT clinics were interviewed by using the questionnaire. Audio-computer-assisted self-interview (ACASI) was used for data collection. Compared with traditional face-to-face interviews and written questionnaires, ACASI has been shown to

decrease under-reporting and to increase the validity and reliability of potentially stigmatized drug use, sex and HIV risk behaviors (Turner, et al., 1998; Perlis, et al., 2004; Waruru. et al., 2005).

The questionnaire consisted of the following questions were asked of each patient:

1) Basic demographic information

2) Drug abuse history

3) Services received in their current MMT clinic, including counseling, psychological and medical treatment services and the utilization of these services

3) Rating of quality of service and the provider-patient relationship

4) Perceived societal discrimination and discrimination in MMT

5) MMT fee is an economic burden or not

6) Daily methadone dosage (this information was double checked with the service record in MMT clinic) and whether they are satisfied with the current dosage

7) Any side effects, treatment of side effects and perceived problems

8) Risky sexual behaviors

9) Continued use of heroin.

The questionnaire including informed consent was pre-tested in a MMT clinic in Kunming city (not a study site.). Based on the results of pre-test, the questionnaire was finalized and used in the field study in the four selected MMT clinics.

The follow up interview of the client was undertaken six months after the first interview. The standard follow up version of the questionnaire was employed during the follow up interview to collect the relevant information from those patients who were still in the MMT since the first

interview. This questionnaire also contained questions about service received since the first interview, interval drug use, methadone dosage, and satisfaction with MMT program, strategies, recent criminality as well as employment status.

The principal investigator and two well-trained young researchers from the Institute for Health Sciences of Kunming Medical University conducted the interviews in the field. The confidential interview was conducted in a private office and lasted about 45 minutes. The same interview procedure and the same interviewers were employed for 6-month follow up interviews.

2.5 Existing data review

The second foci of the quantitative study, the questionnaire survey for the four MMT clinics was conducted by reviewing the existing data of the MMT clinic. The main information about the institutional factors of MMT clinics included:

(1) Number of staff members in the clinic and their responsibility

(2) Professional education level and training experience of staff members

(3) Average salary of the staff members

(4) Number of clients under treatment

(5) Number of drug users who have received treatment in this clinic

(6) Daily hours of operation, dispensing hours and schedules

(7) Hours for counseling and provision for counseling

(8) Missed medication rate

(9) Attitudes of staff and perceived problems

(10) Satisfaction with job.

The questionnaire was developed based on the results of qualitative study (described earlier), the study principal investigator conducted the data collection at beginning of this study.

2.6 Data management

There were two categories of data in this proposed study. One category of data was collected by ACASI and it was directly generated as tab-delimited text record file. This kind of text file was transferred into a SPSS data file using SPSS program. A logic check was done to find outliers and the values that do not make sense using SPSS program. The study investigator went through the original text files to correct or confirm the discordant, missing and illogical values. Each patient was allocated one unique identification number, using this ID number the baseline and follow up databases were combined.

Another category of data was collected from the record data system of the four MMT clinics by using special forms. Similarly, a logic check was done to find outliers and illogical values, and the study investigator went through the original forms to correct or confirm the discordant, missing and illogical values. Using the unique identification number set, the two cleaned-databases for each patient were inked. A combined database was generated which included the baseline, follow up and record data for each patient.

2.7 Data analysis

2.7.1 Analysis strategies

There were three phases of data analysis. In the first phase, variable distributions, range of variables and missing values were checked. In the second phase, descriptive and univariate

analysis were carried out using contingency tables that stratified the observations according to key factors. In the third phase, survival analysis with potential predictors was performed to explore associations between predictors and outcomes. 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 that is 0.3 or less in the univariate analysis then it was introduced into the multivariate Cox model.

2.7.2 Pretreatment characteristics of the MMT patients

Frequency tables, cross tables and graphs were used to describe pretreatment characteristics of the MMT patients. These include (1) the distribution of socio-demographic characteristics of the participants; (2) Onset of Heroin use; (3) Employment history; (4) Family life and support; (5) Drug abuse history; (6) Criminal history; (7) Physical and psychological health status, and (8) Risk sexual behavior.

2.7.3 MMT and services provided to patients

Frequency tables were used to describe MMT and services provided to patients in the four selected MMT clinics. These include (1) Number of staff members in the clinic and their responsibility; (2) Professional education level and training experiences of staff members; (3) Average salary of the staff members; (4) Number of clients under treatment; (5) Number of drug users who ever got treatment in this clinic; (6) The average length of treatment for drug users; (7) Daily hours of operation, dispensing hours and schedules; (8) Hours for counseling; (9) Missed medication rate; and (10) Physical facilities-building and space allocation. These were be compared across clinics and with patient's ratings.

MMT clients' demographic characteristics with Methadone dosage and compliance, satisfaction with service, reported doctor-patient relationship, perceived stigmatization within and outside the methadone clinic and risky sexual behavior were described in cross tables.

2.7.4 Outcome measurement

Patient retention in the MMT program was the major outcome variable in this study. Retention was defined as the client has never stopped taking methadone for a month during the 6-month follow up. According to this study protocol, those clients who did not take any methadone for a month were considered to dropouts no matter they readmitted or not. This was confirmed by the methadone clinic data. If a patient transfers to another methadone maintenance clinic, and was still taking methadone he/she was considered to still be in treatment.

2.7.5 Independent variables

Three categories of independent variables were addressed in this study.

(1) Pretreatment characteristics of the MMT patients. This category of variables included basic demographic information, addiction history and previous experience in drug treatment programs, criminal behavior, family social support, employment and income.

(2) Structural-level factors of MMT programs. This category of variables included neighborhood-facility; staff characteristics and ratios, services provide to the MMT patients and program management and administration.

(3) Process variables. This category of variables described aspects of the treatment process as it impinges on individual patients. For example, methadone maintenance dose, length of stay for this admission, missed methadone during 30 days prior to the date of the first

interview, satisfaction of service, reported doctor-patient relationship, perceived stigmatization within and outside the methadone clinic.

2.7.6 Cox model to determine risk factors

The Cox proportional hazard model is a general regression model because it is not based on any assumptions concerning the nature or shape of the underlying survival distribution. The model assumes that the underlying hazard rate is a function of the independent variables (covariates); no assumptions are made about the nature or shape of the hazard function. Assuming no interaction the model can be written as

$$I(t) = Io(t) \times \exp(\beta 1x1 + \beta 2x2 + \beta 3x3 \ldots)$$

The term h0(t) is called the baseline hazard; it is the hazard for the respective individual when all independent variable values are equal to zero, h(t) is the hazard rate or incident rate at time t. β1, β2, β3 are estimated model coefficients using a maximum partial-likelihood procedure. While no assumptions are made about the shape of the underlying hazard function, the model equations shown above imply two assumptions. First, given two observations with different values for the independent variables, the ratio of the hazard functions for those two observations does not depend on time. The second assumption is that there is a log-linear relationship between the independent variables and the underlying hazard function (Hosmer, 1999; Hill, 2007). The model was used to predict retention in methadone treatment, cessation of drug use and reduction in drug use.

SPSS 17.3was used to run the Cox regression analysis in this study.

3. Results

As shown in Figure 3-2, a total of 523 clients from 4 MMT clinics in Yunnan were recruited and interviewed (questionnaire) from January 2014 to March 2014. After 6-month follow-up, 204 clients were interviewed in the follow-up survey during the period from July 2014 to September 2014.

3.1 Baseline characteristics of study subjects

3.1.1 Demographic characteristics

The basic demographic characteristics of the 523 enrolled participants at the baseline are shown on Table 3-2. Among the participants, 397 (75.9%) were male and 126 (24.1%) were female. 87.5% of the participants were 30 to 50 years old and the average age at the baseline was 38.5 years old. About 85% of participants' education levels were primary school or junior high school graduated, around 10% of participants never completed primary school. Among the 523 participants, 21 graduated from senior high school and 20 of them are from MMT clinic 3 (Kunming). 58% of participants were Han and 42% were minorities, including Dai, Jinpo, Yi, Hani and Bai. 95% of participants lived the residences that were owned by them or their family. 5.4% of participants had been in a controlled environment in the past 30 days before they went to the MMT clinics.

3.1.2 Basic information of participants' employment and financial support

As shown in table 3-3, most participants were unemployed which accounted for 82.0% of the study subjects. For those participants who had a regular or irregular job, the average income was 2410 RMB yuan per month, which was similar to the minimum wage level of Yunnan (2300

RMB yuan); meanwhile, 88% of employed participants reported their income was not stable. 97% of the participants had gotten financial support from their family, relatives and friends; and the financial support was not regular. 61 participants have answered the question about "How much money per month do you get from your family/friends/institution? ", and the average amount was around 993 RMB yuan per month. Given above data, it is not difficult to understand why 90% of the participants evaluated their economical condition as very poor or below the average.

3.1.3 Participants' family and social relations

61.6% of participants were married; 13.8% were divorced. About 95% of participants lived with their spouse, parents and/or offspring; while about 35% of participants were not satisfied to live with families. This study designed 10 relevant descriptions to evaluate the participants' family relationship, such as 'members of my family share many of my interests', 'Most other people are closer to my family than I am' and etc. This study scored 1 point if the participant gave a positive answer and scored 0 point if the participant gave a negative answer. As shown in table 3-4, the average score was 4.3, which revealed that the family relations were not satisfactory and the participants felt guilty and unworthy to their family. Additionally, about 50% of the participants spent most of their free time with friends during the past year. However, 90% of the participants' family members supported them for MMT.

3.1.4 Drug use history of participants

As shown in table 3-5, the average age of the participants who used the drug for first time was about 19 years old, 90% of them used heroin for first time. Most participants in this study were

35~45 years old, therefore most of them tried the first drug in 1990s when it was a peak time of heroin coming into Yunnan. Over about 3-6 months, the participants started using the drug on daily basis. Within 5 years, most participants started injecting heroin on daily basis, so the average age of started injection was around 23 years old. 86% of participants reported they injected heroin three times a day during the month before entering the MMT treatment; about 27% of them shared needles with others during the month before entering the MMT program.

Money spent on drugs varied in different prefectures. 80% of the participants from MMT clinic 1 (Dehong prefecture) spent less than 100 yuan per day on the drug because the county is located on the Myanmar border and the drug was highly accessed. However, about three quarters of the participants in other three clinics had to spent 100~200 yuan per day on drug. Nearly all the participants have tried to quit using before they joined the MMT program, the average times of trying was 3 times. Around 50% and 30% of the participants attempted to quit using drug in government closed-setting rehab centers and in jails respectively, however, two thirds of them were completely voluntary. About 50% of them used some types of modern medication and 28% of them used other methods to quit using drug.

3.1.5 Characteristic of MMT treatment

The basic characteristics of MMT treatment of the 523 enrolled participants at the baseline are shown on Table 3-6. The participants learned about the MMT program through a number of channels, such as Internet, newspapers, posters, health providers, friends and family members. However, the major ways to know the MMT program were by friends and health care providers. As shown in table 3-6, about 50% of the participants knew about the MMT program from their

friends and one fifth learned from health providers. Therefore, health care providers, MMT staff and friends recruited around 95% of the participants to MMT program. Only 6 (1.1%) participants referred by criminal justice system although several programs named "seamlessly link" were implemented to promote the direct referral scheme for drug users who were in jails. With regards to overall goal in MMT program, 55% of participants want to quit both drugs and methadone after a period of time, and 31.4% of participants want to take methadone for lifetime. 40% of the participants had ever dropped out of the MMT program before they rejoined the MMT program at this time. The participants from the MMT clinic 1 (Dehong prefecture) got free methadone; 58% of the participants in other three clinics thought it was an economic burden for them. The average dosage the participants recently received was 47.13 mg/day (with Standard Division was 13.71), less than half of participants (42.6) thought the dosages were appropriate.

With regards to the time spend in traffic to get to the MMT clinic; the participants in different clinics had the different situations. About 40% of participants in Dehong and Dali had to spend more than one hour to get to the clinic, while only less than 20% of participants in Kunming and Honghe spend more than one hour on the way to the clinics. About one third of the participants (30%~38%) in the four selected clinics complained that the location of MMT clinic was inconvenient for them although the time spent in traffic were different. The waiting time for getting the methadone was not so long in the four clinics. As shown in table 3-6, only 12% of the participants had to wait for more than 30 minutes.

The data in table 3-6 shows that availability of supportive services such as psychological counseling and health checkup were poor. Only 19.5% of clients received psychological

counseling at the MMT clinics, and No one received the health checkups on a regular basis nor did they get employment training at the MMT clinics. 23.5% (123) of participants experienced side effects from methadone. However, among the 123 participants, 75% (75) of them reported that they did not get any treatments or help from the MMT clinics.

This study developed ten questions for assessing the provider-client relationship from the clients' perspective. The answer options were presented as 4-point Likert scale. The numeric values on such a scale may range from -2 to +2. For instance, -2 represents 'strongly disagree' while +2 represents 'strongly agree', or -1 represents 'disagree' and +1 represents 'agree'. During the data analysis, we calculated the average score of the ten questions by using the formulation "$\sum$ (point of the ten questions)/10 ". As shown in table 3-6, the average score of the provider-client relationship was 0.16, a bit higher than 0, which revealed that the provider-client relationship was not good. Furthermore, the average scores of the provider-client relationship in four MMT clinics were significantly different (p-value<0.0001) . The score of MMT clinic in Dehong was -0.13, which is a lowest score in the four clinics. Meanwhile, the score is lower than 0, which revealed that the provider-client relationship is not good from the participants' perspective. The highest average score (0.35) was given to the MMT clinic in Kunming, therefore, participants in the MMT clinic in Kunming perceived that the relationship between health providers and client was not bad. The rest two MMT clinics' scores were 0.27 in Dali and 0.07 in Honghe respectively.

This study also developed the four related questions for clients' subjective assessment of MMT program. Similarly, the answer options were presented as 4-point Likert scale and the same

method was used to calculate the average score of the four questions. The data in Table 3-6 showed that the average score was 0.22, a bit higher than 0, which revealed that the clients' subjective assessment of MMT program was not good. Furthermore, the average scores in four MMT clinics were significantly different (p-value<0.0001). The score of MMT clinic in Dehong was -0.25, which is a lowest score in the four clinics. The score is lower than 0, which revealed that the clients were not satisfied with the MMT program in Dehong. The highest average score (0.51) was given to the MMT clinic in Kunming, which revealed that participants in the MMT clinic in Kunming had higher satisfaction of the MMT program. The rest two MMT clinics' scores were 0.27 in Dali and 0.07 in Honghe respectively.

3.1.6 Health status of participants

As shown the table 3-7, most of participants believed their current general health status was OK, which accounted for 74.8% of the total study subjects. About a quarter of the participants reported they need the medical treatment to function in their daily life. Around a half of the participants slept poorly or very badly; and about 60% of the participants were not satisfied with their capacity for work. 75% of the participants reported that they had visited hospital/clinic in the past three months, 11.1 % of them had visited the hospital more than 5 times in the past three months. This study also interviewed the participants about their treatment of psychological and emotional problems. Among the 377 participants who responded to this question, only 16 participants (4.2%) had been treated for psychological or emotional problems in a hospital or inpatient setting; while 8.3% of 338 respondents reported that they have been treated for psychological or emotional problems as an outpatient.

3.1.7 Sexual behaviors of participants

As shown in the table 3-8, 95% of the participants reported they have sex at least one time in the past month, meanwhile, about 8% of them reported they have sex more than 6 times in the past month. With regards to condom use, only 20.7% of the respondents reported that they always used condom when having sex with regular partner(s), while 38.4% of respondents (284) who had sex with casual partner reported that they always use condom. Additionally, most of participants reported they have not had commercial sex in the past month, which accounted for 91.0% of the total study subjects.

3.1.8 Legal status of participants

Data in table 3-9 showed that only 3.1% of the participants were referred by the criminal justice system to the MMT program. 470 participants responded to the question “have you been arrested and charged in your life?”, 35.3% of them reported that they have been arrested and charged in their life.

