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2012

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UNIVERSITY OF CALIFORNIA

Los Angeles

Partnership Status, Continued Drug Use and Treatment Adherence among  
Newly Enrolled Methadone Maintenance Therapy Patients in China

A Dissertation Submitted in Partial Satisfaction of the  
Requirements for the Degree Doctor of Philosophy  
in Epidemiology

By

Dai Wan

2012

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## ABSTRACT OF THE DISSERTATION

Partnership Status, Continued Drug Use and Treatment Adherence among  
Newly Enrolled Methadone Maintenance Therapy Patients in China

By

Dai Wan

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2012

Professor Roger Detels, Chair

**Background:** Social support has been studied by a series of authors as a factor to improve treatment outcome of MMT. The influence of social support could be much more profound in a country like China which has a family-oriented culture. As partnership status (e.g. whether living with a regular partner and/or drug use status of the regular partner) are potentially strong predictors for treatment outcome of MMT, the impact of these factors remains poorly understood. In this study, we aimed to test the hypothesis that living with a drug-using regular sex partner was associated with higher odds to drop out of treatment and increased probability of ongoing substance use while maintained on treatment. We also aimed to find out how actively the regular sex partners had been involved with the treatment support, and to identify the benefits brought by MMT to them and their relationship with the drug user and what the challenges remained for better support.

**Method:** The study was conducted in two provinces in central China. The study was comprised of a qualitative section and a quantitative section. For the qualitative study, 20 patients were recruited from five participating clinics. As 5 of the 20 participants were single, we were able to recruit a total of 15 regular sex partners. The patients and their partners were in-depth interviewed separately. For the quantitative study, a survey was administrated using ACASI in a private room at each clinic with 500 patients recruited from 20 randomly selected clinics. Three and six months after the baseline survey, the treatment status, most recent urine test result for drug use and most recent HIV test result was collected.

**Results:** Participants who had a drug-using regular sex partner were less likely to continue to use substance at 3-months and they were also were less likely to stay in treatment at 6 months after enrollment. Participants who received a higher dose of methadone were less likely to be retained at 3-months. All participating partners had a good experience with methadone by observing the improvement in both physical and psychological health of their partners who had enrolled. The financial burden brought by substance use was greatly relieved. The drug-using partners who had not yet enrolled for MMT themselves planned to enroll after seeing the improvement of their partners. Some partners had played their part in reducing the occurrences of continued drug uses. The overall acceptance of long-term adherence among new patients and their partners was low. Rumors about use of methadone would damage one's kidney and liver were commonly believed by both the patients and their partners. On the other hand, during their short course in treatment the patients and their partners showed high level of satisfaction towards the effectiveness of MMT and the quality of service received. A daily visit to the MMT clinic and cost of medication was logistically manageable for most patients.

**Conclusion:** We urge the staff at MMT clinics to pay special attention on the concordant drug-using couples as they are at greater risk for relapse and drop out in the long run. Special counseling for couples would be helpful. The staff at MMT clinics should work closely with the partners for improved treatment outcomes. The partners are the key contact person to be reached in case a patient starts being absent from treatment. The partners should then be included in the educational programs held at the clinics. The programs also provide the partners an opportunity to meet one another and exchange ideas for better support. Training of the clinic staff is necessary for them to better understand the nature of methadone and how it works then they could better educate their patients. The popular opinion leader approach could be considered to counter the rumors of methadone's bad side effect. The first few months in treatment are vitally important for long-term adherence and therefore the best possible time to educate the patients and partners about the importance of the maintenance nature of MMT.

The dissertation of Dai Wan is approved.

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2012

**DEDICATION**

To My Parents

And

George X. Ouyang



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## ACKNOWLEDGEMENTS

I would like to extend my sincerest gratitude to the members of my doctoral committee, Drs. Abdelmonem A. Afifi, Li Li, Pamina M. Gorbach, and Roger Detels. My dissertation project would not have been accomplished without their guidance and support.

I reserve my greatest thanks for my advisor, Professor Detels who gave me the opportunity to study in UCLA and supported me along the progress of my study, field work and dissertation. I would like to express my great appreciation to Dr. Li, who has been supervising my research during the past few years. The opportunity working with her team is such a valuable experience for me when I started my own research. I also greatly appreciate the guidance and contribution from Dr. Gorbach for my dissertation proposal, data analysis and defense. The input from Dr. Afifi on the statistical analysis of my proposal and dissertation is very helpful. I also want to thank all the professors and staff at Department of Epidemiology, especially Dr. Roberta Malmgren, Wendy Aft, Deborah Shin, and Joy Miller. The support from fellow Fogarty scholars and classmates and friends from school of public health is greatly appreciated, too.

My special thanks go to Dr. Zunyou Wu, Director of National Center for AIDS/STD Prevention and Control, Chinese Center for Disease Prevention and Control and the colleagues of the Division of Health Education and Behavioral Intervention at China CDC. Without their support and assistance this work would not have been possible. I would also like to show my appreciation to my collaborators from CDC of Hubei and Shannxi Province and staff at each participating methadone clinics. Last but not least, this project is not accomplishable without the contribution of all study participants.

This project is funded by UCLA/Fogarty AIDS International Training & Research Program, Grant number: D43 TW000013.

## VITA

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## **CHAPTER I**

### **Introduction**

#### **Background**

Epidemic estimates indicated that at the end of 2011, the estimated number of people living with HIV infection in China was 780,000. Among them, 28.6% were women. There were altogether 154,000 AIDS cases. The country-wide prevalence stood at 0.058% (State Council AIDS Working Committee Office, UN Theme Group on AIDS in China, 2012). Though surpassed by heterosexual transmission in recent years, injecting drug users (IDUs) were still the second largest contributor of HIV infections in China. In 2011, IDUs accounted for 16.9% of newly reported HIV cases. Heroin was the main illicit drug used. About 85% of the IDUs claimed heroin abuse (Sullivan & Wu, 2007). The prevalence of syringe sharing among IDUs has been estimated at 40% (Xiao, Wu & Luo, et al., 2010). In addition to unsafe injecting practices, drug users in China also commonly engage in risky sexual practices that put their partners at a greater risk of HIV infection (Liu, Lian & Zhou et al., 2001; Wu, Detels, & Zhang, 1996).

In the battle to fight against HIV transmission among IDUs, Methadone Maintenance Therapy (MMT) was introduced to China in year 2004. The eight pilot MMT clinics in the five provinces with the highest HIV prevalence were successful in reducing illicit drug abuse, in reducing drug-related criminalities and in improving the IDUs' quality of life and opportunities of employment (Pang, Hao & Mi et al., 2007). The MMT program was then rapidly scaled up throughout the country. By the end of 2011, there were a total of 738 MMT clinics across 623 counties in 28 (out of 31) provinces. The cumulative number of drug addicts who had ever received treatment was 344,000 and 140,000 people were currently receiving treatment (State Council AIDS Working Committee Office, UN Theme Group on AIDS in China, 2012). MMT clients pay 10

Yuan (U.S. \$1.60) for their daily treatment and take methadone once a day under the supervision of a clinic staff. A urine test is required to be taken once a month on a random date. HIV test is required twice yearly.

As its name suggests, MMT is a corrective replacement therapy, rather than a curative treatment (Joseph, Stancliff & Langrod, 2000). Maintenance of usage is then an important indicator of successful treatment. Two years of MMT appears to be the minimum duration before attempting withdrawal (Jaffe & O’Keeffe, 2003). The benefits of long-term methadone maintenance are borne out by data (NIH, 1997). Even patients receiving maintenance for long periods with substantial lifestyle changes often relapse after leaving treatment and their death rates were much higher than for individuals who remained in treatment. For many patients, therefore, years or even lifetime maintenance may be needed (Kleber, 2008).

It has long been reported that methadone has been viewed by both patients and treatment providers alike with some degree of ambivalence (Zweben & Sorensen, 1988). Perceived negative side-effects of methadone, a dislike for the rigid requirements demanded by MMT and fear of withdrawal from methadone upon incarceration or involuntary discharge are reported by opiate-dependent individuals as reasons for not entering MMT (Peterson, Schwartz & Mitchell et al., 2008). Common negative beliefs about methadone include the view that it is harmful to teeth and bones, that it is more damaging to health than heroin, and that withdrawing from methadone is nearly impossible (Stancliff, Myers & Steiner et al., 2002). A series of authors demonstrated that some patients believed that methadone (1) is difficult to discontinue once initiated; (2) interferes with their daily lives; (3) has serious side effects; and (4) has low “status” in the community (Goldsmith, Hunt & Lipton et al., 1984; Hunt, Lipton & Goldsmith et al., 1985). Other studies found that more than half the drug users perceived that MMT was harmful to their

health, thinking that it would damage their immune system or get into their bones (Zaller, Bazazi & Velazquez, 2009; Schwartz, Kelly & O'Grady, 2008). Many drug users believed that high methadone dosages would be harmful to health (Stancliff, Myers & Steiner et al., 2002). Negative attitudes toward methadone can lead many patients to leave MMT programs prematurely (Stancliff, Myers & Steiner et al., 2002), which can result in relapse to heroin use and a return to behaviors that put individuals at high risk for drug-related morbidity and mortality (Gowing, Farrell & Bornemann et al., 2008; Sheerin, Green & Sellman et al., 2004; Langendam, van Brussel & Coutinho et al., 2001). Interventions that correct the negative attitudes and to improve acceptance of long-term adherence would contribute to better treatment retention.