3.2 Overall survival rate of the subjects

The Kaplan-Meier Method was employed to estimate survival rates for this study. The survival rates for each month are shown in table 3-10 and Figure 3-3. As shown in Figure 3-3, the survival rate declined dramatically in the first and second month. Table 3-10 data showed that around 20% of clients dropped out from the MMT clinics in the first month, while around 17% of client dropped out from the MMT clinics in the second month. At the sixth month (the last month of the follow-up), the survival rate was 39.0%. The mean survival time was 3.5 months (Se=0.098) and median was 2.9 months.

3.3 Univariate Analyses: Retention by characteristics of socio-demographics, drug use history, health status, MMT treatment and other related factor

Univarate analyses were carried out in order to build the final Cox model. The results of the univariate analyses for categorical variables and continuous variables were shown in table 3-11 and table 3-12 respectively. For the categorical variables the log-rank test was used to test the difference across strata. For the continuous variables, we employed the univariate Cox proportional hazard regression to test if the variables would be introduced into the multivariate analysis.

In univariate analyses of categorical variables, retention differed significantly with clinic, gender, occupational pattern, main source of money in past month, marital status, needles sharing behavior, money spend on drugs, subjective perception of drug dosage (enough or not?) and numbers of commercial (paid) sex in the past month. The survival functions for the above categorical variables were shown in figure 3-4 to 3-11.

As the data showed in table 3-12, dropout rate differed significantly with family relations and support, provider-clients relationship and client's assessment of MMT program.

Variables with p-value less than 0.30 were entered in the initial multivariate Cox proportional hazards model. These variables included: education level, ethnicity, ownership of the residence, someone's support, attempt to quit, overall goal of MMT, ever dropped out of MMT program, economic burden of MMT, average daily dose, current general status, condoms use with regular partner(s) in the past month and condom use with casual partners.

3.4 Final Cox regression model results

The final Cox model retained the variables, gender, occupation pattern, family relationship and support, current marital status, ever dropped out of MMT, subjective feeling of dosage (enough or not), and the provider-client relationship (showed in table 3-13). Female clients more likely to remain in MMT program, employed clients stayed in MMT program longer than unemployed clients, and the clients who have the good relationship with family stayed in the MMT longer. The average daily dosage of methadone was not related to retention in this study, however, the feeling of the client towards dosage was highly associated with retention, i.e. the client more likely remain in MMT if they subjectively felt the dosage is about right for them. Those clients, who have ever dropped out of MMT previously, more likely drop our again. This study also revealed that the good relationship between provider and clients are positively associated to the retention of MMT.

4. Discussion

4.1 the profile of the MMT clients

In total 523 clients from 4 clinics were investigated in this study at baseline. Overall, the mean age was 38.5 years, 75.9% were male, 61.6% of participants were married, 85% had completed primary school or junior high school, 82.0% were unemployed and 26.6% had shared needles. A national management database for the program was developed in 2004 and was later upgraded to a web-based management database in 2008 (Yin, et al., 2010). Based on this comprehensive database, Sullivan and Wu conducted a study to describe the profile of clients entering the program in the period from March 2004 to March 2010. According to the results from Sullivan's study, among 251,974 clients, the mean age was 34.4 years, 83.8% were male, 54.7% were

single, 81.0% had completed at least junior high school, 70.2% were unemployed and 17% had shared needles (Sullivan, et al., 2014). Comparing the results from above two studies, the clients in our study were older, had a lower education level, higher unemployed rate and more frequently shared needles. Additionally, 58% of clients were Han Chinese in our study while 87.7% were in Sullivan's study. These above disparities revealed that the drug abusers are more vulnerable in the four MMT clinics of Yunnan province due to the underdeveloped socio-economics and other constraints.

There is another national database system on drug abuse in China- China's National Surveillance System on Drug Abuse (NSSDA). Similarly, based this database system, Jia and Lu conducted a study to describe the profile of drug abuser in China in the period from 2008 to 2010. According to results from Jia's study, among 231,523 drug user registered in the system in the period 2008 to 2010, 53.2% were under 35 years old, 88.7% were male, 66.6% were unemployed (Jia, et al., 2014). These data indicated that the younger drug abusers were less likely to participate in the MMT program in China. Several service providers in the four clinics in our study stated a possible reason they believed: *"most of the injected drug users illegally got money for drug. When they become older, they do not want to or are not able to do those (illegal) things. So older drug users are willing to use methadone."* Low coverage of MMT is still a major challenge for MMT program in China (Li, 2013). In the end of 2013, there were 2.47 million registered drug users in China, among whom some 1.33 million were heroin users (National Narcotic Control Commission, 2014) although the total number of drug users is presumed to be much higher. On the other hand, only 410,000 opiate users had ever engaged in MMT cumulatively (WHO, 2014).

4.2 Retention rate and associated factors

This study revealed the cumulative probabilities of retention at 1, 3 and 6months were 80.9%, 47.8% and 39.0%, respectively. The mean survival time was 3.5 months (Se=0.098) and median was 2.9 months. The retention rate reported in this study was lower than the most of the previous studies in China. A study conducted in Yunnan province in 2008 indicated that the cumulative probability of retention at 1, 3 and 6 months was 94%, 75% and 57%, respectively (Che Y et al., 2010); The study by Liu conducted in Guizhou province (another western remote poor province in China) reported the retention rate for the first month was 93.5%; the third month was 81.5% and the 6th month was 68.8% (Liu, et al., 2009). Based on the national management database system, Sullivan and Wu reported that of 221,938 clients with adequate follow-up time, 111,033 (50%) received methadone for 6 months or more. (Sullivan, et al., 2014). Besides the above studies, a study conducted in Kunming of Yunnan in 2008 reported the similar retention rate: the retention rate was 40.0% at the 6 months and 12.8% at 12 months (Jiang et al., 2014). Several studies conducted overseas also reported retention rate consistent with our study, for instance, a study conducted in Australia reported 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).

In our study, seven factors were found to significantly predict retention in the MMT clinics. The seven factors were: female gender, in employment, good family relationships and support, currently married, never dropped out of MMT, subjective feeling of adequate dosage, and good provider-client relationship. Besides the subjective feeling of adequate dosage, the other predictors including female gender, in employment, good family relationship and currently married were also reported in the previous studies. A number of the studies conducted in Yunnan

and China reported the higher dose of methadone was significantly associated with the retention rate. For instance, Che et al. reported that there was no relationship between dose and probability of dropout in periods 1 and 2. However, after 3 months higher average daily dose (>60 mg) was associated with lower probability of dropout (Che, et al., 2010). Cao and his colleagues reported in a six-year cohort study that high daily dosage of methadone (>60 mg) was another important predictor of long-term retention. They also found that an increase of 30 mg in daily dosages reduces the risk of dropout by almost 30% (Cao, et al., 2014).

Plenty of studies conducted in other countries have also clearly demonstrated that higher daily dosages resulted in longer duration of treatment and caused less illicit opioid use and fewer crimes (Gowing et al., 2011; Kerr et al., 2005; Peles et al., 2006). In our study the daily dosage of methadone was not statistically associated to the retention rate in both in univariate analyses and the Cox regression analyses. The possible reason of the inconsistent result maybe: the initiation doses were low and which cause the clients who need high dose more likely to drop out from the MMT at the first week or ten days. These earlier dropouts were not able to participate in our study cohort because of the restriction of our recruitment approach. Therefore, our study was more easily to recruit those clients who were satisfied with low dose methadone into the study cohort. This potential selection bias diluted the association between the daily dosage of methadone and the retention rate, so the association was not statistically significant in our study. However, our study found that the clients' subjective feeling of adequate dosage was significantly associated with retention rate. The clients who felt the dosage was right stayed in the MMT program longer than those clients who felt it was not enough. This suggests that the dosage is not fixed to every clients and it needs to be adjusted according to clients' feeling

individually, however, this request that service providers have more communications with clients, as well as more clinical experiences.

4.3 Limitations of this study

There were certain limitations with internal validity and external validity of this study. First, this study selected the four clinics from four counties in Yunnan according to the concentration of heroin addicts and willingness of participating in our study. As a result, this was not a randomized controlled trial, and its conclusions must be viewed with reservations. Second, self-reporting questionnaire was employed to collect the information in terms current drug using, risky sex behaviors, perceived physical and mental health status. Self-disclosure might be an issue in the study because the results depend entirely on the accurate recollections of the participants. Therefore, the results need to be interpreted with a great deal of care. Third, some information of the participants, such as history of drug use, was retrospectively collected in this study. Therefore, the recall bias in this study needs to be considered.

4.4 Public health implications

This study revealed that around 50% of the clients had dropped out from MMT in the first three months, which also reflected the low quality of care in MMT services. Therefore, we suggest that service providers in MMT should pay more attention on clients during the first three months, improve the quality of services based on clients' needs and demands. More communication and consultation should be provided to clients in order to reducing the early drop out of MMT.

This study indicated that in employment and good provider-client relationship are associated with the higher retention rate of MMT. This result suggests that the MMT program should provide more available and accessible ancillary services to clients in order to help they getting a job, building good relationship with providers. Almost all the China's MMT clinics are either affiliated to CDC or affiliated to hospital (Lin, et al. 2010), as a result, the two types of MMT clinics are lack of experiences psychological counseling, communication skills, employment training and counseling, et al. As recommended by Lin et al, appropriate and ongoing training, especially in the area of motivation enhancement, psychological counseling, and behavior intervention is urgently needed for China's MMT program (Lin & Detels, 2011; Li, et al., 2012). The result suggested that good family relationships and support was associated with high retention of MMT. It implicates that services provided by the MMT clinic should not only include prescribing and dispensing methadone to clients, but also extend counseling, motivating and supporting family members of drug users.

Table 3-1 Sample size and power analysis base on Cox Regression mode

Sample Size(N)	Hazard Ration/Risk Ratio	Event Rate(P)	Std.of variable of interest	R-square	Two-side Alpha	Beta	Power
3819	1.5	0.2	0.5	0.75	0.05	0.2	0.8
2546	1.5	0.3	0.5	0.75	0.05	0.2	0.8
1910	1.5	0.4	0.5	0.75	0.05	0.2	0.8
1528	1.5	0.5	0.5	0.75	0.05	0.2	0.8
2231	1.7	0.2	0.5	0.75	0.05	0.2	0.8
1487	1.7	0.3	0.5	0.75	0.05	0.2	0.8
1116	1.7	0.4	0.5	0.75	0.05	0.2	0.8
893	1.7	0.5	0.5	0.75	0.05	0.2	0.8
1308	2	0.2	0.5	0.75	0.05	0.2	0.8
872	2	0.3	0.5	0.75	0.05	0.2	0.8
654	2	0.4	0.5	0.75	0.05	0.2	0.8
520	2	0.5	0.5	0.75	0.05	0.2	0.8
521	3	0.2	0.5	0.75	0.05	0.2	0.8
347	3	0.3	0.5	0.75	0.05	0.2	0.8
261	3	0.4	0.5	0.75	0.05	0.2	0.8
209	3	0.5	0.5	0.75	0.05	0.2	0.8

Table 3-2 The demographic characteristics of clients in four selected clinics at baseline, % or mean (± S.D.)

	MMT1*	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
Gender							
Male	80(78.4)	102(81.0)	118(76.6)	97(68.8)	397(75.9)	6.053	0.109
Female	22(21.6)	24(19.0)	36(23.4)	44(31.2)	126(24.1)		
AGE	39.9(6.6)	38.2 (6.0)	37.9(6.7)	38.2(6.7)	38.5(6.5)	2.188	0.089
20-30	8(7.8)	5(4.0)	19(12.3)	14(9.9)	46(8.8)	19.983	0.035
30-40	42(41.2)	75(59.5)	78(50.6)	73(51.8)	268(51.2)		
40-50	44(43.1)	44(34.9)	52(33.8)	50(35.5)	190(36.3)		
50+	8(7.8)	2(1.6)	5(3.2)	4(2.8)	19(3.6)		
Education level							
Never completed primary school	20(19.6)	14(11.1)	10(6.5)	15(10.6)	59(11.3)	93.55	<0.001
Primary school	38(37.3)	81(64.3)	68(44.2)	104(73.8)	291(55.6)		
Middle school	44(43.1)	31(24.6)	56(36.4)	21(14.9)	152(29.1)		
High school or above	0(0.0)	0(0.0)	20(13.0)	1(0.2)	21(4.0)		
Ethnicity							
Han	55(53.9)	69(54.8)	117(76.0)	63(44.7)	304(58.1)	268.027	<0.001
Dai	38(37.3)	3 (2.4)	7(4.5)	6(4.3)	54(10.3)		
Bai	0(0.0)	0(0.0)	16(10.4)	0(0.0)	16(3.1)		
Yi	0(0.0)	41(32.5)	11(7.1)	46(46.9)	98(18.7)		
Jinpo	9(8.8)	0(0.0)	1(0.6)	0(0.0)	10(1.9)		
Hani	0(0.0)	13(10.3)	2(1.3)	26(18.4)	41(7.8)		
How long have you lived at your current address							
Mean ±SD	18.55 ±12.43	18.33 ±12.52	16.02 ±12.21	14.40 ±10.89	16.63 ±12.08	7.204	0.066
Median	14.50	15.50	10.00	10.00	10.00		
Is this residence owned by you or your family?							
Yes	98(96.1)	124(98.4)	138(89.6)	137(97.2)	497(95.0)	14.22	0.003
No	4(3.9)	2(1.6)	16(10.4)	4(2.8)	26(5.0)		
Have you been in a controlled environment in the past 30 days?							
No	98(96.1)	118(93.7)	148(96.1)	131(92.9)	495(94.6)	5.527	0.428
Jail/prison	0(0.0)	1(0.8)	3(1.9)	2(1.4)	6(1.1)		
Drug therapy	4(3.9)	7(5.6)	3(1.9)	8(5.7)	22(4.2)		

*: MMT1 represents MMT clinic in Dehong prefecture; MMT2 represent MMT clinic in Dali prefecture; MMT3 represents MMT clinic in Kunming city and MMT4 represents MMT clinics in Honghe prefecture.