The association between low acceptance of long-term treatment and treatment adherence among Chinese patients has been discussed by a series of authors. Liu et al. (2009) reported that patients who expect to be treated for life have higher retention rates than patients who anticipate only short-term treatment. Xu et al. (2012) surveyed 300 first-time MMT patients from 3 clinics in Guangzhou, China regarding their acceptance of long-term adherence to MMT. Over 90% of the participants believed MMT is intended primarily for detoxification. About two thirds of the participants considered one could be completely detoxified and quit using methadone after 2–3 months. About 78% did not consider MMT as a long-term or even lifetime treatment. A total of 84.3% thought that one should attempt to reduce treatment dosage as methadone is harmful to one's health, and 48.5% of the participants held all four negative beliefs. The same group of researchers (Gu, Xu & Lau et al., 2012) reported that patients who held two to three negative beliefs were 3.8 times more likely to drop out of treatment within the first 6 months of starting treatment, and patients who held four negative beliefs were 7.1 times more likely to drop out as

compared with patients who held only one or none negative belief. The findings highlight the fact that the importance of long-term adherence to MMT was not well understood and accepted by the patients in China, which hinders eligible patients from entering the program and promotes premature treatment termination for enrolled patients.

For the above-mentioned reasons, treatment retention remains the major challenge for greater success of MMT in China. Less than 50% of the patients who have ever received MMT are still maintained in treatment. A high dropout rate has been reported from all sites. The 1-year dropout rate was from 50 to 70% (Pang, Hao & Mi et al., 2007; Li, Tan & Sun et al., 2009). Besides, studies have reported that many clients continue to use substances while undergoing MMT, which then contributes to the high drop-out rates from the programs (Lin, Wu & Rou et al., 2010, Liu, Wu & Liang et al., 2008 and Tang & Hao, 2007). Besides, a recent study reported that 44.9% of the participants continued to use heroin while on MMT (Li, Lin & Wan et al., 2012).

Besides low level of understanding and acceptance of the maintenance nature of MMT, social support has been studied by a series of authors as a factor to improve treatment outcome of MMT. Havassy, Hall & Wasserman (1991) has reported that greater structural support (as measured by an index of social integration and by partner status) predicted a lower risk of relapse. Greater experienced partner support for abstinence also predicted lower risk. Other authors reported that support by others may motivate, influence and assist individuals treated for drug dependence to remain abstinent (Janis, 1983). Conversely, the absence of a strong, pro-social interpersonal network may be a major contributor to post-treatment relapse (Hawkins & Catalano, 1985). As drug use is more commonly seen as an individual choice and experience in most Western cultures (Derlega, Winstead & Oldfield III et al., 2003), the influence of social support could be much more profound in a country like China which has a family-oriented culture (Li,

Wu & Wu et al., 2006; Farrer, 2001). Chinese people rarely make decisions without first considering or consulting their family, and whatever an individual experience, he/she often shares it with the family (Muller & Desmond, 1992). Therefore in China, families are considered to be important potential partners in the treatment of drug dependence. For example, families often encourage drug users to initiate and remain in treatment and relapse-prevention programs. Most drug users stay with their families before and after attending treatment programs (Tang, 1995). Family involvement in addiction treatment seems to have led to greater improvement in many behavioral aspects and helped prevent patients from dropping-out (Zhao, Huan & Zhang et al., 2004; McLellan, Kushner & Metzger et al., 1991).

### **Objectives**

As partnership status (e.g. whether living with a regular partner and/or drug use status of the regular partner) are potentially strong predictors for treatment outcome of MMT, the impact of these factors remains poorly understood. In this study, we aimed

1. To test the hypothesis that living with a drug-using regular sex partner was associated with higher odds to drop out of treatment and increased probability of ongoing substance use while maintained on treatment.

Though some studies in China emphasized the importance of social support (especially family support) to desired treatment outcome of MMT program and suggested involvement of family members in behavioral interventions for MMT patients (Lin, Wu & Detels, 2011), few studies have actually collected information from the family members' point of view. The changes brought by MMT to the family and the family members are largely unknown. In this study, we aimed



2. To find out how actively the regular sex partners had been involved with the treatment support, and to identify the benefits brought by MMT to them and their relationship with the drug user and what the challenges remained for better support.

We also aimed

3. To find out the level of understanding and acceptance of the maintenance nature of MMT among the new patients' and their regular partners' and any other possible perceived difficulties for long-term adherence including perceived side effects and logistic difficulties.

### **Sites**

The study was conducted in two provinces in central China, Hubei and Shaanxi. The number of drug users has increased rapidly in these two provinces in recent years. Hubei ranks no. 6 in China regarding number of MMT clinics and Shaanxi's rank is no. 7. By April 2011, there were 52 MMT clinics (including three mobile clinics) in Hubei province serving 8,020 patients. The cumulative number of patients receiving treatment in Hubei was 20,231. In Shaanxi province, there were a total of 36 clinics (including one mobile clinic) serving 7,961 patients. The cumulative number of patients was 18,312.

### **Design**

The study was comprised of a qualitative section and a quantitative section.

For the qualitative study, 20 patients were recruited from five randomly selected clinics in the two participating provinces. The inclusion criteria were: 1) aged 18-55 years old, 2) reported a history of injecting drug use, 3) enrolled in MMT no longer than 30 days prior to recruitment. As 5 of the 20 participants were single, we were able to recruit a total of 15 regular sex partners. The regular sex partners had to fulfill the following criteria to be eligible: 1) aged 18-55 years old, 2)

seeing the participating patient on a regular basis for at least three months prior to recruitment. A study flyer was distributed by clinic staff to potential patients during their daily visit. If a patient was interested, the PI herself then approached him/her and introduced the study protocol. All patients were explained that the research was not part of their treatment, and that their decision about whether to participate would not affect their treatment and service they were going to receive. If a patient gave oral consent to participate, the PI then passed him/her a copy of the flyer to invite his/her regular sex partner for those who had a regular partner. If they both agreed to participate, informed consent was then administered to assure that participation was completed voluntary. The patient and his/her partner gave informed consent separately. The interviews lasted approximately 40–70 minutes, and took place in a private room at each clinic. The patients and their partners were interviewed separately without the presence of each other. All interviews were digitally audio-recorded for analysis and quality control. There were no personal identifiers linked to the recorded interviews. The interviews were semi-structured according to specific guidelines, and included a set of open-ended probes to be used when necessary. The interview guide covered the following domains for the patients: 1) drug use history, 2) detoxification history, 3) experience with MMT, and 4) relationship with the regular partner and other family members. Major domains for the interview with the partners were: 1) relationship with the patient, 2) understanding of the patient's drug use, 3) understanding of the patient's previous detoxification attempts, and 3) understanding of MMT.

For the quantitative study, twenty clinics were randomly selected from the two participating provinces, among them 11 clinics were located in Hubei Province and the remaining 9 clinics were in Shaanxi Province. There were a total of 266 participants recruited from the clinics in Hubei Provinces whereas another 234 participants were recruited from Shaanxi Province. The

eligible participants had to fulfill the following inclusion criteria: 1) aged 18-55 years old, 2) reported history of injecting drug use, 3) enrolled in MMT no longer than 30 days prior to recruitment. A study flyer was distributed by clinic staff to potential patients during their daily visit to the MMT clinic. If a patient was interested, the PI herself then approached him/her and introduced the study protocol. All patients were told that the research was not part of their treatment, and that their decision about whether to participate would not affect their treatment and the service they were going to receive. The survey was administrated using ACASI in a private room at each clinic. The participants read the questions from a touch-screen tablet computer by themselves or they could listen to a question by touching the audio button next to that question. A study investigator was standing by at the exit of the room to answer any possible questions a participant might have during the survey. There were a total of 107 multiple-choice questions and an average patient took 30-40 minutes to finish the survey. The information collected included a participant's demographic characteristics, their drug-use history, detoxification history and experience with MMT. For those who had a regular sex partner, the demographics of the regular partner and the drug-use characteristics of the partner were also collected.

### **Analysis**

For the qualitative study, the digitally recorded interviews were transcribed verbatim in Chinese, the original language. Cross-checking and confirmations of the transcriptions were done to assure the quality of work. The data were analyzed using ATLAS.ti 7.0 (Muhr, 1997), a qualitative data analysis software package available in Chinese. A grounded theory approach was used to analyze the data (Glaser & Strauss, 1967). The final coding system for the methadone patients had a total of 25 codes and another 18 codes for the partners. Analyses were conducted

by identifying the themes occurring most frequently, and putting them in the context of other information conveyed by the participants (Sandelowski, 1986). All transcriptions, coding, and analyses were completed in Chinese, and the results were translated into English.

For the quantitative study, SAS 9.2 was used for data analysis of this study. The number of participants who retained on treatment and who continued to use drugs at each follow-up was compared across demographic characteristics, partnership status and treatment-related variables. At 6-month follow-up, analysis was done with the participants who remained in treatment at 3-month follow-up. Among the 500 participants recruited at baseline, 413 was retained in treatment at 3-month and 329 was retained at 6-month. There were 9 participants who dropped out at 3-month but re-enrolled at 6-month. By excluding the 9 participants we ended up with a sample of 320 participants for 6-month analysis. Logistic regression models were then fitted to identify factors predicting treatment retention and continued substance use at each follow-up. The variables included in the regression models were identified either by the univariate analysis or had been reported in the literature. As our sample was not a simple random sample since the patients were nested under clinics and were volunteers, patients recruited from the same clinic were expected to be correlated. We adopted a generalized linear mixed model to account for the correlations. The PROC GLIMMIX model in SAS gave subject-specific estimates. The random effect models and the simple logistic models identified the same group of predictors. Therefore only the estimates of the random effect models were reported.

Detailed information about study design, methods, and results are illustrated in the following chapters.

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## Chapter II

### Importance, Feasibility and Low Acceptance of Long-term Treatment Adherence to Methadone Maintenance Therapy in China

#### Abstract

**Introduction:** The association between low acceptance of long-term methadone maintenance treatment and treatment adherence among Chinese patients has been discussed by a series authors. It has been reported that patients who expect to be treated for life have higher retention rates than patients who anticipate only short-term treatment.

**Method:** In this study, we in-depth interviewed 20 newly enrolled MMT patients and their regular sex partners recruited from five clinics in China. We focused on whether they understood and accepted the maintenance nature of MMT. Other possible perceived difficulties for long-term adherence queried including perceived side effects and logistic difficulties which were also discussed.

**Results:** We found that the overall acceptance of long-term adherence among new patients and their partners was low. Most of the participants thought their addiction could be cured with MMT and they could quit in a few months. Rumors about use of methadone would damage one's kidney and liver were commonly believed by both the patients and their partners. On the other hand, during their short course in treatment the patients and their partners showed high level of satisfaction towards the effectiveness of MMT and the quality of service received. A daily visit to the MMT clinic and cost of medication was logistically manageable for most patients.

**Discussion:** The findings of the study highlight the importance and feasibility of long-term adherence to MMT, as well as the low acceptance level of the concept among newly enrolled patients and their regular sex partners in China.

## **Introduction**

Methadone Maintenance Therapy (MMT) was initially proposed by Dole and Nyswander in 1967 to deal with chronic or long-term and relapsing disorder of opioid dependence (Dole & Nyswander, 1967). Since then there have been numerous studies demonstrating the effectiveness of MMT. By administering on a daily basis a prescribed dose, MMT can reduce craving, suppress opioid withdrawal and free drug addicts from the daily cycle of seeking, buying and using heroin (Kleber, 2008). Besides reducing illicit opioid use and drug-related morbidity and mortality, MMT was also shown to reduce the participants' risk of human immunodeficiency virus (HIV) infection. The participants were less likely to be involved in criminal activities, and their overall functioning was improved (Metzger, Woody & McLellan, et al., 1993).

As its name suggests, MMT is a corrective replacement therapy, rather than a curative treatment (Joseph, Stancliff & Langrod, 2000). Maintenance of usage is then an important indicator of successful treatment. Two years of MMT appears to be the minimum duration before attempting withdrawal (Jaffe & O'Keeffe, 2003). The benefits of long-term methadone maintenance are borne out by data (NIH, 1997). Even patients receiving maintenance for long periods with substantial lifestyle changes often relapse after leaving treatment and their death rates were much higher than for individuals who remained in treatment. For many patients, therefore, years or even lifetime maintenance may be needed (Kleber, 2008).

It has long been reported that methadone has been viewed by both patients and treatment providers alike with some degree of ambivalence (Zweben & Sorensen, 1988). Perceived negative side-effects of methadone, a dislike for the rigid requirements demanded by MMT and fear of withdrawal from methadone upon incarceration or involuntary discharge are reported by opiate-dependent individuals as reasons for not entering MMT (Peterson, Schwartz & Mitchell et

al., 2008). Common negative beliefs about methadone include the view that it is harmful to teeth and bones, that it is more damaging to health than heroin, and that withdrawing from methadone is nearly impossible (Stancliff, Myers & Steiner et al., 2002). A series of authors demonstrated that some patients believed that methadone (1) is difficult to discontinue once initiated; (2) interferes with their daily lives; (3) has serious side effects; and (4) has low “status” in the community (Goldsmith, Hunt & Lipton et al., 1984; Hunt, Lipton & Goldsmith et al., 1985). Other studies found that more than half the drug users perceived that MMT was harmful to their health, thinking that it would damage their immune system or get into their bones (Zaller, Bazazi & Velazquez, 2009; Schwartz, Kelly & O'Grady. 2008). Many drug users believed that high methadone dosages would be harmful to health (Stancliff, Myers & Steiner et al., 2002). Negative attitudes toward methadone can lead many patients to leave MMT programs prematurely (Stancliff, Myers & Steiner et al., 2002), which can result in relapse to heroin use and a return to behaviors that put individuals at high risk for drug-related morbidity and mortality (Gowing, Farrell & Bornemann et al., 2008; Sheerin, Green & Sellman et al., 2004; Langendam , van Brussel & Coutinho et al., 2001). Interventions to correct the negative attitudes and to improve acceptance of long-term adherence would contribute to better treatment retention. MMT was initiated in China in 2004 with 8 pilot clinics in 5 provinces. As the pilot clinics were proven to be great success (Pang, Hao & Mi et al., 2007), MMT coverage was then rapidly scaled up throughout the country. By the end of 2011, there were a total of 738 MMT clinics across 623 counties in 28 (out of 31) provinces. The cumulative number of drug addicts who had ever received treatment was 344,000 of whom 140,000 people were currently receiving treatment (State Council AIDS Working Committee Office, UN Theme Group on AIDS in China, 2012). With all the benefits brought by MMT to the patients and the society as a whole, treatment

retention remains the major challenge to greater success. As we could read from the statistics, less than 50% of the patients who have ever received MMT remain in treatment. High dropout rates have been reported throughout all sites. The 1-year dropout rate ranged from 50 to 70% (Pang, Hao & Mi et al., 2007; Li, Tan & Sun et al., 2009).

The association between low acceptance of long-term treatment and treatment adherence among Chinese patients has been discussed by a series of authors. Liu et al. (2009) reported that patients who expect to be treated for life have higher retention rates than patients who anticipate only short-term treatment. Xu et al. (2012) surveyed 300 first-time MMT patients from 3 clinics in Guangzhou, China regarding their acceptance of long-term adherence to MMT. Over 90% of the participants believed MMT is intended primarily for detoxification. About two thirds of the participants considered one could be completely detoxified and quit using methadone after 2–3 months. About 78% did not consider MMT as a long-term or even lifetime treatment. A total of 84.3% thought that one should attempt to reduce treatment dosage as methadone is harmful to one's health, and 48.5% of the participants held all four negative beliefs. The same group of researchers (Gu, Xu & Lau et al., 2012) reported that patients who held two to three negative beliefs were 3.8 times more likely to drop out of treatment within the first 6 months of starting treatment, and patients who held four negative beliefs were 7.1 times more likely to drop out as compared with patients who held only one or none negative belief. The findings highlight the fact that the importance of long-term adherence to MMT was not well understood and accepted by the patients in China, which hinders eligible patients from entering the program and promotes premature treatment termination for enrolled patients.

In this study, we in-depth interviewed 20 newly enrolled MMT patients and their regular sex partners recruited from five clinics in Shaanxi and Hubei province in China regarding what were

there concerns about long-term adherence to MMT treatment. We focused on whether they understood and accepted the maintenance nature of MMT. Other possible perceived difficulties for long-term adherence queried included perceived side effects and logistic difficulties, which were also discussed.

## **Method**

### **Study sites and participants**

The study was conducted in two provinces in central China, Hubei and Shaanxi. The number of drug users has increased rapidly in these two provinces in recent years. Hubei ranks no. 6 in China regarding number of MMT clinics and Shaanxi's rank is no. 7. By April 2011, there were 52 MMT clinics (including three mobile clinics) in Hubei province serving 8,020 patients. The cumulative number of patients receiving treatment in Hubei was 20,231. In Shaanxi province, there were a total of 36 clinics (including one mobile clinic) serving 7,961 patients. The cumulative number of patients was 18,312. Figure 1 mapped the geographic location of the study sites. 20 patients were recruited from five randomly selected clinics in the two provinces. The inclusion criteria were: 1) aged 18-55 years old, 2) reported a history of injecting drug use, 3) enrolled in MMT no longer than 30 days prior to recruitment. As 5 of the 20 participants were single, we were only able to recruit a total of 15 regular sex partners. The regular sex partners had to fulfill the following criteria to be eligible: 1) aged 18-55 years old, 2) seeing the participating patient on a regular basis for at least three months prior to recruitment.