Table 3-3 Basic information of employment and financial support among the clients in four selected clinics at baseline, % or mean (± S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
Occupation pattern							
Regular work	1(1.0)	5(4.0)	6(3.9)	1(0.7)	13(2.5)	12.141	0.059
Irregular work	16(15.7)	11(8.7)	31(20.1)	23(16.3)	81(15.5)		
Unemployed	85(83.3)	110(87.3)	117(76.0)	117(83.0)	429(82.0)		
Income (n=94)							
Mean (SD)	2473.53 (546.04)	2221.88 (647.29)	2437.84 (705.57)	2450.00 (652.58)	2410.64 (651.50)	0.543	0.654
How stable is your monthly income from your current job (n=94)							
Unstable	15(88.2)	14(87.5)	33(89.2)	21(87.5)	83(88.3)	0.053	0.997
Fairly stable	2(11.8)	2(12.5)	4(10.8)	3(12.5)	11(11.7)		
Does someone contribute to your support in any way?							
No	0(0.0)	0(0.0)	4(4.5)	5(3.5)	12(2.3)	9.82	0.02
Yes	102(100.0)	126(100.0)	147(95.5)	136(96.5)	511(97.7)		
Is it a regular (such as daily, weekly or monthly) allowance? (n=511)							
no	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	-	-
yes	102(100.0)	126(100.0)	147(100.0)	136(100.0)	511(100.0)		
How much money per month do you get from your family/friends/institution? (n=61)							
Mean (SD)	1026.92 (876.93)	975.00 (846.97)	950.00 (684.24)	1043.33 (692.53)	993.44 (739.34)	0.057	0.982
During the past 30 days, what has been the main source of money?							
Paid jobs or business activities	17(16.7)	16(12.7)	37(24.0)	24(17.0)	94(18.0)	9.843	0.131
Family/members/relatives /friends/institution	81(79.4)	108(85.7)	114(74.0)	116(82.3)	419(80.1)		
Other source	4(3.9)	2(1.6)	3(1.9)	1(0.7)	83(1.9)		
How would you evaluate your current economic condition?							
Very poor	80(78.4)	52(41.3)	69(44.8)	41(29.1)	242(46.3)	62.830	<0.001
Below average	17(16.7)	59(46.8)	69(44.8)	77(54.6)	222(42.4)		
Average	5(4.9)	12(9.5)	14(9.1)	21(14.98)	52(9.9)		
Above average	0(0.0)	3(2.4)	2(1.3)	2(1.4)	7(1.3)		

Table 3-4 Basic information of the clients' family/social relations in four selected clinics at baseline, % or mean (± S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
What is your current marital status							
Never married	10(9.8)	22(17.5)	21(13.6)	19(13.5)	72(13.8)	22.309	0.100
Married	67(65.7)	83(65.9)	90(58.4)	82(58.2)	322(61.6)		
Separated	2(2.0)	2(1.6)	10(6.5)	4(2.8)	18(3.4)		
Divorced	19(18.6)	16(12.7)	23(14.9)	32(22.7)	90(17.2)		
Remarried	2(2.0)	1(0.8)	1(0.6)	2(1.4)	6(1.1)		
Widowed	2(2.0)	2(1.6)	9(5.8)	2(1.4)	15(2.9)		
How many persons are there in your family (including yourself)							
Mean ±SD	2.35 ±0.908	2.94 ±0.990	2.77 ±0.904	2.94 ±0.935	2.78 ±0.958	9.711	<0.001
With whom do you live?							
Parents	23(19.2)	53(26.2)	61(27.7)	68(30.9)	205(26.9)	-	-
Wife/ husband officially married to you	69(57.5)	84(41.6)	88(40.0)	84(38.2)	325(42.7)		
Live-in sex partner	5(4.2)	7(3.5)	7(3.2)	3(1.4)	22(2.9)		
Offspring	20(16.7)	54(26.7)	58(26.4)	57(25.9)	189(24.8)		
Brother, sister or relative	2(1.7)	4(2.0)	6(2.7)	8(3.6)	20(2.6)		
Friend	1(0.8)	0(0.0)	0(0.0)	0(0.0)	0(0.0)		
Are you satisfied to be living with these people?							
No	28(27.5)	40(31.7)	40(26.0)	25 (17.7)	22(25.4)	10.973	0.089
Indifferent	7(6.9)	10(7.9)	12(7.8)	20(14.2)	49(9.4)		
Yes	37(65.7)	76(60.3)	102(66.2)	96(68.1)	341(65.2)		
The score of family relationship							
Mean ±SD	4.21 ±1.19	4.19 ±1.16	4.41 ±1.03	4.37 ±1.02	4.31 ±1.09	1.337	0.261
With whom did you spend most of your free time with during the past year?							
Family	18(17.6)	21(16.7)	44(28.6)	34 (24.1)	117(22.4)	8.436	0.208
Friends	55(53.9)	65(49.2)	71(46.1)	68(48.2)	256(48.9)		
Alone	29(28.4)	43(34.1)	39(25.3)	39(27.7)	150(28.7)		
How many close friends (exclude family members) do you have?							
Mean ±SD	2.53 ±0.805	2.42 ±0.763	2.49 ±0.716	2.49 ±0.780	2.48 ±0.761	0.409	0.747
Do your family members support you for MMT?							
Yes	93(91.2)	120(95.2)	142(92.2)	130 (92.2)	485(92.7)		
No	2(2.0)	2(1.6)	2(1.3)	5(3.5)	11(2.1)		
They don't know about it	7(6.9)	4(3.2)	10(6.5)	6(4.3)	27(5.2)		

Table 3-5 Drug use history of the participants in four selected clinics at baseline, % or mean (± S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
Age of use drugs for the first time							
Mean ±SD	19.45 ±5.37	18.38 ±5.36	18.79 ±5.34	18.81 ±4.98	18.82 ±5.26	0.783	0.504
Median	18.50	17.00	18.00	18.00	18.00		
What kind of drug did you use the first time?							
Opium	15(14.7)	9(7.1)	6(3.9)	7(5.0)	37(7.1)	20.869	0.002
Heroin	86(84.3)	114(92.5)	138(89.6)	132(93.6)	470(89.9)		
Morphine	1(1.0)	3(2.4)	10(6.5)	2(1.4)	16(3.1)		
Age of start using drugs on a daily basis							
Mean ±SD	19.97 ±5.45	18.85 ±5.36	19.37 ±5.37	19.36 ±5.03	19.36 ±5.29	0.842	0.471
Median	19.00	17.50	19.00	18.00	18.00		
What kind of drugs did you use most							
Opium	2(2.0)	4(3.2)	3(1.9)	8(5.7)	17(3.3)	6.159	0.406
Heroin	99(97.1)	121(96.0)	148(96.1)	129(91.5)	497(95.0)		
Morphine	1(1.0)	1(0.8)	3(1.9)	4(2.8)	9(1.7)		
Age of start injecting drugs on a daily basis							
Mean ±SD	23.19 ±6.37	22.86 ±5.99	22.55 ±5.51	22.61 ±5.57	22.76 ±5.81	0.290	0.832
Median	23.00	22.00	21.00	22.00	22.00		
How many times did you use drugs during the month before entering the MMT program?							
Did not use	4(3.9)	6(4.8)	10(6.5)	6(4.3)	26(5.0)	11.212	0.737
Once a week or less	2(2.0)	2(1.6)	3(1.9)	3(2.1)	10(1.9)		
More than once a week but less than once a day	1(1.0)	4(3.2)	2(1.3)	2(1.4)	9(1.7)		
Once a day	1(1.0)	1(0.8	1(0.6)	0(0.0)	3(0.6)		
2-3 times a day	89(87.3)	97(77.0)	128(83.1)	121(85.8)	435(83.2)		
More than 3 times a day	5(4.9)	16(12.7)	10(6.5)	9(6.4)	40(7.6)		
Have you ever share needles with others during the month before entering the MMT program?							
NO	73(71.6)	90(71.4)	119(77.3)	102(72.3)	384(73.4)	1.691	0.639
YES	29(28.4)	36(28.6)	35(22.7)	39(27.7)	139(26.6)		

To be continue

Table 3-5 Drug use history of the participants in four selected clinics at baseline, % or mean (± S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
How much did you spend on drugs during the month							
No	8(7.8)	13(10.3)	16(10.4)	11(7.8)	48(9.2)	208.935	<0.001
below 30	27(26.5)	4(3.2)	0(0.0)	3 (2.1)	34(6.5)		
30-100	53(52.0)	30(23.8)	6(3.9)	24(17.0)	113(21.6)		
100-200	8(7.8)	72(51.7)	113(73.4)	95(67.4)	288(55.1)		
200-400	4(3.9)	4(3.2)	14 (9.1)	6(4.3)	28(5.4)		
beyond 400	2(2.0)	3(2.4)	5(3.2)	2(1.4)	12(2.3)		
How many times did you try to quit using drugs?							
Mean ±SD	3.34 ±0.98	3.33 ±1.03	3.27 ±1.01	3.23 ±1.08	3.29 ±1.03	0.331	0.803
Median	3.00	3.00	3.00	3.00	3.00		
Where were you for your MOST RECENT attempt?							
At home	10(9.8)	11(8.7)	11(7.1)	8(5.7)	40(7.6)	13.296	0.150
In government closed-setting rehab centers	55(53.9)	58(46.0)	78(50.6)	69 (48.9)	260(49.7)		
In jails/prisons	29(28.4)	33(26.2)	50(32.5)	51(36.2)	163(31.2)		
In other facilities (such as hospitals or private clinics/centers)	8(7.8)	24(19.0)	15(9.7)	13(9.2)	60(11.5)		
What method(s) did you use during your MOST RECENT attempt?							
Stopped yourself without any medication	1(1.0)	1(0.8)	2(1.3)	1(0.7)	5(1.0)	5.764	0.927
Using some types of modern medication to reduce pain	47(46.1)	65(51.6)	76(49.4)	71(50.4)	259(49.5)		
Using traditional medicine, acupuncture and acupressure, etc.	13(12.7)	9(7.1)	12(7.8)	11(7.8)	45(8.6)		
Using traditional medicine	10(9.8)	20(15.9)	20(13.0)	17(12.1)	67(12.8)		
Other method(s)	31(30.4)	31(24.6)	44 (28.6)	41(29.1)	147(28.1)		
In your most recent attempt to quit, did you want to do it, or were you forced by others							
It was completely voluntary	71(69.6)	90(71.4)	102(66.2)	90(63.8)	353(67.5)	2.071	0.558
I was forced but I also wanted to quit	31(30.4)	36(28.6)	52(33.8)	51(36.21)	170(32.5)		

Table 3-6 Characteristic of MMT treatment of participants in four selected clinics at baseline, % or mean (± S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
How did you learn about the MMT program							
Internet	5(4.9)	12(9.5)	9(5.8)	11(7.8)	37(7.1)	7.318	0.948
Newspaper/magazine/booklets	5(4.9)	5(4.0)	7(4.5)	11(7.8)	28(5.4)		
Poster	9(8.8)	13(10.3)	17(11.0)	18(12.8)	57(10.9)		
Health care providers	23(22.5)	24(19.0)	35(22.7)	31(22.0)	113(21.6)		
Friend	51(50.0)	61(48.4)	71 (46.1)	60(42.6)	243(46.5)		
Family member	9(8.8)	11(8.7)	15(9.7)	10(7.1)	45(8.6)		
How were you recruited to the MMT program?							
Referred by health care providers	16(15.7)	23(18.3)	19(12.3)	24(17.0)	82(15.7)	10.051	0.611
Suggested by criminal justice system	0(0.0)	1(0.8)	3(1.9)	2(1.4)	6(1.1)		
Recommended by friend	49(48.0)	51(40.5)	60(39.0)	52(36.9)	212(40.5)		
Recruited by MMT staff	33(32.4)	41(32.5)	64(41.6)	55(39.0)	193(36.9)		
It was your decision and went there yourself	4(3.9)	10(7.9)	8 (5.2)	8(5.7)	30(5.7)		
What is your overall goal in the MMT program							
To take MMT for life time, and not use drugs anymore	34(33.3)	46(36.5)	46(29.9)	38(27.0)	164(31.4)	3.861	0.695
To use MMT for life time, and reduce the use of drugs	14(13.7)	14(11.1)	21(13.6)	23(16.3)	72(13.8)		
Try to quit drugs and MMT after a period of time	54(52.9)	66(52.4)	87(56.5)	80(56.7)	287(54.9)		
Have you ever dropped out of MMT program							
Yes	37(36.3)	62(49.2)	65(42.2)	54(38.3)	218(41.7)	4.843	0.184
No	65(63.7)	64(50.8)	89(57.8)	87(61.7)	305(58.3)		
Is the payment for MMT an economic burden for you							
Yes	0(0.0)	96(76.2)	120(77.9)	92(65.2)	308(58.9)	187.089	<0.001
No	102(100.0)	30(23.8)	34(22.1)	49(34.8)	215(41.1)		
How much methadone do you currently receive every day?							
Mean ±SD	49.41 ±15.14	47.69 ±13.81	46.23 ±12.89	45.96 ±13.31	47.13 ±13.71	1.583	0.193
Median	40.00	40.00	40.00	40.00	40.00		
Do you think the dosage is?							
About right	45(44.1)	52(41.3)	61(39.6)	65(46.1)	223(42.6)	1.456	0.693
Too little	57(55.9)	74(58.7)	93(60.4)	76(53.9)	600(57.4)		
How much time do you spend in traffic to get to the MMT clinic every day?							
Less then 30 MINUTES	32(31.4)	20(15.9)	53(34.4)	64(45.4)	169(32.3)	52.308	<0.001
30-60 MINUTES	25(24.5)	55(43.7)	71(46.1)	53(37.6)	204(39.0)		
MORE THAN 60 MINUTES	45(44.1)	51(40.5)	30(19.5)	24(17.0)	150(28.7)		
Is the location of MMT clinic is convenient for you?							
Yes	64(62.7)	87(69.0)	105(58.2)	105(74.5)	361(69.0)	3.887	0.274
No	38(37.3)	39(31.0)	49(31.8)	36(25.5)	162(31.0)		

To be continue

Table 3-6 Characteristic of MMT treatment of participants in four selected clinics at baseline, % or mean (± S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
How long on average do you wait before you get treatment everyday?							
BELOW 10 MINUTES	5(4.9)	14(11.1)	4(2.6)	3(2.1)	26(5.0)	21.203	0.012
10-20 MINUTES	28(27.5)	49(38.9)	53(34.4)	42(29.8)	172(32.9)		
20-30 MINUTES	55(53.9)	49(38.9)	78(50.6)	79(56.0)	261(49.9)		
MORE THAN 30 MINUTES	14(13.7)	14(11.1)	19(12.3)	17(12.1)	64(12.2)		
Have you received psychological counseling at the MMT clinic?							
Yes	17(16.7)	19(15.1)	42(27.3)	24(17.0)	102(19.5)	8.568	0.036
No	85(83.3)	107(84.9)	112(72.7)	117(83.0)	421(82.5)		
Have you received HIV education at the MMT clinic?							
Yes	83(81.4)	104(82.5)	123(79.9)	112(79.4)	422(80.7)	0.517	0.915
No	19(18.6)	22(17.5)	31(20.1)	29(20.6)	101(19.3)		
Have you received health checkups on a regular basis at the MMT clinic							
Yes	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	-	-
No	102(100.0)	126(100.0)	154(100.0)	141(100.0)	523(100.0)		
Have you experienced side effects from methadone?							
Yes	21(20.6)	33(26.2)	35(22.7)	34(24.1)	123(23.5)	1.068	0.785
No	81(79.4)	93(73.8)	119(77.3)	107(75.9)	400(76.5)		
Do you receive treatment for methadone side effects?(n=123)							
Yes, outside the MMT program	1(4.8)	2(6.1)	0(0.0)	2(5.9)	5(4.1)	5.994	0.430
Yes, from MMT program	7(33.3)	6(18.2)	8(22.9)	4(11.8)	25(20.3)		
No	13(61.9)	25(75.8)	27(77.1)	28(82.4)	93(75.6)		
Do you receive employment training or counseling in the MMT program?							
Yes	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	-	-
No	102(100.0)	126(100.0)	154(100.0)	141(100.0)	523(100.0)		
How much do you agree with each of the following statements regarding the services staff in your MMC?							
Mean ±SD	-0.13 ±0.82	0.27 ±0.77	0.35 ±0.83	0.07 ±0.80	0.16 ±0.83	8.425	<0.001
How much do you agree with each of the following statements regarding the MMT program?							
Mean ±SD	-0.25 ±1.31	0.39 ±1.24	0.51 ±1.29	0.09 ±1.28	0.22 ±1.31	8.337	<0.001

Table 3-7 Health status of participants in four selected clinics at baseline, % or mean (S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
How do you rate your current general health level?							
Very good	1(1.0)	1(0.8)	1(0.6)	2(1.4)	5(1.0)	11.381	0.497
Good	21(20.6)	14(11.1)	28(18.2)	32(22.7)	95(18.2)		
OK	78(76.5)	102(81.0)	114(74.0)	97(68.8)	391(74.8)		
Poor	2(2.0)	8(6.3)	9(5.8)	9(6.4)	28(5.4)		
Very bad	0(0.0)	1(0.8)	2(1.3)	1(0.7)	4(0.8)		
Do you need any medical treatment to function in your daily life?							
Yes	24(23.5)	26(20.6)	45(29.2)	32(22.7)	127(24.3)	3.179	0.365
No	78(76.5)	100(79.4)	109(70.8)	109(77.3)	396(75.7)		
Do you sleep well?							
Good	6(5.9)	5(4.0)	12(7.8)	13(9.2)	36(6.9)		
OK	51(50.0)	56(44.4)	76(49.4)	57(40.4)	240(45.9)		
Poor	33(32.4)	50(39.7)	44(28.6)	55(39.0)	182(34.8)		
Very bad	12(11.8)	15(11.9)	22(14.3)	16(11.3)	65(12.4)		
How satisfied are you with your capacity for work?							
Very good	9(8.8)	12(9.5)	20(13.0)	7(5.0)	48(9.2)	10.797	0.546
Good	8(7.8)	16(12.7)	19(12.3)	15(10.6)	58(11.1)		
OK	20(19.6)	23(18.3)	20(13.0)	21(14.9)	84(16.1)		
Poor	61(59.8)	68(50.4)	88(57.1)	89(60.3)	306(58.5)		
Very bad	4(3.9)	7(5.6)	7(4.5)	9(6.4)	27(5.2)		
How many doctor or hospital/clinic visits (exclude visiting MMT clinic) did you have in the past three months?							
No	31(30.4)	36(28.6)	36(23.4)	31(22.0)	134(25.6)	8.850	0.451
1-2 times	43(42.2)	48(38.1)	61(39.6)	67(47.5)	219(41.9)		
3-5 times	15(14.7)	31(24.6)	38(24.7)	28(19.9)	112(21.4)		
more than 5 times	13(12.7)	11(8.7)	19(12.3)	15(10.6)	58(11.1)		
Have you been treated for any psychological or emotional problems? (in a hospital or inpatient setting, n=377)							
Yes	3(3.9)	3 (3.2)	4(3.8)	6(6.0)	16(4.2)	1.096	0.778
No	74(96.1)	91(96.8)	102(96.2)	94(94.0)	361(95.8)		
Have you been treated for any psychological or emotional problems? (Outpatient/private patient=338)							
Yes	5(7.7)	11(12.9)	7(7.3)	5(5.4)	28(8.3)	3.564	0.313
No	60(92.3)	74(87.1)	89(92.7)	87(94.6)	310(91.7)		
Experienced serious depression (Past 30 Days, N=428)							
YES	40(47.1)	43(43.0)	63(49.2)	54(47.0)	200(46.7)	0.883	0.829
NO	45(52.9)	57(57.0)	65(50.8)	61(53.0)	228(53.3)		
Experienced serious anxiety or tension (Past 30 Days, N=420)							
YES	37(44.0)	37(36.3)	36(30.0)	29(25.4)	139(33.1)	8.554	0.036
NO	47(56.0)	65(63.7)	84(70.0)	85(74.6)	281(66.9)		
Experienced hallucinations (Past 30 Days, N=486)							
YES	30(30.9)	23(19.5)	29(20.9)	19(14.4)	101(20.8)	9.457	0.024
NO	67(69.1)	95(80.5)	110(79.1)	113 (85.6)	385(79.2)		
Experienced trouble understanding, concentrating or remembering violence(Past 30 Days, N=504							
YES	61(61.0)	87(71.3)	96(66.2)	88(64.2)	332(65.9)	2.832	0.418
NO	39(39.0)	35(28.7)	49(33.8)	49 (35.8)	172(34.1)		
Experienced trouble controlling violent behavior including episodes or rage or violence (Past 30 Days, N=435)							
YES	42(50.6)	43(41.0)	60(48.0)	73(59.8)	218(50.1)	8.369	0.039
NO	41(49.4)	62(59.0)	65(52.0)	49(40.2)	217(49.9)		

Table 3-8 Sexual behavior among participants in four selected clinics at baseline, % or mean (S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
How many times did you have sex in the past month?							
None	5(4.9)	5(4.0)	8(5.2)	7(5.0)	25(4.8)	4.081	0.997
One	19(18.6)	26(20.6)	29(18.8)	29(20.6)	103 (19.7)		
Two	48(47.1)	62(49.2)	75(48.7)	67(47.5)	252(48.2)		
3-5	22(21.6)	19(15.1)	28(18.2)	26(18.4)	95(18.2)		
6-10	4(3.9)	8(6.3)	5(3.2)	6(4.3)	23(4.4)		
More than 10	4(3.9)	6(4.8)	9 (5.8)	6(4.3)	25(4.8)		
How often did you use condoms when having sex with your regular partner(s) in the past month?(N=362)							
Every time	18(21.4)	19(21.1)	19(18.8)	19(21.8)	75 (20.7)	17.504	0.290
Often	9(10.7)	13(14.4)	14(12.9)	8(9.2)	44(12.2)		
Sometimes	36(42.9)	31(34.4)	35(34.7)	35(40.2)	137(37.8)		
Rarely	19(22.6)	25(27.8)	30(29.7)	22(25.3)	96(26.5)		
Never	2(2.4)	2(2.2)	3 (3.0)	3(3.4)	10 (2.8)		
How often did you use condoms when you had sex with casual partners? (N=284)							
Every time	21(39.6)	31(47.0)	31(35.2)	26(33.8)	109 (38.4)		
Often	17(32.1)	15(22.7)	19(21.6)	26(33.8)	77(27.1)		
Sometimes	10(18.9)	8(12.1)	16(18.2)	14(18.2)	48(16.9)		
Rarely	4(7.5)	9(13.6)	14(15.9)	9(11.7)	36(12.7)		
Never	1(1.9)	3(4.5)	8(9.1)	2(2.6)	14 (4.9)		
How many people did you have commercial (paid) sex with in the past month?							
None	93(91.2)	115(91.3)	137(89.0)	131(92.9)	476(91.0)	15.557	0.412
One	1(1.0)	3(2.4)	2(1.3)	0(0.0)	6 (1.1)		
Two	2(2.0)	3(2.4)	1(0.6)	3(2.1)	9(1.7)		
3-5	2(2.0)	1(0.8)	1 (0.6)	2(1.4)	6(1.1)		
6-10	1(1.0)	1(0.8)	9(5.8)	3(2.1)	14(2.7)		
More than 10	3（2.9)	3(2.4)	4(2.6)	2(1.4)	12 (2.3)		

Table 3-9 Legal status of participants in four selected clinics at baseline, % or mean (S.D.)

	MMT1	MMT2	MMT3	MMT4	TOTAL	F/χ^2	P
Was your admission to MMT prompted or suggested by the criminal justice system?							
No	96(94.1)	122(96.8)	151(98.1)	138(97.9)	507(96.9)	3.801	0.284
Yes	6(5.9)	4 (3.2)	3(1.9)	3(2.1)	16(3.1)		
Are you on probation or parole?							
No	102(100.0)	126(100.0)	154(100.0)	141(100.0)	523(100.0)	-	-
Yes	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)		
Have you been arrested and charged in your life?(n=470)							
No	57(64.0)	77(67.5)	91(65.5)	79(61.7)	304(64.7)	0.954	0.812
Yes	32(36.0)	37(32.5)	48(34.5)	49(38.3)	166(35.3)		

Table 3-10 Survival rate by months on treatment

Months	Case on treatment (N)	Survival rate %
0	523	100.00
1	423	80.88
2	331	63.29
3	250	47.80
4	229	43.79
5	215	41.11
6	204	39.01

Table 3-11 Univariate Analyses: Retention by socio-demographics characteristics, drug use history, health status, MMT treatment and related factors

	Number of Subjects (%)	Retention at 6 month	95%CI	Log-rank P value
MMT clinic				
MMT1	102(19.5)	0.284	0.196-0.372	**0.020**
MMT2	126(24.1)	0.437	0.351-0.523	
MMT3	154(29.4)	0.461	0.383-0.539	
MMT4	141(27.0)	0.355	0.277-0.433	
Gender				
Male	397(75.9)	0.365	0.318-0.412	**0.018**
Female	126(24.1)	0.476	0.390-0.562	
AGE				
20-30	46(8.8)	0.370	0.231-0.590	0.844
30-40	268(51.2)	0.396	0.337-0.455	
40-50	190(36.3)	0.400	0.329-0.471	
50+	19(3.6)	0.316	0.106-0.526	
Education level				
Never completed primary school	59(11.3)	0.458	0.331-0.585	**0.278**
Primary school	291(55.6)	0.361	0.306-0.416	
Middle school	152(29.1)	0.441	0.363-0.519	
High school or above	21(4.0)	0.286	0.092-0.480	
Ethnicity				
Han	304(58.1)	0.414	0.359-0.469	**0.256**
Minorities	219(41.9)	0.361	0.298-0.424	
Is this residence owned by you or your family?				
Yes	497(95.0)	0.400	0.357-0.443	**0.156**
No	26(5.0)	0.231	0.068-0.394	
Occupation pattern				
Regular work	13(2.5)	0.846	0.650-1.042	**0.004**
Irregular work	81(15.5)	0.457	0.349-0.565	
Unemployed	429(82.0)	0.366	0.321-0.411	
Does someone contribute to your support in any way?				
no	12(2.3)	0.667	0.400-0.934	**0.083**
yes	511(97.7)	0.386	0.343-0.429	
During the past 30 days, what has been the main source of money?				
Paid jobs or business activities	94(18.0)	0.511	0.409-0.613	**0.017**
Family/members/relatives /friends/institution	419(80.1)	0.370	0.323-0.417	
Other source	10(1.9)	0.200	0.047-0.447	
How would you evaluate your current economic condition?				
Very poor	242(46.3)	0.388	0.327-0.449	0.346
Below average	222(42.4)	0.374	0.311-0.437	
Average or higher	59(11.3)	0.475	0.348-0.602	

To be continue

Table 3-11 Univariate Analyses: Retention by socio-demographics characteristics, drug use history, health status, MMT treatment and related factors (Cont.)

	Number of subjects (%)	Retention at 6 month	95%CI	Log-rank P value
What is your current marital status				
Never married	72(13.8)	0.264	0.162-0.366	**<0.001**
Married	322(61.6)	0.472	0.417-0.527	
Other	129(24.6)	0.264	0.188-0.340	
How many persons are there in your family (including yourself)				
1	37(7.1)	0.297	0.150-0.444	0.324
2	166(31.7)	0.446	0.370-0.522	
3	231(44.2)	0.372	0.309-0.435	
4	55(10.5)	0.382	0.253-0.511	
5	34(6.5)	0.382	0.219-0.545	
Are you satisfied to be living with these people?				
No	133(25.4)	0.368	0.286-0.450	0.598
Indifferent	49(9.4)	0.449	0.310-0.588	
Yes	341(65.2)	0.393	0.342-0.444	
Do your family members support you for MMT?				
Yes	485(92.7)	0.398	0.355-0.441	0.365
No	38(7.3)	0.316	0.169-0.463	
How many times did you use drugs during the month before entering the MMT program?				
Did not use	26(5.0)	0.269	0.098-0.440	0.579
less than once a day	22(4.2)	0.364	0.162-0.566	
2-3 times a day	435(83.2)	0.405	0.358-0.452	
More than 3 times a day	40(7.6)	0.350	0.203-0.497	
How many times did you share needles with others during the month before entering the MMT program?				
NO	384(73.4)	0.414	0.365-0.463	**0.036**
YES	139(26.6)	0.311	0.253-0.409	
How much did you spend on drugs during the month				
No	48(9.2)	0.312	0.181-0.443	**0.047**
below 100	147(28.1)	0.327	0.251-0.403	
beyong 200	328(62.7)	0.433	0.380-0.486	
In your most recent attempt to quit, did you want to do it, or were you forced by others				
It was completely voluntary	353(67.5)	0.371	0.320-0.422	**0.120**
I was forced but I also wanted to quit	170(32.5)	0.435	0.361-0.509	

To be continue

Table 3-11 Univariate Analyses: Retention by socio-demographics characteristics, drug use history, health status, MMT treatment and related factors (Cont.)

	Number of subjects (%)	Retention at 6 month	95%CI	Log-rank P value
What is your overall goal in the MMT program				
To take MMT for life time, and not use drugs anymore	164(31.4)	0.457	0.381-0.533	**0.095**
To use MMT for life time, and reduce the use of drugs	72(13.8)	0.306	0.200-0.412	
Try to quit drugs and MMT after a period of time	287(54.9)	0.376	0.319-0.433	
Have you ever dropped out of MMT program				
Yes	218(41.7)	0.344	0.281-0.407	**0.0543**
No	305(58.3)	0.426	0.371-0.481	
Is the payment for MMT an economic burden for you				
Yes	308(58.9)	0.425	0.370-0.480	**0.061**
No	215(41.1)	0.344	0.281-0.407	
How much methadone do you currently receive every day? (dosage at the baseline)				
BELOW 60	401(76.7)	0.406	0.367-0.455	**0.194**
MORE THAN 60	122(23.3)	0.344	0.260-0.428	
Do you think the dosage is?				
About right	223(42.6)	0.323	0.262-0.384	**0.006**
Too little	300(57.4)	0.443	0.386-0.500	
Average daily dose				
< 40 mg	65(12.4)	0.277	0.167-0.387	**0.125**
40-60 mg	135(25.8)	0.370	0.288-0.452	
> 60	323(61.8)	0.424	0.371-0.477	
How much time do you spend in traffic to get to the MMT clinic every day?				
BELOW 30 MINUTES	169(32.3)	0.367	0.294-0.440	0.624
30-60 MINUTES	204(39.0)	0.407	0.340-0.474	
MORE THAN 60 MINUTES	150(28.7)	0.400	0.322-0.478	
Is the location of MMT clinic is convenient for you?				
Yes	361(69.0)	0.404	0.353-0.455	0.420
No	162(31.0)	0.364	0.290-0.438	
How long on average do you wait before you get treatment everyday?				
BELOW 30 MINUTES	26(5.0)	0.392	0.347-0.437	0.786
MORE THAN 30 MINUTES	64(12.2)	0.391	0.271-0.511	
Have you received psychological counseling at the MMT clinic?				
Yes	102(19.5)	0.343	0.251-0.435	0.314
No	421(82.5)	0.404	0.357-0.451	

To be continue

Table 3-11 Univariate Analyses: Retention by socio-demographics characteristics, drug use history, health status, MMT treatment and related factors (Cont.)