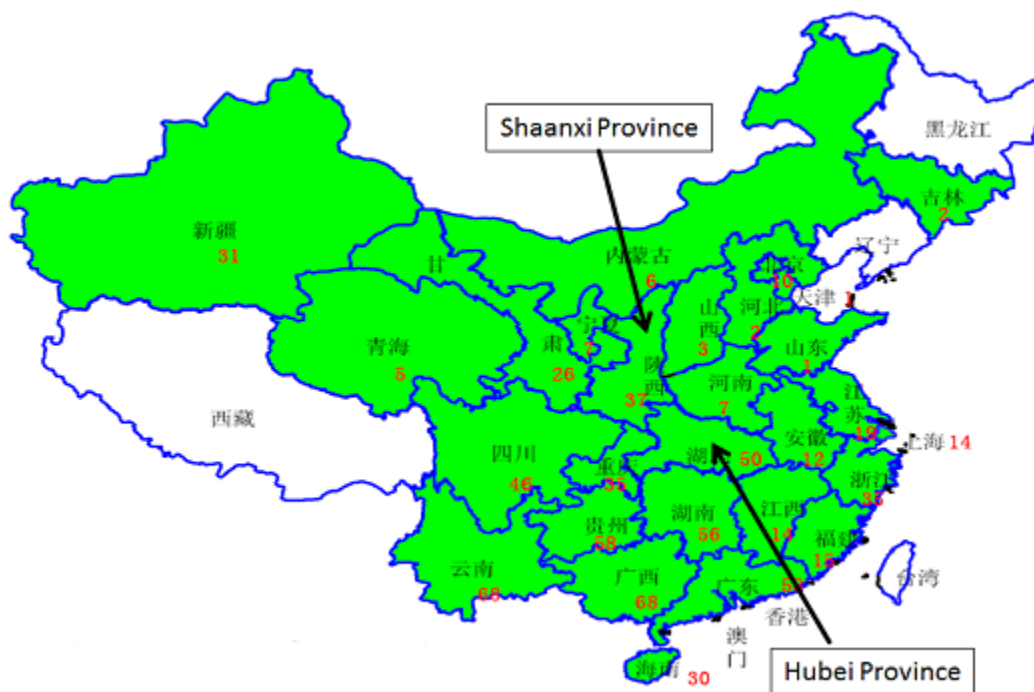


Figure 1: Geographic location of the study sites

### Data collection

A study flyer was distributed by clinic staff to potential patients during their daily visit. If a patient was interested, the PI herself then approached him/her and introduced the study protocol. All patients were explained that the research was not part of their treatment, and that their decision about whether to participate would not affect their treatment and service they were going to receive. If a patient gave oral consent to participate, the PI then passed him/her a copy of the flyer to invite his/her regular sex partner for those who had a regular partner. If they both agreed to participate, informed consent was then administered to assure that participation was completed voluntary. The patient and his/her partner gave informed consent separately. Prior to the interview, all participants were told in detail about the study purpose, procedures, and potential benefits and risks. All participants received 3 coupons for their participation which allowed the patients three free methadone treatments (about \$5). The regular partners received no

direct monetary benefit but only free treatment provided to their partner which was stated in the informed consent. The study was approved by the Institutional Review Boards (IRB) of both the University of California, Los Angeles (UCLA), and the Chinese Centre for Disease Control and Prevention (CCDC).

The interviews lasted approximately 40–70 minutes, and took place in a private room at each clinic. The patients and their partners were interviewed separately without the presence of each other. All interviews were digitally audio-recorded for analysis and quality control. There were no personal identifiers linked to the recorded interviews. The interviews were semi-structured according to specific guidelines, and included a set of open-ended probes to be used when necessary. The interview guide covered the following domains for the patients: 1) drug use history, 2) detoxification history, 3) experience with MMT, and 4) relationship with the regular partner and other family members. Major domains for the interview with the partners were: 1) relationship with the patient, 2) understanding of the patient's drug use, 3) understanding of the patient's previous detoxification attempts, and 3) understanding of MMT.

### Data Analysis

The digitally recorded interviews were transcribed verbatim in Chinese, the original language. Cross-checking and confirmations of the transcriptions were done to assure the quality of work. The data were analyzed using ATLAS.ti 7.0 (Muhr, 1997), a qualitative data analysis software package available in Chinese. A grounded theory approach was used to analyze the data (Glaser & Strauss, 1967). The final coding system had a total of 25 codes for the patients and 18 codes for the partners. Analyses were conducted by identifying the themes occurring most frequently, and putting them in the context of other information conveyed by the participants (Sandelowski,

1986). All transcriptions, coding, and analyses were completed in Chinese, and the results were translated into English.

## **Results**

Among the 20 participating patients, there were 5 single patients and the rest 15 patients had a regular sex partner. There were 1 female single patient and 4 male single patients. Among the 15 patients who had a partner, 10 were males and 5 were females. We then recruited 10 female partners and 5 male partners accordingly. In this study, only heterosexual partners were considered. The mean age of the participating patients was 41.2 years and the mean age of their partners was 37.3 years. The majority of the participating couples were married (14 out of 15 pairs). On average, the couples had been together for 8.6 years.

By analyzing both the patients' and their regular partners' understanding and attitude towards MMT, we found that the overall acceptance of long-term adherence among new patients and their partners was low. The majority of the participants did not understand the maintenance nature of MMT. They were not aware from past detoxification failures that a corrective replacement therapy like MMT, rather than a curative treatment, was the way to deal with drug addictions. Most of the participants thought their addiction could be cured with MMT and they could quit in a few months. Rumors about use of methadone would damage one's kidney and liver were commonly believed by both the patients and their partners.

On the other hand, all patients had good experience with methadone during their short course in treatment. They were freed from cravings for drugs which put them back to normal life. Both the patients and partners showed high level of satisfaction towards the effectiveness of MMT and the quality of service received. A daily visit to the MMT clinic for most patients was logistically manageable. The time and money spent for taking methadone was affordable for most of the



patients and partners, which made long-term adherence feasible. Five themes were identified and the themes were summarized in Table 1. The supportive quotes were given below.

(1) Short-term, intensive treatment was proven not an effective way to control drug addiction.

All patients had repeated detoxification attempts including self-drug-abstinence at home with/without taking medications, formal hospitalization for treating drug addiction, forced detoxification in prison or at labor camp prior to their MMT enrollment. All previous attempts worked at the beginning but relapses occurred as soon as the patients got connected with their drug-sharing circle again.

“I took medicines by myself at home. I was once taken by police for forced detoxification. (Sighed) Slang says “10 years of abstinence. Relapse with one use”. Once you used drugs, you got addicted to it. You thought you had quit, but the addiction haunted. I was still in the circle. I was not able to get out of it. I once quit for more than a year without even one use (of drugs). It was when I was sent back to my hometown which was very rural. But once I got back here I got connected with those people again. I did not actively approach them but the chances of getting drugs were around.” - *A 40 years old male patient*

“He was once taken by police and sent for forced detoxification. It was useless. He repeatedly quit then relapsed. He quit when he was hospitalized and the few days immediately after being released. Once he met those drug-using friends, he can’t resist the temptation. He was then out of control again.” - *A 45 years old female partner*

“I took medicines by myself. I quit for one and a half years. I relapsed because of the circle. I was given the chance to get drugs.” - *A 41 years old female patient*

(2) Level of acceptance of long-term adherence to MMT was low.

Past detoxification failures did not make the patients and partners understand the importance of MMT's maintained nature. The majority of the participants made only short term treatment plans (usually a few months). They were hoping for a cure, rather than a replacement.

“I want to quit MMT in half a year. I think I am even able to quit now.” - *A 29 years old male patient*

“I don't want her to take methadone for long. As soon as methadone overtook her heroin addiction, she should stop taking methadone. We don't have particular difficulty to adhere, I just don't want to have her taking methadone for long time.” - *A 45 years old male partner*

“As long as his addiction was eradicated, he should quit MMT. We then could start a new life. That's also what he plans.” - *A 45 years old female partner*

(3) Rumors about severe side effects of methadone were prevalent among peers.

The patients experienced only minor side effects including constipation and drowsiness which was explained by the clinic staff at the beginning of treatment. The symptoms were relieved for most of the patients as the treatment went on. Rumors of side effects included severe damage to liver and kidney by taking methadone.