	Number of subjects (%)	Retention at 6 month	95%CI	Log-rank P value
Have you received HIV education at the MMT clinic?				
Yes	422(80.7)	0.393	0.346-0.440	0.964
No	101(19.3)	0.386	0.292-0.480	
Have you experienced side effects from methadone?				
Yes	123(23.5)	0.374	0.288-0.460	0.733
No	400(76.5)	0.398	0.351-0.445	
How do you rate your current general health level?				
Good	100(19.1)	0.310	0.220-0.400	**0.070**
OK	391(74.8)	0.417	0.3680-.466	
Poor	32(6.1)	0.344	0.179-0.509	
Do you need any medical treatment to function in your daily life?				
Yes	127(24.3)	0.425	0.339-0.511	0.600
No	396(75.7)	0.381	0.334-0.428	
Do you sleep well?				
Good	36(6.9)	0.306	0.155-0.457	0.506
OK	240(45.9)	0.408	0.345-0.471	
Poor	247(47.1)	0.389	0.328-0.450	
How satisfied are you with your capacity for work?				
Good	106(20.3)	0.387	0.295-0.479	0.555
OK	84(16.1)	0.440	0.334-0.5456	
Poor	333(63.6)	0.381	0.328-0.434	
Have you been treated for any psychological or emotional problems? (in a hospital or inpatient setting, n=377)				
Yes	16(4.2)	0.438	0.195-0.681	0.431
No	361(95.8)	0.396	0.345-0.447	
Have you been treated for any psychological or emotional problems? (Outpatient/private patient=338)				
Yes	28(8.3)	0.429	0.245-0.613	0.581
No	310(91.7)	0.390	0.335-0.445	

To be continue

Table 3-11 Univariate Analyses: Retention by socio-demographics characteristics, drug use history, health status, MMT treatment and related factors

	Number of subjects (%)	Retention at 6 month	95%CI	Log-rank P value
How many people did you have sex with in the past month?				
None	25(4.8)	0.480	0.284-0.676	0.716
One	103 (19.7)	0.350	0.258-0.442	
Two	252(48.2)	0.381	0.320-0.442	
3-5	95(18.2)	0.400	0.302-0.498	
More than 6	48(9.2)	0.479	0.338-0.620	
How often did you use condoms when having sex with your regular partner(s) in the past month?				
Every time	75 (20.7)	0.400	0.288-0.512	**0.054**
Often	44(12.2)	0.477	0.330-0.624	
Sometimes	137(37.8)	0.358	0.027-0.438	
Rarely	96(26.5)	0.500	0.400-0.600	
Never	10 (2.8)	0.800	0.553-1.047	
How often did you use condoms when you had sex with casual partners?				
Every time	109 (38.4)	0.431	0.339-0.523	**0.163**
Often	77(27.1)	0.312	0.208-0.416	
Sometimes	48(16.9)	0.208	0.092-0.324	
Rarely	36(12.7)	0.389	0.230-0.584	
Never	14 (4.9)	0.286	0.049-0.523	
How many people did you have commercial (paid) sex with in the past month?				
None	476(91.0)	0.393	0.350-0.436	**0.029**
1-2	15 (2.9)	0.600	0.353-0.847	
3-10	20(3.8)	0.400	0.184-0.616	
More than 10	12 (2.3)	0.083	-0.074-0.240	

Table 3-12 Summary of univariate analyses for retention rate for continuous variables

Variable	Wald	Hazard Ration	95% CI	P-value
Number of close friends (exclude family members)	0.272	1.038	0.903~1.192	0.602
Age of use drugs for the first time	0.036	0.998	0.977~1.019	0.849
Age of start using drugs on a daily basis	0.013	0.999	0.978~1.020	0.911
Family relations and support	**4.328**	**0.898**	**0.811~0.994**	**0.038**
Provider-clients relationship	**42.942**	**0.644**	**0.564~0.734**	**0.000**
Clients' assessment of MMT program	**40.698**	**0.765**	**0.704~0.830**	**0.000**

Table 3-13 Final Cox model with hazard ratios for dropout

	Wald	Exp(B)	95.0% CI for Exp(B)		P value
			Lower	Upper	
Gender					
Male	-	-	-	-	-
Female	7.649	.680	.518	.894	.006
Occupation pattern					
Unemployed	13.247				.0001
Irregular work	7.071	.646	.469	.892	.008
Regular work	6.566	.161	.040	.651	.010
The score of family relationship (points)					
5-10	4.142	.902	.817	0.996	.042
Current marital status					
Never married					
Married	15.794	.631	.503	0.792	.0001
Have you ever dropped out of MMT program					
Yes	-	-	-	-	-
No	5.104	.775	.621	.967	.024
The provider-client relationship					
6-10 points	46.705	0.630	0.552	0.719	0.000
Do you think the dosage is?					
Too little					
About right	8.525	.847	.757	.949	.004
Average daily dose					
< 40 mg	3.213				.201
40-60 mg	2.583	1.305	.943	1.805	.108
> 60	1.391	1.168	.902	1.513	.238

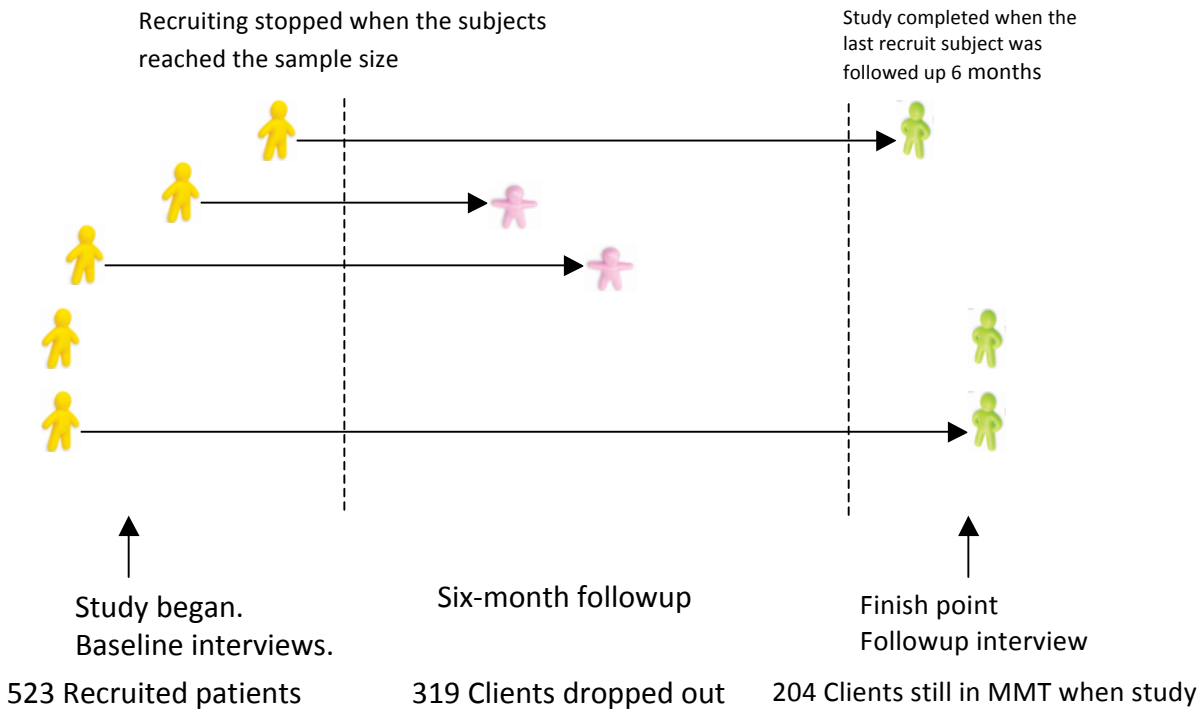

Figure 3-1. Study design Chart

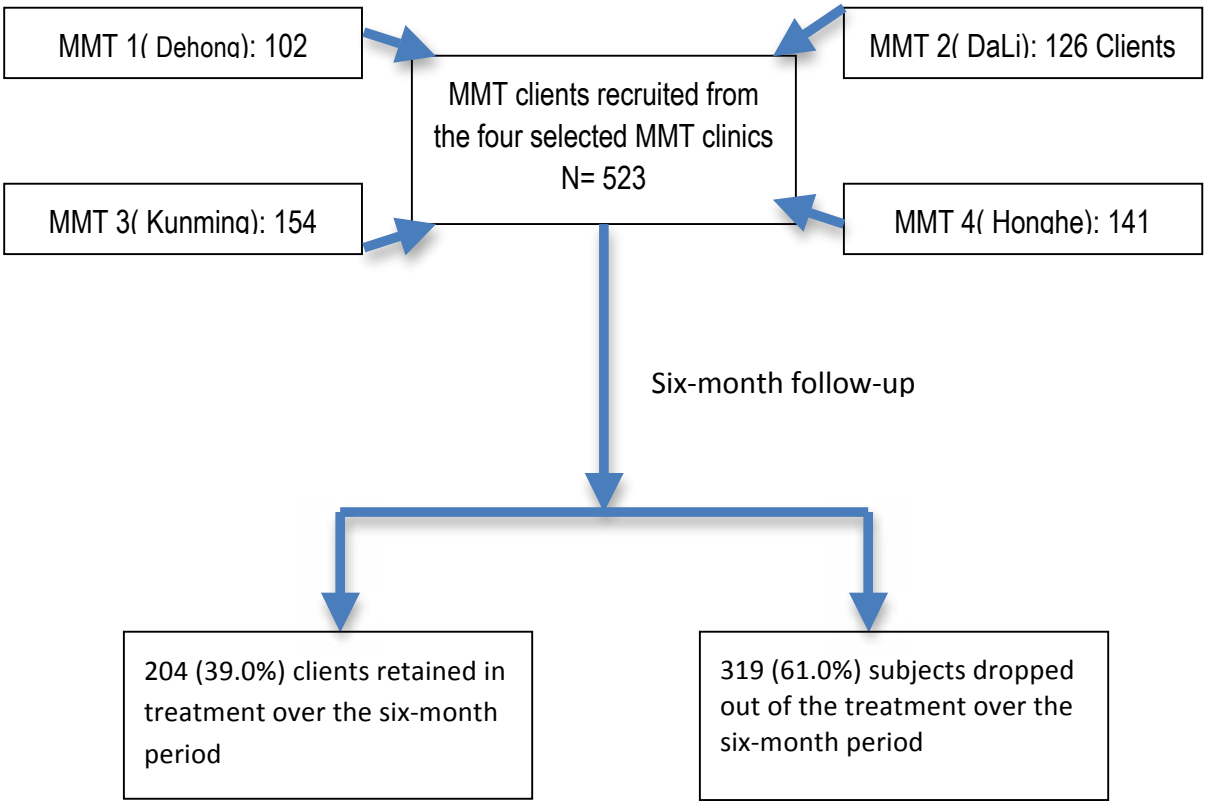

Figure 3-2. Overall retention rate of 523 subjects over six-month follow-up period.

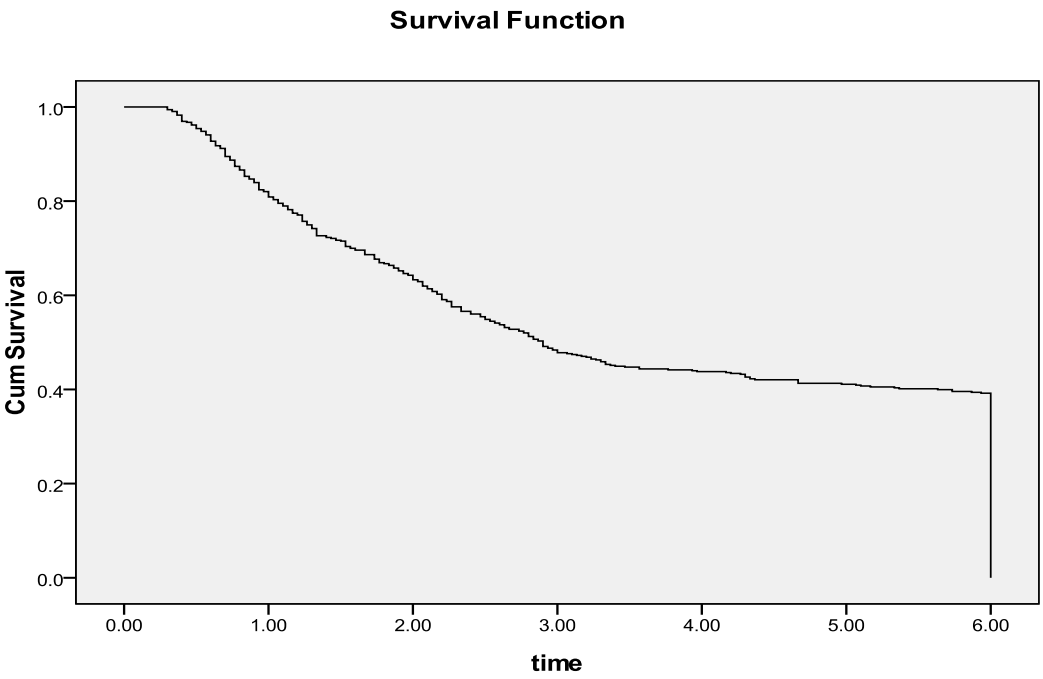

Figure 3-3 Kaplan–Meier survival estimate of retention probability in the subjects

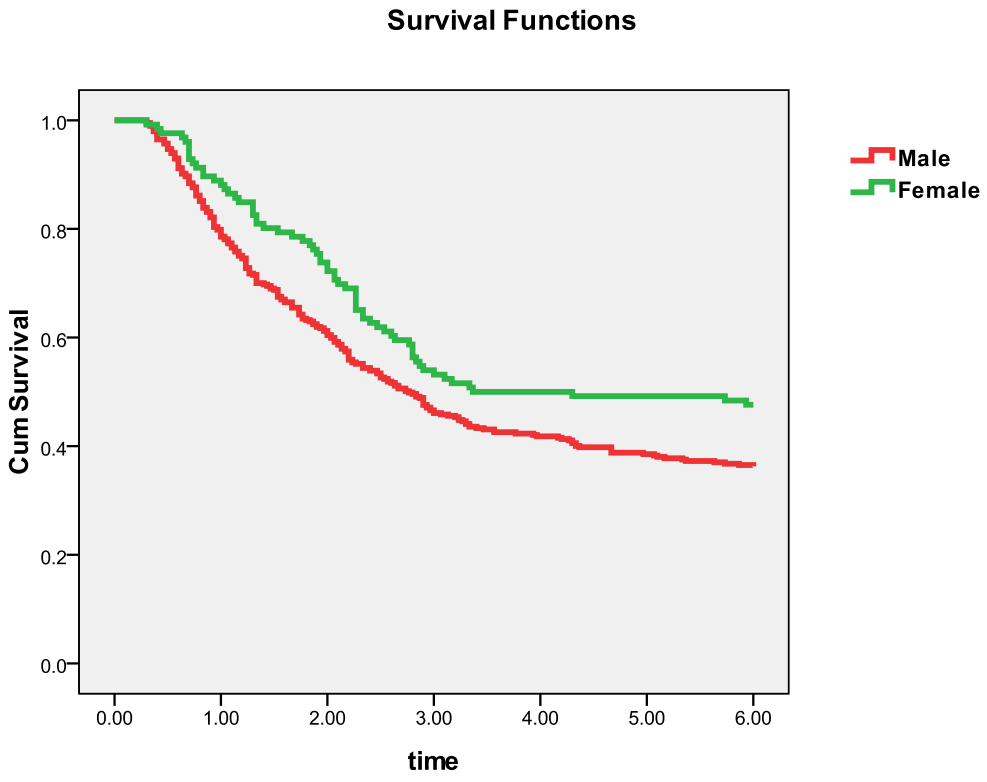

Figure 3-4 Kaplan–Meier survival estimate of retention probability in the participants by gender

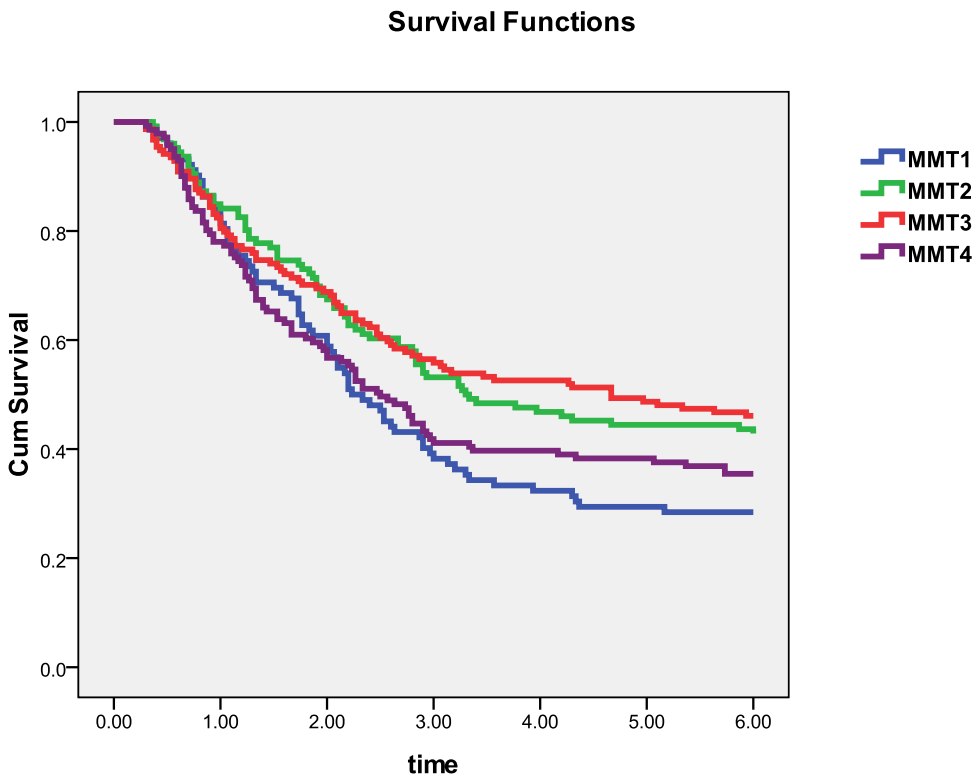

Figure 3-5 Kaplan–Meier survival estimate of retention probability in the participants by clinics