“My friend attending the same clinic told me methadone could badly damage my liver and kidney. So I did not want to take it for long.” - *A 39 years old female patient*

“I wished my husband could quit methadone as soon as possible. I heard methadone would do harm to one's kidney and liver. Once he thought methadone had taken over heroin, he should try to quit this treatment immediately.” - *A 37 years old female partner*

“I heard a lot of rumors about the side effects of methadone which I did not really understand. I then consulted the physician at my clinic. He comforted me but I did not

think he actually understood the side effects well. I heard methadone would damage your liver and kidney but I had no choice.” - *A 34 years old male patient*

(4) Good adherence to methadone treatment kept one away from drugs.

Regular methadone intake as prescribed on a daily basis reduced one’s cravings for drugs effectively and improved their overall quality of life. Absences from treatment would increase one’s chance to relapse.

“Methadone worked better (than all past attempts). As long as you were taking it, you did not think about drugs.” - *A 39 years old male patient*

“When you were taking methadone, you did not have the craving for drugs. But for one day you did not take methadone, you again experienced the cravings. Methadone kept you normal.” - *A 37 years old male partner*

“An hour after taking methadone, I was totally normal like anyone else. It kept you normal for at least 24 hours. It was hard to tell after 24 hours, though. Some people, those younger ones could even go to work after taking methadone. When I was taking drugs, one use kept you comfortable for at most 4 hours. You had to have another use after that, otherwise craving for drugs occupied your mind. Methadone changed me completely. I would have come to take it earlier.” - *A 43 years old female patient*

(5) Good adherence to methadone treatment was logistically manageable.

The cost of methadone treatment (10¥/Day, about \$1.6) was affordable for the majority of the patients. Time management required some effort but was still achievable.

“Not a big deal actually. It was a bit troublesome since you need to allocate some time to come to the clinic every day. Now I have purchased a monthly pass then I could make

appointment by phone with the staff if I had to come in late then they would wait for me.

It solved the problem of time management.” - A 27 years old female partner

“Not a problem. It costs only 20 Yuan (about \$3.2) per day for two people which are a minor cost to me. We would adhere to treatment as long as needed.” - A 29 years old male patient

“It was not a problem for me. You should travel less when you were under treatment. I think I could manage that.” - A 46 years old male patient

## **Discussion**

The effectiveness of MMT was greatly appreciated by this group of newly enrolled patients and their partners. All patients claimed that MMT was the best detoxification experience they have had, and successfully suppressed the craving for substance with only minor side effects experienced. The patients returned to a close-to-normal life style with methadone. Couple began to make plans for their future as a family. The patients understood from their own experience that one intake of methadone worked for 1-2 days only, so daily adherence to treatment was necessary for methadone to be effective. The patients and their partners did not learn from past detoxification failures that one had to adhere to MMT for a long-term on a daily basis to continuously control their drug addiction. In our sample, only 3 (out of 35) participants understood methadone is supposed to be a maintenance therapy. This low level of acceptance for long-term treatment is a big obstacle for good adherence in the long run. The propaganda that methadone should be taken for years or even for a life-time could hinder potential patients from getting enrolled at all. The best possible time to educate the patients and partners could be 1-2 months after enrollment allowing some time for the benefits of MMT to be perceived. The choice of the timing would also prevent premature drop-outs for some patients who consider

their condition has been well-controlled and stabilized. The first few months in treatment are therefore vitally important for long-term adherence.

Rumors of the side effect of methadone should be countered as soon as a new patient is enrolled. Though the participants of our study showed an overall high level of satisfaction about the service provided, few of them discussed their concerns about MMT with the clinic staff. Some participants mentioned that they did not think the clinic staff understand the side effects of methadone fully so they did not trust what they said. Training of the staff is necessary for them to better understand the nature of methadone and how it works. It would also improve the professional image of the staff in the eyes of the patients and partners. The popular opinion leader approach could also be considered to educate the patients to counter the rumors of methadone's bad side effects. As the rumors were mainly from so-called "friends" of the participants, the words from such "friends" who are popular and respected in the circle would be more persuasive. Patients who have been in treatment for a relatively long time are good candidates to be opinion leaders. Their real-life experience would be the most convincing stories for the fellow patients. Educational messages conveyed this way could not only reach the patients in treatment, but also those potential patients who have not yet enrolled.

The majority of the patients perceived adherence to MMT as logistically manageable, which showed the feasibility of long-term adherence. Time management was more a burden than the financial cost for many patients, especially for those who had a full-time job. One participating clinic of our study set good example to run a trial for a prepaid monthly methadone pass. The patients are offered a monthly pass at a slightly discounted price at the beginning of each month. The pass holders also have the privileges to make appointments with the staff by phone in case they are not able to make a visit during the normal operating hours. Making payment of a

month's treatment in advance is also considered a motivation of the participating patients to adhere closely for the month. Some participants mentioned that they were not able to accept travelling assignments from work since MMT "tied" them locally. The patients could be freed if temporary transfers could be made in case they need to travel for work or for leisure. Such transfers are feasible in the sense that all MMT patients in China have a unique identification number and all MMT clinics are connected online by the national surveillance system. The freedom of travelling does not seem to be so important in the short-run, but it would help the patients in the long-term and promote long-term adherence. Three participants mentioned that they planned to quit MMT as soon as possible since they would eventually return to their hometown, where was more rural and where MMT was not available. With the rapid scaling-up of MMT in China, especially the promotion of mobile clinics in rural areas, more patients in need would have the chance to receive MMT.

There are some limitations of the study that should be noted. The data were collected from a region with moderate drug-use problems. MMT patients in this area might differ from their counterparts in more heavily drug-affected regions of China. As a qualitative study, the sample was not representative of all newly enrolled patients, limiting the generalizability of the results.

Nonetheless, the findings of the study highlight the importance and feasibility of long-term adherence to MMT, as well as the low level acceptance of the concept among newly enrolled patients and their regular sex partners in China. The service providers should be better educated about the nature of methadone and they could then educate their patients and their partners. Patients who have good long-term adherence to treatment could be identified and trained as peer educators to reach both the patients in treatment and those who have not for education about how methadone works and show that the severe side effects are just rumors. More flexible operating

hours, temporary transfers between clinics, better treatment coverage for all would contribute to promotion of long-term treatment adherence.

Table 1: A summary of the themes.

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List of themes
1. Short-term, intensive treatment was proven not an effective way to control drug addiction.
2. Level of acceptance of long-term adherence to MMT was low.
3. Rumors about severe side effects of methadone were prevalent among peers.
4. Good adherence to methadone treatment kept one away from drugs.
5. Good adherence to methadone treatment was logistically manageable.

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## CHAPTER III

### **Benefits and Concerns towards Methadone Maintenance Therapy from A New Patient's**

#### **Regular Sex Partner's Perspective**

##### **Abstract**

**Introduction:** Social support has been studied by a series of authors as a factor to improve treatment outcome of MMT. For a country with a family-oriented culture like China, families are considered to be important potential partners in the treatment of drug dependence.

**Method:** In this study, we interviewed 15 regular sex partners of 15 newly enrolled MMT patients in-depth to find out how actively they had been involved with the treatment support, the benefits brought by MMT to them and their relationship with the drug user and what the challenges remained for better support.

**Results:** All participating partners had a good experience with methadone by observing the improvement in both physical and psychological health of their partners who had enrolled. The financial burden brought by substance use was greatly relieved. The five drug-using partners who had not yet enrolled for MMT themselves planned to enroll after seeing the improvement of their partners. The partners' attitude towards MMT was biased by rumors in the drug-using circle that methadone could bring great harms to the patients' health in the long-run. Some partners had played their part in reducing the occurrences of continued drug uses.

**Discussion:** The findings of the study highlight the benefit brought by MMT to the drug users' family as a whole. The regular sex partners are identified to be the best candidates to monitor a drug user's adherence to MMT and keep him/her away from continued drug uses. They should therefore be more closely contacted by clinic staff and more actively involved in the educational

programs. The partners were in need of professional advice from MMT clinics to better support the patients.

## **Introduction**

Since the introduction of Methadone Maintenance Therapy (MMT) as a replacement treatment for chronic opioid dependence in 1967 (Dole & Nyswander, 1967), numerous studies have demonstrated the effectiveness of MMT. By a daily prescribed dose, MMT can reduce craving, suppress opioid withdrawal and free drug addicts from the daily cycle of seeking, buying and using heroin (Kleber, 2008). Besides reducing illicit opioid use and drug-related morbidity and mortality, MMT was also shown to reduce the participants' risk of human immunodeficiency virus (HIV) infection (Metzger, Woody & McLellan, et al., 1993). In the battle to fight against HIV transmission among IDUs, MMT was initiated in China in 2004. The eight pilot MMT clinics in the five provinces with the highest HIV prevalence were proven to be a great success in reducing illicit drug abuse, in reducing drug-related criminalities, in improving the IDUs' quality of life and family relationships, and in increasing the opportunities for employment (Pang, Hao & Mi et al., 2007). The MMT program was then rapidly scaled up throughout the country. By the end of 2011, there were a total of 738 MMT clinics across 623 counties in 28 (out of 31) provinces. The cumulative number of drug addicts who had ever received treatment was 344,000 and 140,000 people were currently receiving treatment (State Council AIDS Working Committee Office, UN Theme Group on AIDS in China, 2012).

Social support has been studied by a series of authors as a factor to improve treatment outcome of MMT. Havassy, Hall & Wasserman (1991) has reported that greater structural support (as measured by an index of social integration and by partner status) predicted a lower risk of relapse. Greater experienced partner support for abstinence also predicted lower risk. Other authors reported that support by others may motivate, influence and assist individuals treated for drug dependence to remain abstinent (Janis, 1983). Conversely, the absence of a strong, pro-social

interpersonal network may be a major contributor to post-treatment relapse (Hawkins & Catalano, 1985). As drug use is more commonly seen as an individual choice and experience in most Western cultures (Derlega, Winstead & Oldfield III et al., 2003), the influence of social support could be much more profound in a country like China which has a family-oriented culture (Li, Wu & Wu et al., 2006; Farrer, 2001). Chinese people rarely make decisions without first considering or consulting their family, and whatever an individual experience, he/she often shares it with the family (Muller & Desmond, 1992). Therefore in China, families are considered to be important potential partners in the treatment of drug dependence. For example, families often encourage drug users to initiate and remain in treatment and relapse-prevention programs. Most drug users stay with their families before and after attending treatment programs (Tang, 1995). Family involvement in addiction treatment seems to have led to greater improvement in many behavioral aspects and helped prevent patients from dropping-out (Zhao, Huan & Zhang et al., 2004; McLellan, Kushner & Metzger et al., 1991).

Though some studies in China emphasized the importance of social support (especially family support) to desired treatment outcome of MMT program and suggested involvement of family members in behavioral interventions for MMT patients (Lin, Wu & Detels, 2011), few studies have actually collected information from the family members' point of view. The changes brought by MMT to the family and the family members are largely unknown. In this study, we interviewed 15 regular sex partners of 15 newly enrolled MMT patients in China in-depth to find out how actively they had been involved with the treatment support, the benefits brought by MMT to them and their relationship with the drug user and what the challenges remained for better support.

## **Method**

### Study sites and participants

The study was conducted in two provinces in central China, Hubei and Shaanxi. The number of drug users has increased rapidly in these two provinces in recent years. Hubei ranks no. 6 in China regarding number of MMT clinics and Shaanxi ranks no. 7. By April 2011, there were 52 MMT clinics (including three mobile clinics) in Hubei province serving 8,020 patients. The cumulative number of patients receiving treatment in Hubei was 20,231. In Shaanxi province, there were a total of 36 clinics (including one mobile clinic) serving 7,961 patients and the cumulative number of patients was 18,312.

Fifteen regular sex partners of newly enrolled patients were recruited from five randomly selected clinics in the two provinces. The inclusion criteria for the drug users were: 1) aged 18-55 years old, 2) reported history of injecting drug use, 3) enrolled in MMT no longer than 30 days prior to recruitment. Their regular sex partners had to fulfill the following criteria to be eligible: 1) aged 18-55 years old, 2) seeing the participating patient on a regular basis for at least three months prior to recruitment.

### Data collection

A study flyer was distributed by clinic staff to potential patients during their daily visit. If a patient was interested, the PI herself then approached him/her and introduced the study protocol. If a patient gave oral consent to participate, the PI then gave him/her a copy of the flyer to invite their regular sex partner. If they both agreed to participate, informed consent was then administered to assure that participation was completed voluntary. The patient and his/her partner had to give informed consent separately.



Prior to the interview, details of the study purpose, procedures, and potential benefits and risks of the study were explained. It was made clear that the research was not part of the treatment the patients received, and that their decision about whether to participate would not affect the treatment and service they were going to receive. The participating partners received 3 coupons for their participation which allowed the patients three free methadone treatments (about \$5). The participating partners received no direct monetary benefit but only free treatment provided to the patients which was stated in the informed consent. The study was approved by the Institutional Review Boards (IRB) of both the University of California, Los Angeles (UCLA), and the Chinese Center for Disease Control and Prevention (CCDC).

The interviews lasted approximately 40–70 minutes, and took place in a private room at each clinic. The partners were interviewed individually without the presence of the patient. All interviews were digitally audio-recorded for analysis and quality control. There were no personal identifiers linked to the recorded interviews. The interviews were semi-structured according to specific guidelines, and included a set of open-ended probes to be used when necessary. The interview guide covered the following domains 1) relationship with the patient, 2) understanding of the patient's drug use, 3) understanding of the patient's previous detoxification attempts, and 3) understanding of MMT.

#### Data Analysis

The digitally recorded interviews were transcribed verbatim in Chinese, the original language. Cross-checking and confirmations of the transcriptions were done to assure the quality of work. The data were analyzed in Chinese using ATLAS.ti 7.0 (Muhr, 1997), a qualitative data analysis software package. A grounded theory approach was used to analyze the data (Glaser & Strauss, 1967). The final coding system had a total of 18 codes. Analyses were conducted by identifying

the themes occurring most frequently, and putting them in the context of other information conveyed by the participants (Sandelowski, 1986). All transcriptions, coding, and analyses were completed in Chinese, and the results were later translated into English.

## **Results**

Among the 15 participating partners, 10 were females and 5 were males. The mean age of all partners was 37.2 years. There were 14 partners were married to the participating patient. On average, the couples had been together for 8.6 years. We found that all 15 participating partners cared about the treatment progress of the patients and many of them were actively involved in monitoring the patients' adherence to treatment. All of them had a good experience with methadone by observing the improvement in both physical and psychological health of their partners who had enrolled. The financial burden brought by substance use was greatly relieved, too. All these improvements were motivations for the partners to make future plans with the patients as a family. All patients had had various detoxification failures prior to their MMT enrollment including self-abstinence, hospitalization or forced detoxification etc. Some partners took MMT as the last chance allowed for the patients to quit drugs and to stay in this relationship and all of them were satisfied and inspired by the progress their partners made. There were five drug-using partners who had not yet enrolled for MMT themselves and all of them mentioned they planned to enroll after seeing the improvement of their partners.

On the other hand, the partners did not understand MMT well. Their attitude towards MMT was biased by rumors in the drug-using circle that methadone could bring great harms to the patients' health in the long-run. Only one participating partner understood she needed to support her partner on treatment for a long time, even for a life-time. Some partners observed or suspected the patients' continued substance use and they had played their part in reducing its occurrences.

They were in need of professional advice from MMT clinics to better support the patients. The perceived benefits and concerns towards MMT from the partners' perspective were summarized in the five themes listed in Table 1. The corresponding quotes were given below.

(1) Improved health condition of the patient was observed by the partner.

“He changed! His energy level was regained. He used to lack interest in anything. Now his appetite was much better. He began to ask me to cook something he liked.” - A 43 years old female partner

“He used to be very skinny and lost all his appetite. After taking methadone, from my observation I thought his overall condition was improved. He began to lead a normal life again.” - A 40 years old female partner

“He looked much healthier and vigorous after taking methadone.” - A 37 years old female partner

(2) Family financial burden was greatly relieved.

“We used to be very poor. Now we could save some money. We could buy what other kids have for our child.” - A 36 years old female partner

“We used to be richer than most of our friends. We run our own furniture business. We had to sell our business to cover the cost of drugs. Methadone was much cheaper than drugs. We plan to start a small business next year.” - A 41 years old female partner

“It costs 200 Yuan to buy heroin lasting for four hours. Methadone costs 10 Yuan for 1-2 days. We should have started MMT earlier. We could save a lot of money then.” - A 31 years old female partner

(3) The improvement brought by methadone promoted intention to enroll for MMT of drug-using partners.

“I did not enroll since I was scared and I was not sure whether it worked. It helps my husband a lot. I plan to get enroll soon.” - A 34 years old female partner

“I saw my husband changed. He said he felt much better. I plan to talk to a staff at the clinic after this interview.” - A 37 years old female partner

“I was just released from prison for forced detoxification. Now I am free of drugs. In case I would be involved with drugs again in future? Oh, I would definitely choose methadone. It works well for him.” - A 35 years old female partner

(4) Rumors about severe side effects of methadone were prevalent among the partners.

“I heard that methadone would damage one’s livers and kidneys. As long as his addiction was eradicated, he should quit MMT. We then could start a new life. That’s also what he plans.” - A 45 years old female partner

“I hope she could take less methadone and visit less frequently in future. Now she comes everyday. Maybe she could then visit every two or three days. It is not a long-time thing. It has lots of side-effect.” - A 45 years old male partner

“I wish he could quit both heroin and methadone in a near future. Methadone is medicine. One can’t take medicine for years.” - A 27 years old female partner

(5) The partners took an active role in monitoring the patients’ adherence to treatment and in reducing continued substance uses.