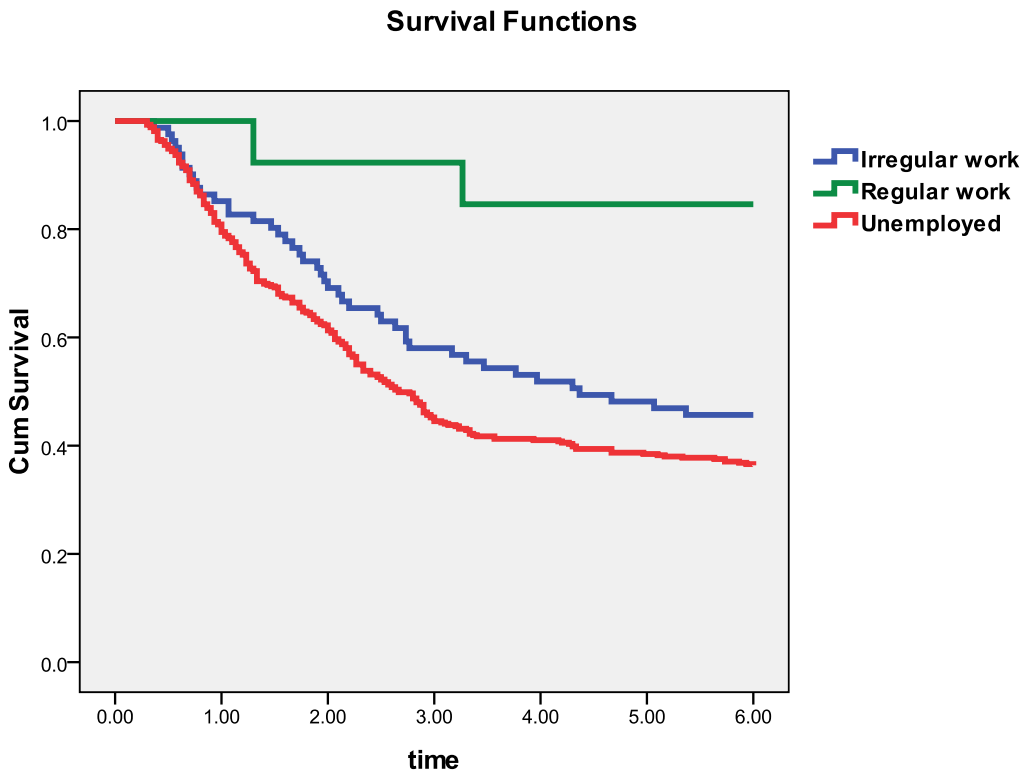

Figure 3-6 Kaplan–Meier survival estimate of retention probability in the participants by occupational pattern

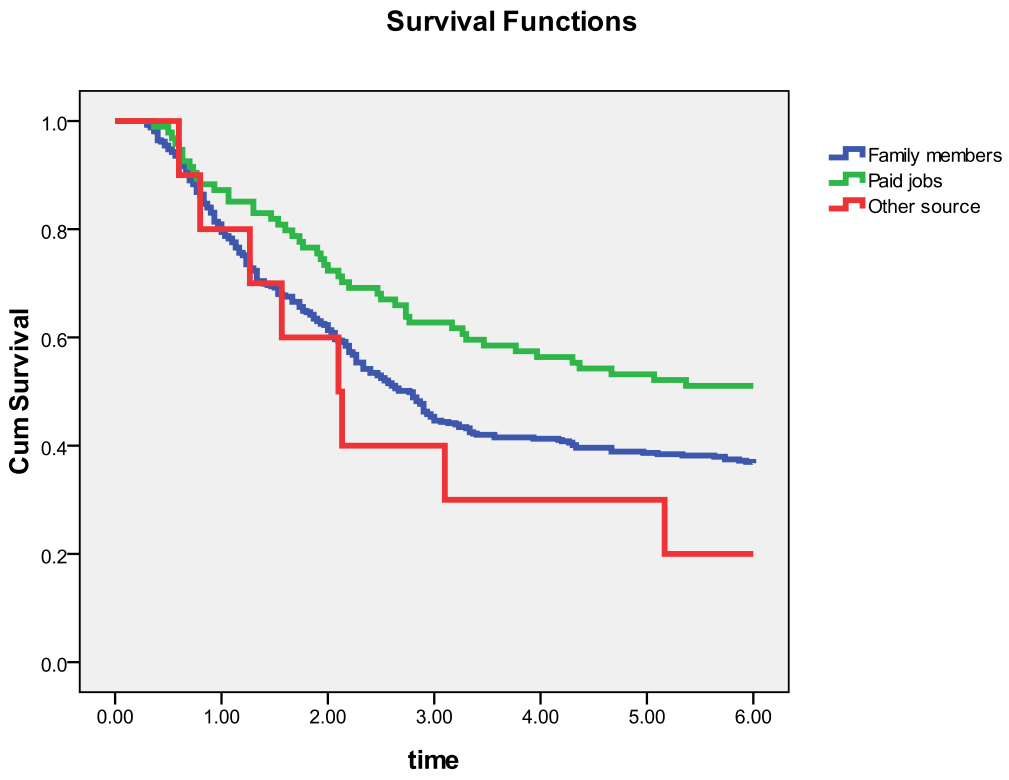

Figure 3-7 Kaplan–Meier survival estimate of retention probability in the participants by the main source of money（During the past 30 days）

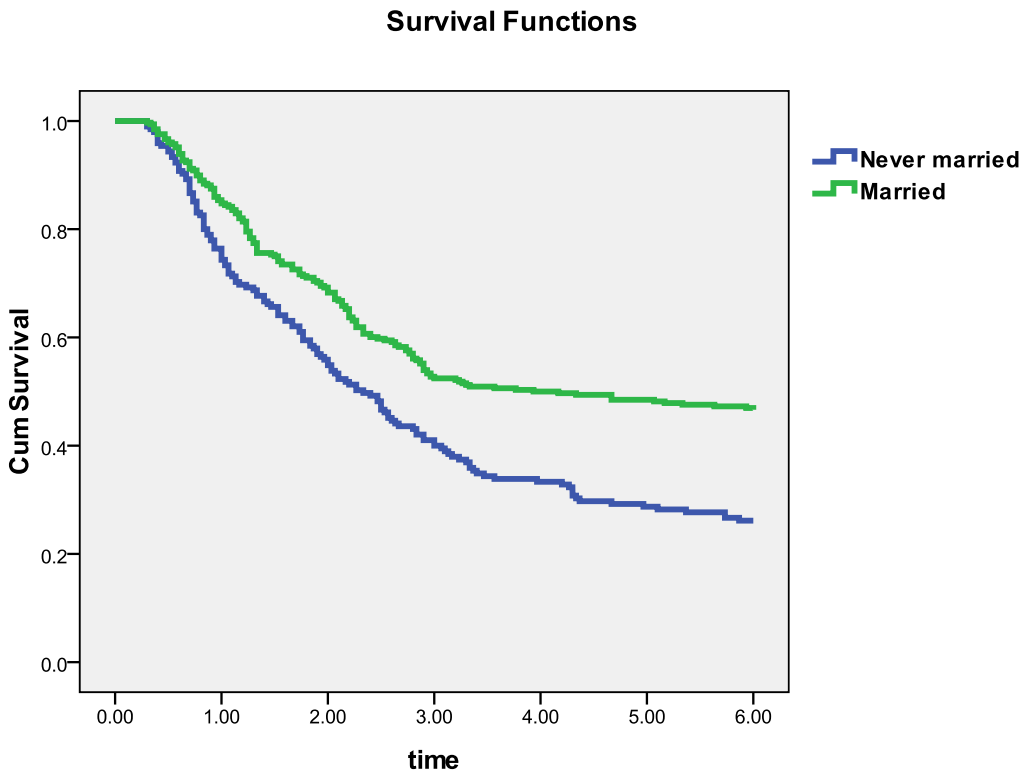

Figure 3-8 Kaplan–Meier survival estimate of retention probability in the participants by marital status

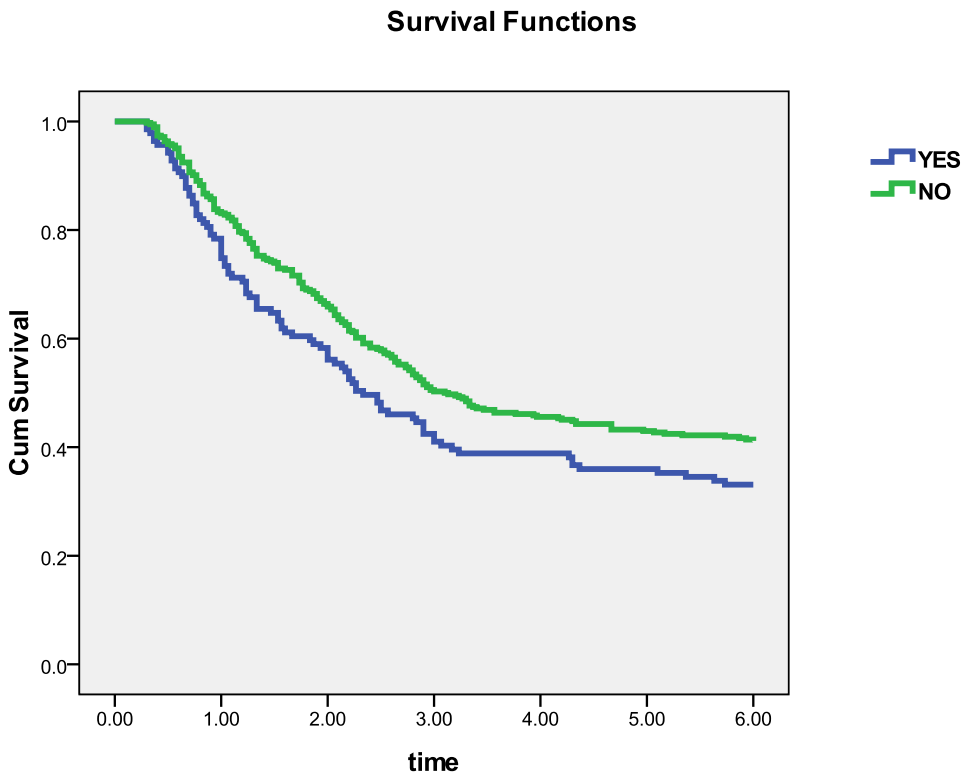

Figure 3-9 Kaplan–Meier survival estimate of retention probability in the participants by share needles

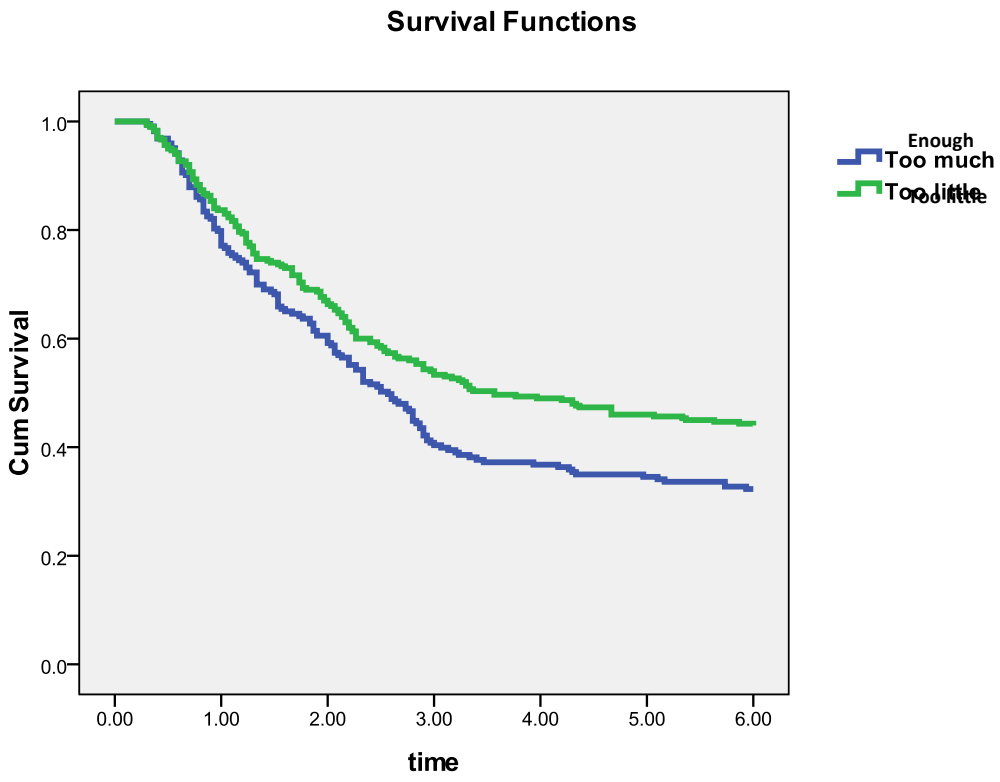

Figure 3-10 Kaplan–Meier survival estimate of retention probability in the participants by the dosage methadone

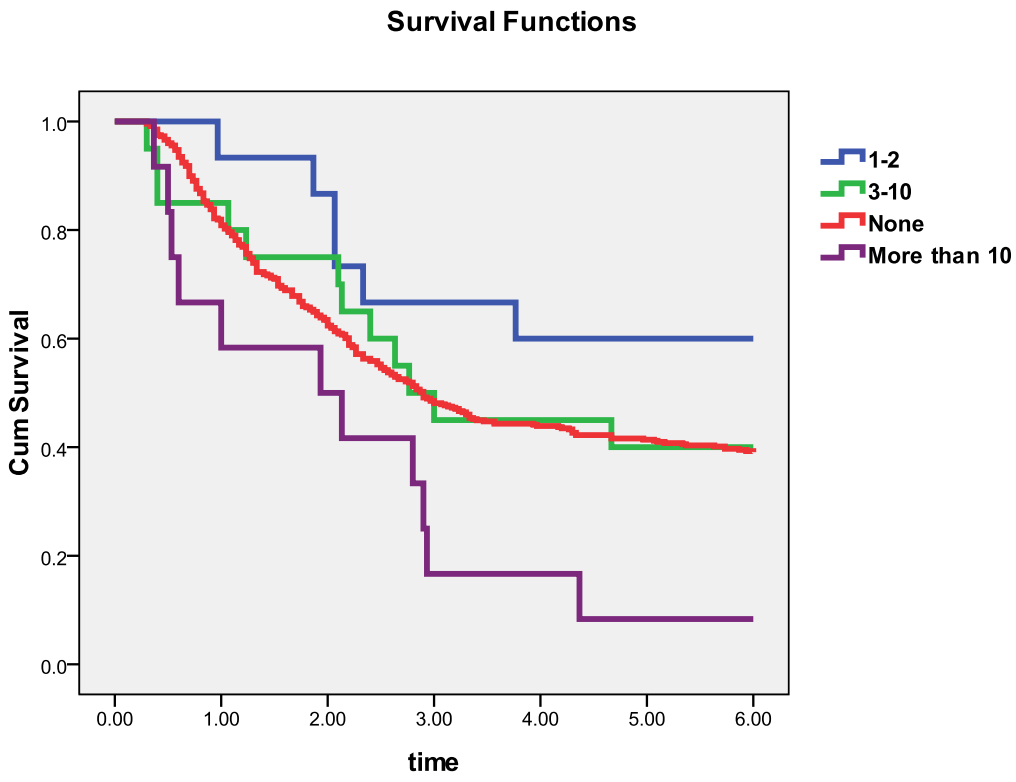

Figure 3-11 Kaplan–Meier survival estimate of retention probability in the participants by commercial (paid) sex

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Chapter IV Research Article 3

The effect of Methadone Maintenance Treatment on Clients' employment, drug use, family relationship, heath status and sexual behavior

ABSTRACT

Objective: This study examined effect of methadone maintenance treatment (MMT) for 204 drug users who entered methadone maintenance between baseline and 6-month follow-up. Effects of MMT included employment, family relationship, physical and mental health status and sexual behaviors.