“When I was busy, I would ask my mother-in-law to accompany him to the clinic. We then could make sure he came for treatment every day and he did not meet those drug-using friends on his way to the clinic.” - A 43 years old female partner

“I kept all his money. He could only get money with good reasons.” - A 33 years old female partner

“I know he still uses that thing (heroin) sometimes. What I can do is trying to keep him away from that circle. When I answered the door and saw those drug-users looking for him, I would find an excuse to get them away.” - A 40 years old female partner

## **Discussion**

We could read from the responses that MMT not only benefits the drug users, but also their partners and their relationship, which had been severely damaged by their repeated relapses. The partners were encouraged by the observation of the improvement in the drug users' health. The stabilized emotional status is another important contributor to more harmonic relationship. The expenses on drugs used to range from a few hundreds to a thousand of Yuan per day. Now the families could make savings by paying only 10 Yuan (about \$1.6) for each methadone treatment. The family's financial situation would be further improved in the long-run as many unemployed drug users began to plan for job seeking after less than a month enrollment with MMT. Many participating partners mentioned that they were about to give up the relationship as they were discouraged by the repeated failures of detoxification. All of them agreed that MMT is the best treatment for drug addiction and they regain the confidence of the families' future.

The motivated partners are perfect candidates to give support for better treatment adherence. The partners either accompany the drug user to the clinic or make phone calls to make sure the drug user has visited MMT clinic as planned. All participating partners mentioned they knew well whether the drug user attended treatment or not every day. By controlling the drug users' daily allowance and keeping the drug-using circle of friends away, the partners also contributed to reduce the chances of continued substance abuses. We suggest the staff at MMT clinics work

closely with the partners for improved treatment outcomes. As reported by clinic staff, a drug user usually becomes unreachable after being absent from treatment for a few days. The partners then are the key contact person to be reached. If a drug user could be contacted within the first few days of absence, the chance to get him/her back into treatment is much higher.

On the other hand, the prevalence of misunderstanding of methadone's side effects among the partners makes the acceptance of long-term treatment low as it also is among the drug users. The partners should then be included in the educational programs held at the clinics. The importance of long-term adherence to treatment should be a key educational message to reach both the patients and their partners. The programs also provide the partners an opportunity to meet one another and exchange ideas for better support.

Our participants included five drug-using partners who were not yet enrolled in MMT. These partners should have the top priorities to be persuaded for enrollment since their drug-using status would greatly improve the enrolled patients' chances to discontinued substance uses. Even for the both-enrolled drug-using couples, the probabilities for continued substance uses and drop-outs are much higher as documented in literatures (Tutten & Jones, 2003; Westermeyer, & Boedicker, 2000). We urge the staff at MMT clinics to pay special attention on the concordant drug-using couples as they are at greater risk for relapse and drop out in the long run. Special counseling for couples would be helpful.

There are some limitations of the study that should be noted. The data were collected from a region with moderate drug-use problems. MMT patients in this area might differ from their counterparts in more heavily drug-affected regions of China. As a qualitative study, the sample was not representative of all newly enrolled patients and their partners, limiting the generalizability of the results. The participants of our study are newly enrolled patients and their

partners. For a longer course in treatment more factors including relapses or logistic burden could complicate the partners' burden for treatment support. Besides, regular partners who care more about the drug users' treatment outcome were more likely to participate in this study. Besides, we did not interview other significant others of the drug users like parents or siblings who could also greatly contribute to treatment support, especially for single drug users under MMT. Nonetheless, the findings of the study highlight the benefit brought by MMT to the drug users' family as a whole. The regular sex partners are identified to be the best candidate to monitor a drug user's adherence to MMT and keep him/her away from continued drug uses. They should therefore be more closely contacted by clinic staff and more actively involved in the educational programs.

Table 1: A summary of the themes.

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List of themes
1. Improved health condition of the patient was observed by the partner.
2. Family financial burden was greatly relieved.
3. The improvement brought by methadone promoted intention to enroll for MMT of drug-using partners.
4. Rumors about severe side effects of methadone were prevalent among the partners.
5. The partners took an active role in monitoring the patients' adherence to treatment and in reducing continued substance uses.

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## CHAPTER IV Partner Drug Use, Continued Substance Abuse and Treatment Adherence Among Newly Enrolled Methadone Maintenance Therapy Patients in China

### Abstract

**Introduction:** Drug users' personal social circles, especially among sexual partners, were suggested to be associated with continued drug use, continued injecting, treatment retention, and higher rates of relapse.

**Method:** We recruited 500 newly enrolled MMT patients from twenty randomly selected methadone clinics in two provinces of China to test the hypothesis that living with a drug-using regular sex partner is associated with poorer adherence to MMT and increased probability of ongoing substance uses. Each participant completed a survey at baseline with ACASI and their treatment status and the most recent urine test result were collected 3 and 6 months after the baseline survey. A generalized linear mixed model was adopted to identify significant covariates and account for intra-clinic correlations.

**Results:** There were 56 (11.6%) participants having a concordant drug-using regular partner. The majority of the participants (51.6%) were living with a regular sex partner who had never used drugs. There were 413 participants who remained in treatment after 3-months and among them, 320 were also retained after 6-months. A total of 80 participants tested positive for illicit drug uses at 3-months and 49 tested positive at 6-months. By considering the variables together and adjusting for intra-clinic correlations, participants who had a drug-using regular sex partner were less likely (AOR=0.84, CL [0.720, 0.972]) to continue to use substance at 3-months. Participants who had more detoxification failures prior to their methadone enrollment were less likely to stay in treatment at 3-months (AOR=0.92, CL [0.843, 0.995]). Surprisingly, participants who received a higher dose of methadone were less likely to be retained at 3-months (AOR=0.96, CL

[0.930, 0.999]). For the participants who remained in treatment at 3-months, participants who had a concordant drug-using regular partner were less likely to stay in treatment at 6 months after enrollment (AOR=0.94, CL [0.896, 0.993]). After 6-months, first-time MMT patients were better retained compared with those who previously enrolled (AOR=1.04, CL [1.007, 1.071]).

**Discussion:** The findings highlight the impact of having a drug-using regular sex partner's on a new MMT patient's treatment adherence and outcome. As drug-using couples are more vulnerable to continued substance use and premature treatment termination compared to sole users, special effort needs to be made to keep them in treatment. Education about the importance of long-term treatment adherence is another key to improve treatment adherence in the long-run. The first few months in MMT for newly enrolled patients are considered the key period for intervention to keep patients in the long term. Special attention should be paid to the patients who have had many prior detoxification failures. Patients who have a history to drop-out from MMT could survive the first 3-months but are more likely to drop-out again after 6-months. This group of patients therefore needs to be monitored especially closely.

## **Introduction**

Epidemic estimates indicated that at the end of 2011, the estimated number of people living with HIV infection in China was 780,000. Among them, 28.6% were women. There were altogether 154,000 AIDS cases. The country-wide prevalence stood at 0.058% (State Council AIDS Working Committee Office, UN Theme Group on AIDS in China, 2012). Though surpassed by heterosexual transmission in recent years, injecting drug users (IDUs) were still the second largest contributor of HIV infections in China. In 2011, IDUs accounted for 16.9% of newly reported HIV cases. Heroin was the main illicit drug used. About 85% of the IDUs claimed heroin abuse (Sullivan & Wu, 2007). The prevalence of syringe sharing among IDUs has been estimated at 40% (Xiao, Wu & Luo, et al., 2010). In addition to unsafe injecting practices, drug users in China also commonly engage in risky sexual practices that put their partners at a greater risk of HIV infection (Liu, Lian & Zhou et al., 2001; Wu, Detels, & Zhang, 1996).

In the battle to fight against HIV transmission among IDUs, Methadone Maintenance Therapy (MMT) was introduced to China in year 2004. The eight pilot MMT clinics in the five provinces with the highest HIV prevalence were successful in reducing illicit drug abuse, in reducing drug-related criminalities and in improving the IDUs' quality of life and opportunities of employment (Pang, Hao & Mi et al., 2007). The MMT program was then rapidly scaled up throughout the country. By the end of 2011, there were a total of 738 MMT clinics across 623 counties in 28 (out of 31) provinces. The cumulative number of drug addicts who had ever received treatment was 344,000 and 140,000 people were currently receiving treatment (State Council AIDS Working Committee Office, UN Theme Group on AIDS in China, 2012). MMT clients pay 10 Yuan (U.S. \$1.60) for their daily treatment and take methadone once a day under the supervision of a clinic staff. A urine test is required to be taken once a month on a random date. As the

benefits of long-term methadone maintenance are borne out by data (NIH, 1997), treatment retention remains the major challenge for greater success of MMT in China. Less than 50% of the patients who have ever received MMT are still maintained in treatment. A high dropout rate has been reported from all sites. The 1-year dropout rate was from 50 to 70% (Pang, Hao & Mi et al., 2007; Li, Tan & Sun et al., 2009). Besides, studies have reported that many clients continue to use substances while undergoing MMT, which then contributes to the high drop-out rates from the programs (Lin, Wu & Rou et al., 2010, Liu, Wu & Liang et al., 2008 and Tang & Hao, 2007). A recent study reported that 44.9% of the participants continued to use heroin while on MMT (Li, Lin & Wan et al., 2012).