Methods: A prospective cohort study was employed in this study. 523 clients from the four selected MMT clinics from four city/prefectures of Yunnan Province were recruited into the cohort, beginning on January 2014 and followed up until September 2014. In total, 523 clients completed questionnaire interview at baseline and 204 clients who still remained in MMT clinics were interviewed at six-month follow up. To evaluate the effects of MMT program, this study compared the baseline information and followed up information among the 204 clients who were remaining in the MMT program.

Results: Clients remaining in MMT reduced their heroin using and only 3 clients (1.5%) reported sharing needles in last month at the follow up. The MMT improved the sexual function and the average times of having sex in last month were 2.87 and 3.37 at the baseline and follow up, respectively. Meanwhile, the proportion of having commercial (paid) sex also increased from 8.8% at the baseline to 17.2% at the follow up. These may reveal that the MMT improved the clients' sexual function, which may lead some of clients seeking the commercial (paid) sex in order to meet their sexual needs. MMT clients' condom usage was increased through the 6-

month treatment, but only 30% of MMT clients reported always using condoms when they had sex with regular partner(s) and 47.5% of MMT clients always used condoms when they had sex with causal partner(s). This study also documented that the physical health status of clients retained in the program was improved significantly. However, the psychological health status underwent no considerable improvement through the 6-month MMT. This study showed that there were no statistically significant changes in terms of MMT services utilization between the baseline and follow up.

Conclusions: This study showed that the positive changes in terms of heroin usage, health status and risk sex behaviors for those 204 clients remaining in the treatment. Thus, increasing the coverage and increasing retention of MMT depends on improving the quality of services. Retention in MMT has been demonstrated to reduce drug use and improve the quality of life of those continuing patients. The issue now is to increase the retention rate so that more drug users may benefit.

Key words: Methadone Maintenance Treatment, Effect, Yunnan, China, prospective cohort study, drug users, HIV/AIDS

1. Introduction

Methadone was synthesized in Germany in the 1940s and was used as treatment agent in the mid-1960s for opioid dependence by Dole & Nyswander (1965), functioning as a type of legal opioid substitution therapy (Marsch, 1998). Since the mid-1960s, many researchers have demonstrated the beneficial effects of participation in methadone maintenance programs. These beneficial effects include reduction of illicit drug use, injecting related behavior, criminal behavior, deaths due to overdose, and also with reduced risk of spread of HIV/AIDS, hepatitis C, and other infectious diseases, as well as increases of employment and quality of life among IDUs (Ball, 1991; Gottheil, et al., 1993; Gunne, 1981; Newman, 1979; Strain, et al., 1993; Joseph, et al., 2000).

2. The effectiveness of Methadone Maintenance Treatment (MMT)

2.1 Reduction of illicit drug use

Considerable of evidence has proven that MMT is effective to reduce illicit drug use, especially heroin use among the drug users. A comprehensive evaluation study on MMT programs was conducted in the three east coast of the US by Ball and Ross in 1980s. They followed 617 male heroin addicts for 2 years and found that 70% of patients reduced their heroin use after six months of treatment; by the fourth year, 92% of these patients who stayed in MMT treatment reported no use of heroin and 97% reported no use of other opiates (Ball & Ross, 1991). Marsch conducted a meta-analysis of 11 MMT studies and reported that a statistically significant relationship between MMT and reduction of illicit opiate drug use was found (Marsch, 1998). A repeated cross-sectional survey was carried out in the first phase of eight MMT clinics in China by Peng and et. al, they found that the proportion of clients who injected drugs was reduced from

69.1 to 8.9 and 8.8%, and the frequency of injection in the past month was reduced from 90 times per month to twice per month (Peng, et. al, 2007). Gossp's 2005 study showed that on entry to treatment, there was a prompt and substantial drop in heroin use reported in all clinics (Gossp, 2005).

2.2 Reduced risk of spread of HIV/AIDS, hepatitis C and other infectious diseases

Both the randomized controlled trails and observational studies proved that MMT also prevents transmission of HIV among infected drug users by its reduction of needle-sharing (Hall,1998; Ball & Ross,1991). A large prospective cohort study in the USA has also found that MMT protected against HIV infection (Metzger, 1993). Metzger compared the prevalence and incidence of human immunodeficiency virus (HIV) infection among IDUs in methadone treatment programs and out of methadone treatment in an 18 months follow up study. They found that over 18 months, the odds of HIV infection were 5.4-times greater among those who were not in MMT compared with those who were (Metzger, 1993). Some researchers also believe that Methadone maintenance also can support the early diagnosis of health problems such as HIV/AIDS, because HIV testing can be provided (Meise et al., 2009).

Dolan et al. conducted a randomized controlled MMT trial with a prison population in New South Wales. They found that participants who had been treated by methadone reported a significantly lower prevalence of heroin injection, syringe sharing, and scored lower on an HIV Risk-taking Behavioral Scale than participants who received standard drug treatment and time-limited methadone treatment (Dolan, 2003).

David R. Gibson and his colleagues reviewed 38 studies published since 1987 that examined effectiveness, they found that substantial evidence that methadone maintenance treatment is effective in preventing HIV disease among IDU. Thirty-four of the 38 studies they reviewed contained evidence that methadone maintenance reduces HIV risk behavior and/or HIV seroconversion. Seventeen of these reported statistically significant differences between in-treatment and out-of-treatment IDU; five showed that continuous as opposed to interrupted treatment was associated with decreased risk of infection with HIV (Gibson, 1999).

Since HBV and HCV have a similar transmission pattern as HIV, so MMT programs show the benefit on reduction of HBV and HCV infection as well. Shi and his colleagues conducted a follow-up study among 102 MMT patients, after 6 months follow-up, they found that no participant seroconvert to HCV positivity during the 6 months of MMT (Shi, et, al., 2007).

2.3 Reduction of criminal activities and increase of employment and quality of life

Illicit drug users are more likely at a higher risk of being involved in crimes because of their extreme craving for heroin. Many studies have explored that illicit drug use is highly associated with criminal activities. The money frequently comes from property crime, fraud and drug dealing committed by the users as well as from lawful sources (Grabosky, 1995). The studies also found that participation in MMT program can reduce criminal activity among IDUs (Ball & Ross, 1991; Coid et al., 2000). For example, in a comprehensive study, Coid and his colleagues (2000) found that participation in a community Methadone Treatment Program contributed to decreases in criminal activity. Methadone treatment was associated with a fall in the level of financial gain from criminal activities, and a decrease in the number of reported arrests by the

police during the treatment period. They found that burglaries and thefts were reduced by half and the effect on drug dealing was even greater. Amato and his colleagues reported that patients on substitution therapy were less likely to be involved in crimes (3% involvement in crimes vs 12% among drug users without treatment (Amato et al., 2005). Ball and Ross followed 617 male heroin addicts for 2 years and found that the number of offences during methadone maintenance had been reduced to about 20% of pre-treatment levels (Ball & Ross, 1991). A number of meta-analysis studies on the effectiveness of MMT programs also show that a positive association between the reduction of criminal activities and MMT participation. For instance, Marsch reported that there is a consistent, statistically significant relationship between retention in MMT and the reduction of property-related crimes in her meta-analysis study. (Marsch, 1998). Mattick and his colleagues reviewed eleven randomized clinical trials on the efficacy and MMT intervention. The results of this meta-analysis indicate that there was a greater reduction in criminal activity(3 RCTs, RR=0.39; 95%CI: 0.12-1.25) and mortality(4 RCTs, RR=0.48; 95%CI: 0.10-2.39) among the MMT patients, but these differences were not statistically significant (Mattick, et al., 2009).

2.4 Increase of employment and quality of life

Besides reducing criminal activities among IDUs, MMT programs also increase employment and quality of life. Dole and colleague's study indicated that patient's employment rate was increasing upon entry into the program (Marsch, 1998). Peng and et al. conducted a repeated cross-sectional survey in China, they report that patients' societal and familial functions improved significantly. The employment rate of patients increased from 22.9% at beginning of the MMT program to 43.2% after 6 months of treatment (Peng, et al., 2005). Torrents and et al.

assessed changes in health-related quality of life over a 3-year follow-up period in a cohort of 135 opioid dependent patients (Torrens, 1997).

Very few studies were conducted to evaluate whether MMT programs can help the patients become drug-free. In a German study, 10% of patients who were in substitution maintenance programs became drug-free from both the primary and substitute drug (Kraft, et al., 1997). However, the model of MMT originally proposed by Dole and Nyswander (high doses of methadone, long duration of treatment, intensive rehabilitative services) was modified during its popularization in the 1970s in the USA and Australia. The goal of many programs moved from maintenance towards abstinence from all opioid drugs, including methadone (Ward, et al., 1999).

3. Objective

To evaluated the effectiveness of MMT in terms of employment and financial support, family/social relations, drug using behavior, sexual behaviors, health status and services provision and utilization of MMT in the four MMT clinics.

4. Methods

4.1. Study design

A cohort study was conducted to evaluate the MMT program effectiveness in terms of clients' employment and financial support, family/social relations, drug using behavior, sexual behaviors, health status and services provision and utilization of MMT in the four MMT clinics. The cohort recruitment started on January 1st, 2014. According to the protocol, the study recruited and interviewed (questionnaire) a total of 523 clients from the four selected MMT

clinics from January 2014 to March 2014. The follow-up interviews started in July 2014, and were completed in September 2014. In this study, retention is defined as the client has never stopped taking methadone for a month during the 6-month follow up. According to this study protocol, those clients who had not taken any methadone for a month were considered to dropouts no matter they readmitted or not. In total, 204 clients who remained in the MMT program were interviewed in the follow-up survey. To evaluate the impact of MMT program, this study compared the baseline information and followed up information among the 204 clients who were remaining in the MMT program.

4.2. Study subjects

523 patients were recruited from 4 methadone clinics in Yunnan province, after 6-month follow-up, 319 clients dropped out from MMT clinic. There were 204 clients remained in the MMT and interviewed by employing the follow-up questionnaire. The baseline information and followed up information were compared among the 204 patients.

Among the 204 clients who still remained in the MMT, 70.6% were male and 75% were married. Besides gender and marital status, there was no statistically significant difference in terms of age, education level, ethnicity, age of use drug for first time and age of start injecting drug on a daily basis between those remaining in MMT and those dropping out. For details please see table 4-1.

4.3. Data analysis

This study aimed to evaluate the change of patients' drug using behavior, medical status, sexual behavior, employment status, legal, family social supports and physical and psychological status

over the course of follow up in the four MMT clinics. In this study, we included only those 204 clients who were remaining in MMT program at follow up. Client's changes were compared those 204 clients at baseline and follow up. For continuous variables, the Paired t-test was used to test difference between baseline and follow up. For categorical variables, the McNemar test or McNemar-Bowker test was used. SPSS 17 was used to run the statistics testing.

5. Results

5.1 Employment and financial support

As shown in table 4-2, there were no significant changes in terms of clients' employment and financial support. Some positive changes were observed although the statistic test showed they were not significant. For instance, at baseline 76.5% of clients were unemployed and 70.6% at follow-up; at baseline only 12.5% of clients reported their monthly income were fairly stable and 18.3% at follow-up.

5.2 Family and social relations

This study designed 10 relevant descriptions to evaluate the participants' family relationship, such as 'My family gives me the moral support I need', 'Most other people are closer to my family than I am', 'I have a deep sharing relationship with a number of members of my family' and etc. This study scored 1 point if the participant gave a positive answer and scored 0 point if the participant gave a negative answer. The average score represents the general assessment of clients' family relationship. As shown in table 4-3 at the baseline the average score of clients' family relationship was 4.37, which increased to 4.87 at the 6-month follow up (t-test, $p<0.001$). This increasing showed that the clients have changed the relationship with their family members.

For instance, the proportion of reporting 'I have a deep sharing relationship with a number of members of my family' increased from 34.5% at baseline to 61.3% after 6-month MMT treatment (data is not show in table).

5.3 Drug using behavior

Compared with the baseline survey, the clients' drug using behaviors were changed considerably. As shown in table 4-4, 96.6% of clients used heroin in the past month at the baseline, which decreased to 3.9% at the follow up ($p<0.0001$). The proportion of needles sharing from 22.5% at the baseline decreased to 1.5% at the follow up ($p<0.0001$). The proportions of using heroin and needles sharing were founded very low in this study, which may because of self-disclosure of respondents. Some of the current clients did not report their real status of drug using behaviors because they were afraid that the disclosure would bring negative effect to their treatment in MMT clinic.

5.4 Sexual behaviors

Data in table 4-5 indicated that clients at baseline and follow up significantly differed in the average times of having sex in last month ($p < 0.01$). Average times of having sex was 2.87 reported by clients at the baseline, which was 3.37 times at the follow up. 5.9% of clients self-reported having on sex in the past month at the baseline survey, and only 1.0%(2 clients) at the follow up interview ($p=0.003$). The data also showed that the proportion of having commercial (paid) sex increased from 8.8% at the baseline to 17.2% at the follow up interview ($p=0.039$). The above data indicated that the MMT might increase the clients' sexual activities/interest, which may lead the increase of seeking the commercial (paid) sex.

With regards to condom use, 20.3% of the clients who had regular sex (158) reported that they always used condom when having sex with regular partner(s) at the baseline, which increased to 30.4% (p=0.0003) of the client who had regular sex (184) at the follow up. Similarly, the proportion of always using condom when having sex with casual partner(s) was increased from 38.7% at the baseline to 47.5% at the follow up, although the change was not statistically significant (P=0.2076).

5.5 Physical and psychological health status

This study compared the health status of 204 clients retained in the MMT program at baseline and follow up, the data showed that the physical health status were improved in the 204 clients. 36.3% of clients rated their current general health status as 'good' or 'very good' at the follow up comparing to 15.2% at the baseline (P<0.001). The clients' reported that the quality of sleep has improved comparing to the baseline. At baseline 53.4% of clients reported that sleep 'well' or 'OK', and 73.0% at the follow up. After 6-month MMT treatment, the clients' satisfaction with capacity for work was also improved. 53.9% of clients were satisfied with their capacity for work at the follow up, and 38.2% at the baseline (p=0.006).

Psychological problems of the baseline and follow up were also presented in Table 4-6. This showed that, there was no significant difference between the baseline and follow up for the mental health status, which included serious depression, serious anxiety or tension, hallucinations, trouble understanding, concentrating or remembering and trouble controlling violent behavior including episodes or rage or violence.

5.6 Services provision and utilization of MMT

Table 4-7 showed that information related MMT services provision and utilization of 204 clients who retained in treatment at baseline and follow up. The overall clients' assessment towards MMT program was improved comparing the baseline and follow up. The score was generated from the four statement: i) The MMT program has improved my quality of life; ii) The MMT program has improved my health; iii) The MMT program has helped me improve my family relationships and iv) Overall, I am satisfied with my experiences with the MMT program. The average scores were 0.662 and 0.934 at the baseline and follow up respectively p=0.009). This revealed that the clients who retained the MMT program increasing the acceptance and the satisfaction of MMT along with staying in the program. However, except for the overall assessment of MMT program, there was no statistically significant changes in terms of MMT services provision and utilization between the baseline and follow up. For instance, there were on significant improvement of provision and utilization of supportive services, such as psychological counseling, treatment for side effects, although the clients had already been in MMT program for at least six months.

6. Discussion

As stated in the results, clients remaining in MMT reduced their heroin using, 96.1 % clients self-reported to be abstaining from use of heroin at the follow up. Additionally, only 3 clients (1.5%) reported sharing needles in last month at the follow up. These findings were consistent with other studies conducted both in China and oversea (Peng L, etc 2007; Shi J, etc., 2007, Wald J & Hall W, 1999). Since eight pilot clinics established in 2004, China has rapidly scaled

up MMT program nationwide. 738 clinics that had already served over 340 000 clients cumulatively as of the end of 2011, and China's MMT Program is now recognized as the largest single opioid agonist maintenance treatment program in the world (Pang L, etc 2007; Yin W, etc., 2010; Sullivan SG & Wu Z 2014.) Given the situation, the MMT program in China has made a considerable reduction of drug use in the country. Estimation was reported by Wenyuan Yin, in 2008 and 2009, respectively, consumption of heroin was reduced by 17.0 tons and 22.4 tons, and $US939 million and US$1.24 billion in heroin trade were avoided. In Yunnan province, MMT program cumulatively served 137,724 drug users for last decade. Assuming 0.6 gram heroin consumed per drug user per day and 370 Yuan (US$ 60) per gram, in total 30.16 tons heroin was reduced and US$ 1.83 billion in heroin trade was avoided.

This study documented that the MMT improved the sexual function and the average times of having sex in last month were 2.87 and 3.37 at the baseline and follow up, respectively. These findings were consistent with other studies conducted in China (Bai Xian, etc, 2009; Ailikemuyahufu & Zhang R, etc, 2009). Bai et al documented that 67.3% of MMT clients self-reported there was improvement in terms of sexual functions by MMT treatment. Ailikemuyahufu and Zhang reported that the average times of having sex in last month were 2.70 and 4.86 during the period when they were using heroin and after 12-month treatment. Other studies conducted in western counties note that methadone patients report an increase in libido upon entering methadone treatment, as com- pared to the period when they were using heroin (Herman Joseph, etc., 2000).

Interestingly, along with the increasing of times of having sex, the proportion of having commercial (paid) sex also increased from 8.8% at the baseline to 17.2% at the follow up. These may reveal that the MMT improved the clients' sexual function, which may lead some of clients seeking the commercial (paid) sex in order to meet their sexual needs. This hypotheses need to be researched and proved in further studies. Meanwhile, increasing of having commercial (paid) sex among the clients who retained in MMT program should be considered.

Despite the finding that MMT clients' condom usage was increased through the 6-month treatment, we cannot ignore the fact that only 30% of MMT clients reported always using condoms when they had sex with regular partner(s) and 47.5% of MMT clients always used condoms when they had sex with causal partner(s). These findings suggested that relevant health education and provision the free condom in MMT clinics must be encouraged and strengthened. Numerous studies have demonstrated the effectiveness of MMT for improving the clients' physical and mental health (Lowinson et al., 1997; Žilvinas Padaiga et al., 2007). This study also documented that the physical health status of clients retained in the program was improved significantly. However, the psychological health status underwent no considerable improvement through the 6-month MMT. McLellan's study stated that: "At 24 weeks, methadone alone resulted in minimal improvements; methadone plus counseling resulted in significant improvements over methadone alone; and enhanced methadone services, including a broad range of psychosocial services plus methadone, had the best outcomes of all (McLellan et al., 1993)." According this, our study findings suggested that the treatment of psychological problems might need long-term treatment and comprehensive services.

This study showed that there were no statistically significant changes in terms of MMT services utilization between the baseline and follow up. Furthermore, because of the low availability and accessibility of ancillary services provided in the MMT clinics, only 19.6% of clients have received psychological counseling and 23.8 % have received the treatment for their side effects in the MMT clinic at the follow up. 87.8% of clients have received health education at the MMT clinic, but the topics of health education only limited to HIV/AIDS. Fortunately, China's methadone maintenance program has recognized that comprehensive services are associated with improved treatment outcome. "Increasing the quality of services and providing comprehensive service" were set as the first priority of the MMT program in China (Yin, et al., 2010). In December 2014 the State Ministry of Health and Family Planning Commission, Ministry of Public Security and the State Food and Drug Administration jointly issued *"The Regulation for the administration of drug maintenance therapy".* According to the Regulation, the MMT clinics must provide the comprehensive ancillary services to clients in MMT besides the regular methadone maintenance treatment. The ancillary services included: psychological counseling, psychosocial support, health education, HIV/HCV/syphilis counseling and testing, referrals for related health issues (SHFPC, 2014). To achieve this goals, services staff capacity building through well-designed intensive training and encouraging the multi-sector cooperation at both national and local level have been implementing in China (Yin, et al., 2010).

There were certain limitations with internal validity and external validity of this study. First, it should be noted that this study were inherently biased because it only was able to measure outcomes among the 39% of clients who still retained the MMT program after 6-month follow up. Clients who were able to retain in MMT program for 6 months had better compliance than

those who dropped out. Therefore, the results of this study overestimated the impact of MMT programs on the totality of drug users. Second, this study only followed up for 6 months due to the limited time and budget. Therefore, the outcomes of MMT, especially the long-term outcomes, could not be fully evaluated. Third, self-reporting questionnaire was employed to collect the information in terms current drug using, risky sex behaviors, perceived physical and mental health status. Self-disclosure might be an issue in the study because the results depend entirely on the accurate recollections of the participants. Therefore, the results need to be interpreted with a great deal of care.

Nevertheless, even with the limitations noted above, this study showed that the positive changes in terms of heroin usage, health status and risk sex behaviors for those 204 clients remaining in the treatment. Thus, increasing the coverage and increasing retention of MMT depends on improving the quality of services. The comprehensive approach and services must be provided to clients rather than only prescribing methadone dose. Additionally, human resource development and capacity building for MMT services staff, as well as the multi-sector cooperation must be considered and enhanced as recommended by Liu et al (Liu, et al, 2008). Retention in MMT has been demonstrated to reduce drug use and improve the quality of life of those continuing patients. The issue now is to increase the retention rate so that more drug users may benefit.

Table 4-1 Demographic information of retained clients and dropouts of MMT program

Characteristics	Retained clients (%) N=204	Dropouts (%) N=319	P-value
Gender			
Male	144(70.6)	253(79.3)	**0.023**
Female	60(29.4)	66(20.7)	
AGE			
20-30	17(8.3)	29(9.1)	0.903
30-40	106(50.2)	162(50.8)	
40-50	75(36.8)	115(36.1)	
50+	6(2.9)	13(4.1)	
Education level			
Never completed primary school	27(13.2)	32(10.0)	0.223
Primary school	105(51.5)	186(58.3)	
Middle school	66(32.4)	86(27.0)	
High school or above	6(2.9)	15(4.7)	
Ethnicity			
Han	125(38.7)	179(43.9)	0.243
Minority	79(61.3)	140(56.1)	
Current marital status			
Never married	51(25.0)	144(45.1)	**0.000**
Married	153(75.0)	175(54.9)	
Age of use drugs for the first time (mean +-SD)	18.89±5.50	18.78±5.09	0.813
Age of start using drugs on a daily basis (mean +-SD)	19.41±5.51	19.32±5.16	0.851
Age of start injecting drugs on a daily basis	22.77±5.95	22.75±5.72	0.963

Table 4-2 the comparison of employment/financial support of the 204 clients remaining in the treatment baseline and follow-up

	Baseline	Follow-up	T/χ^2	P
Occupation pattern				
Regular work	11(5.4)	11(5.4)	2.154	0.179
Irregular work	37(18.1)	49(24.0)		
Unemployed	156(76.5)	110(70.6)		
Income (n=100)				
Mean ±SD	2401.04 ±596.57	2232.50 ±677.78	1.832	
How stable is your monthly income from your current job (baseline: n=48, follow-up: n=60)				
Unstable	42(87.5)	49(81.7)	0.684	0.408
Fairly stable	6(12.5)	11(18.3)		
Does someone contribute to your support in any way?				
no	8(3.9)	11(5.4)	0.497	0.481
yes	196(96.1)	193(94.6)		
On average, how much money per month do you get from your family/friends/institution?(n=38)				
Mean ±SD	1178.57 ±784.78	1079.41 ±598.45	0.184	0.170
How would you evaluate your current economic condition?				
Very poor	87(44.4)	85(44.0)	0.547	0.909
Below average	81(41.3)	83(43.0)		
Average	23(11.7)	22(11.4)		
Above average	5(2.6)	3(1.6)		

Table 4-3 the comparison of family and social relations of the 204 clients remaining in the treatment baseline and follow-up

	Baseline	Follow-up	T/χ^2	P
How many persons are there in your family (including yourself)				
Mean ±SD	2.76 ±0.938	2.77 ±0.935	0.011	0.916
Are you satisfied to be living with these people?				
No	49 (24.0)	44(21.6)	0.993	0.609
Indifferent	22(10.8)	28(13.7)		
Yes	133(65.2)	132(64.7)		
Score of family relationship				
Mean ±SD	4.37 ±1.06	4.87 ±1.32	-4.146	<0.001
With whom did you spend most of your free time with during the past year?				
Family	41 (20.1)	38(18.6)	0.141	0.932
Friends	105 (51.5)	107(52.5)		
Alone	58(28.4)	54(28.9)		
Do your family members support you for MMT?				
Yes	192 (94.1)	195(95.6)	0.336	0.845
No	2 (1.0)	1(0.5)		
They don't know about it	10(4.9)	8(3.9)		

Table 4-4 the comparison of drug using behavior of the 204 clients remaining in the treatment baseline and follow-up

	Baseline	Follow-up	T/χ^2	P
How many times did you use drugs in past month?				
Did not use	7 (3.4)	196(96.1)	365.966	<0.0001
Once a week or less	3 (1.5)	5(2.5)		
More than once a week but less than once a day	5(2.5)	3(1.5)		
2-3 times a day	175(85.8)	0(0.0)		
More than 3 times a day	14(6.9)	0(0.0)		
Did you share needles with others during in past month?				
NO	158(77.5)	201(98.5)	51.845	<0.001
YES	46(22.5)	3(1.5)		

Table 4-5 the comparison of sexual behaviors of MMT of the 204 clients remaining in the treatment baseline and follow-up

	Baseline	Follow-up	T/χ^2	P
How many times did you have sex in the past month?				
Average times	2.87	3.37		0.001
None	12(5.9)	2(1.0)	17.987	0.003
One	36(17.6)	33(16.2)		
Two	96(47.1)	79(38.7)		
3-5	37(18.1)	61(29.9)		
6-10	10(4.9)	19(9.3)		
More than 10	13(6.4)	10(4.9)		
How often did you use condoms when having sex with your regular partner(s) in the past month?				
Every time	32(20.3)	56(30.4)	21.010	0.0003
Often	21(13.3)	44(23.9)		
Sometimes	49(31.0)	54(29.3)		
Rarely	48(30.4)	25(13.6)		
Never	8(5.1)	5(2.7)		
Total	158	184		
How often did you use condoms when you had sex with casual partners?				
Every time	48(38.7)	47(47.5)	5.88	0.2076
Often	40(32.3)	24(24.2)		
Sometimes	21(16.9)	10(10.1)		
Rarely	13(10.5)	14(14.1)		
Never	2(1.6)	4(4.0)		
Total	124	99		
How many people did you have commercial (paid) sex with in the past month?				
None	186(91.2)	169(82.8)	11.700	0.039
One	3(1.5)	12(5.9)		
Two	6(2.9)	14(6.9)		
3-5	2(1.0)	5(2.5)		
6-10	6(2.9)	3(1.5)		
More than 10	1(0.5)	1(0.5)		

Table 4-6 the comparison of health status of MMT of the 204 clients remaining in the treatment baseline and follow-up

	Baseline	Follow-up	T/χ^2	P
How do you rate your current general health level?				
Very good	2(1.0)	4(2.0)	24.614	**<0.001**
Good	29(14.2)	70(34.3)		
OK	162(79.4)	122(59.8)		
Poor	10(4.9)	6(2.9)		
Very bad	1(0.5)	2(1.0)		
Do you need any medical treatment to function in your daily life?				
Yes	53(26.0)	51(25.0)	0.052	0.820
No	151 (74.0)	153(75.0)		
Do you sleep well?				
Good	11(5.4)	46(22.5)	32.517	**<0.001**
OK	98(48.0)	103(50.5)		
Poor	69(33.8)	42(20.6)		
Very bad	26(12.7)	13(6.4)		
How satisfied are you with your capacity for work?				
Very good	18(8.8)	18(8.8)	14.284	**0.006**
Good	23(11.3)	41(20.1)		
OK	37(18.1)	51(25.0)		
Poor	120(58.9)	93(45.6)		
Very bad	6(2.9)	1(0.5)		
How many doctor or hospital/clinic visits (exclude visiting MMC) did you have in the past three months?				
No	52(25.5)	54(26.5)	0.212	0.976
1-2 times	83(40.7)	81(39.7)		
3-5 times	50(24.5)	52(25.5)		
more than 5 times	19(9.3)	17(8.3)		
How many times have you been treated for any psychological or emotional problems? (in a hospital or inpatient setting=296)				
yes	7(4.7)	6(4.1)	0.067	0.796
No	142(95.3)	141(95.9)		
Experienced serious depression (Past 30 Days)				
No	87(51.8)	96(54.9)	0.325	0.569
Yes	81(48.2)	79(45.1)		
Experienced serious anxiety or tension (Past 30 Days)				
No	106(63.5)	114(67.5)	0.589	0.443
Yes	61(36.5)	55(32.5)		
Experienced hallucinations(Past 30 Days)				
No	158(81.4)	151(82.1)	0.024	0.876
Yes	36(18.6)	33 (17.9)		
Experienced trouble understanding, concentrating or remembering(Past 30 Days)				
No	73(36.7)	76(40.4)	0.572	0.450
Yes	126(63.3)	112 (59.6)		
Experienced trouble controlling violent behavior including episodes or rage or violence(Past 30 Days)				
No	92(52.9)	91(54.8)	0.129	0.719
Yes	82(47.1)	75 (45.2)		

Table 4-7 the comparison of services utilization of MMT of the 204 clients remaining in the treatment baseline and follow-up

	Baseline	Follow-up	T/χ^2	P
What is your overall goal in the MMT program				
To take MMT for life time, and not use drugs anymore	75(36.8)	80(39.2)	1.162	0.559
To use MMT for life time, and reduce the use of drugs	22(10.8)	27(13.2)		
Try to quit drugs and MMT after a period of time	107(52.5)	97(47.5)		
Is the payment for MMT an economic burden for you				
Yes	131(64.2)	130(63.7)	0.011	0.918
No	73(35.8)	74(36.3)		
How much time do you spend in traffic to get to the MMT clinic every day?				
BELOW 30 MINUTES	62(30.4)	60(29.4)	0.382	0.826
30-60 MINUTES	82(40.2)	88(43.1)		
MORE THAN 60MINUTES	60(29.4)	56(27.5)		
Is the location of MMT clinic is convenient for you?				
Yes	145(71.1)	157(77.0)	1.835	0.176
No	59(28.9)	47(23.0)		
Have you received psychological counseling at the MMT clinic?				
Yes	35(17.2)	40(19.6)	0.408	0.523
No	169(82.8)	164(80.4)		
Have you received HIV education at the MMT clinic?				
Yes	166(81.4)	179(87.8)	3.172	0.075
No	38(18.6)	25(12.3)		
Have you experienced side effects from methadone?				
Yes	46(22.5)	42(20.6)	0.232	0.630
No	158(77.5)	162(79.4)		
Do you receive treatment for methadone side effects?(n=88)				
Yes, outside the MMT program	2(4.3)	2(4.8)	0.587	0.746
Yes, from MMT program	8(17.4)	10(23.8)		
No	36(78.3)	30(71.4)		
Do you receive employment training or counseling in the MMT program?				
Yes	0(0.0)	0(0.0)	-	-
No	204(100.0)	204(100.0)		
Provider-clients relationship				
Mean ±SD	0.446 ±0.704	0.456 ±0.676	-0.136	0.892
Clients' assessment of MMT program				
Mean ±SD	0.662 ±1.125	0.934 ±0.949	-2.638	**0.009**

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