Three types of factors can be considered in examining retention in MMT, patient factors, program factors, and community factors. A number of patient-related factors are identified to be associated with longer tenure in treatment including older age, female gender and higher levels of motivation for treatment (Deck and Carlson, 2005; Mertens & Weisner, 2000; Simpson, Joe & Rowan-Szal, 1997). Program-related factors include higher dosage of methadone (Bao, Liu & Epstein et al., 2009; Amato, Davoli & Perucci, 2005) and higher level of patient satisfaction with the treatment program and counselor (Lin, Wu & Detels, 2011; Villafranca, McKellar & Trafton et al., 2006). Community-level factors have been less frequently studied, but have been of increasing interest in recent years (Brown, O'Grady, & Battjes, 2004) and also appear to play a role in patient retention. Similar factors have been found to be associated with ongoing drug abuse including higher dosage (Kamal, Flavin & Campbell, 2007), counseling and comprehensive services (Lin, Wu & Rou et al., 2010; Ilgen, Jain & Kim, 2008).

Besides the above-mentioned, frequently discussed factors, drug users' personal social circles, especially among sexual partners, were suggested to be associated with continued drug use,

continued injecting, treatment retention, and higher rates of relapse (Tutten & Jones, 2003; Wasserman & Boedicker, 2001). Valente & Vlahov (2001) showed that most contemporary syringe-sharing occurred within limited social circles (e.g. close friendships, sexual relationships and family ties). It has been reported that interventions which work with injectors to supplant their drug-using friends with non-drug-using contacts may be the most successful in achieving sustained behavioral risk reductions (Costenbader, Astone & Latkin, 2006). The impact of drug-using in an IDU's close social network could be more profound for a family-oriented society like China. Che et al. (2010) reported, based on a cohort study in Yunnan, China, that patients' early dropout was related to ethnicity, clinic accessibility, living with drug users and methadone dose. Those who lived with a drug user were 2.71 times (Hazard ratio, 95% CI: 1.55–4.74) to drop out. A series of studies worldwide reported that respectively 40.8-56.0% of male IDUs and 68.4-71.7% of female IDUs have a drug-using regular sex partner (Crepaz & Marks, 2002; Anderson, Cheney & Clatts et al., 1996; Corby & Wolitski, 1996). A recent study in China found that 10.3% of male IDUs and 25% of female IDUs have a regular sex partner who is also an IDU (Gonzales, Marinelli-Casey & Shoptaw et al., 2006).

As partnership status (e.g. whether living with a regular partner and/or drug use status of the regular partner) are potentially strong predictors for treatment outcome of MMT, the impact of these factors remains poorly understood. We hypothesize that living with a drug-using regular sex partner is associated with poorer adherence to MMT and increased probability of ongoing substance use while maintained on treatment. The participants of our study were recruited from twenty randomly selected methadone clinics in two provinces of China, who were enrolled with MMT no more than 30 days prior to recruitment. The treatment status and the most recent urine



test result were collected from the participants three months and six months after the baseline survey.

## **Method**

### **Sample size**

The study was a prospective study with the major exposure variable defined as “having a drug-using regular sex partner” and the main outcome variable as “remaining in treatment 6 months after enrollment”. PASS was used to calculate sample size. Based on existing statistics and literature, the following assumptions were made (Fleiss, Levin, & Paik, 2003). (1) Alpha was fixed at 0.05. (2) The width of the confidence interval was fixed at 1.5. (3) The exposed to unexposed ratio was set to be 1:2 or 1:3. (4) Probability of remaining in treatment for unexposed varied from 0.3 to 0.8 by 0.1 increments. (5) The minimum odds ratio was taken as 1.75, 2.00 or 2.25. Based on the calculation, a sample of 420 newly enrolled IDUs would provide us enough power (details omitted).

As a second step, we used the design effect (DEFF) to account for nesting effect within each clinic, which inflated the sample size calculated in the first step. The adjusted sample size was  $N = DEFF \times N^*$ , where  $DEFF = [1 + (m-1) ICC]$  and  $m$  was the mean number of patients per clinic and  $N^*$  was the sample size required without considering the clustering effect. The intra-class correlation (ICC) was estimated to be .01 by most studies. And an ICC was expected to be smaller with more clusters (clinics) and less subjects in each cluster (patients) (Smeeth, 2002). By adopting an ICC of .01 we had an adjusted sample size of 475. For an ICC of .02, the adjusted sample size was 529. Considering budget and manpower constricts, we reached the decision of recruiting an average of 25 patients from each of the 20 clinics for a total number of 500 participants.

## Study Sites and Participants

The study was conducted in two provinces in central China, Hubei and Shaanxi. The number of drug users has increased rapidly in these two provinces in recent years. Hubei ranks no. 6 in China regarding number of MMT clinics and Shaanxi ranks no. 7. By April 2011, there were 52 MMT clinics (including three mobile clinics) in Hubei province serving 8,020 patients. The cumulative number of patients receiving treatment in Hubei was 20,231. In Shaanxi province, there were a total of 36 clinics (including one mobile clinic) serving 7,961 patients and the cumulative number of patients was 18,312. Twenty clinics were randomly selected from the two participating provinces, among them 11 clinics were located in Hubei Province and the remaining 9 clinics were in Shaanxi Province. There were a total of 266 participants recruited from the clinics in Hubei Provinces whereas another 234 participants were recruited from Shaanxi Province.

The eligible participants had to fulfill the following inclusion criteria: 1) aged 18-55 years old, 2) reported history of injecting drug use, 3) enrolled in MMT no longer than 30 days prior to recruitment. A study flyer was distributed by clinic staff to potential patients during their daily visit to the MMT clinic. If a patient was interested, the PI herself then approached him/her and introduced the study protocol. All patients were told that the research was not part of their treatment, and that their decision about whether to participate would not affect their treatment and the service they were going to receive. All participants received two coupons for their participation which allowed them two free methadone treatments (about \$3.2). The study was approved by the Institutional Review Boards (IRB) of both the University of California, Los Angeles (UCLA), and the Chinese Centre for Disease Control and Prevention (CCDC).

## Data Collection

The baseline recruitment started 1<sup>st</sup> August 2011 and ended 30<sup>th</sup> September 2011. The study participants were those who were enrolled in MMT during 1<sup>st</sup> July 2011 and 20 September 2011. The participants were first-time enrollers or the dropouts who had enrolled again officially during the stated period of time. Following the criteria in the national methadone practice handbook, a drop-out was defined as a patient who was absent from MMT for seven consecutive days with no sound reasons. For our study, we only recruited the dropouts whose re-enrollment was at least 30 days after their last day in treatment. A regular sex partner was defined as someone who had been seeing the participant on a regular basis for at least three months prior to study recruitment.

The survey was administrated using ACASI in a private room at each clinic. The participants read the questions from a touch-screen tablet computer by themselves or they could listen to a question by touching the audio button next to that question. The participants could then make choices by touching the desired answer. They could always go back to a specific question if they made a mistake or changed their mind. A study investigator was standing by at the exit of the room to answer any possible questions a participant might have during the survey. There were a total of 107 multiple-choice questions and an average patient took 30-40 minutes to finish the survey. The information collected included a participant's demographic characteristics, their drug-use history, detoxification history and experience with MMT. For those who had a regular sex partner, the demographics of the regular partner and the drug-use characteristics of the partner were also collected. Three months (between 10/1/2011 to 12/30/2011) and six months (between 1/1/2012 to 3/30/2012) after the baseline survey, the PI contacted staff at each clinic to find out whether a participant was still on treatment and the most recent urine test result.

## Data analysis

SAS 9.2 (SAS Institute Inc, Cary, NC) was used for data analysis of this study. The number of participants who remained in treatment and who continued to use drugs at each follow-up was compared across demographic characteristics, partnership status and treatment-related variables. At 6-month follow-up, only those participants who also had remained in treatment at 3-months were included in the analysis. Among the 500 participants recruited at baseline, 413 was retained in treatment at 3-month and 329 was retained at 6-month. There were 9 participants who dropped out at 3-month but re-enrolled at 6-month. By excluding the 9 participants we ended up with a sample of 320 participants for 6-month analysis. Logistic regression models were then fitted to identify factors predicting treatment retention and continued substance use at each follow-up. The variables included in the regression models were identified either by the univariate analysis or had been reported in the literature. Predictors “number of prior (non-methadone) detoxification failures”, “methadone dose” and “household monthly income” were rescaled by 1/100 to make the estimates more presentable.

Our sample was not a simple random sample since the patients were nested under clinics and were volunteers. Patients recruited from the same clinic were expected to be correlated. We then adopted a generalized linear mixed model to account for the correlations. The PROC GLIMMIX model in SAS gave subject-specific estimates. The random effect models and the simple logistic models identified the same group of predictors. Therefore only the estimates of the random effect models were reported.

## Results

The sample characteristics are summarized in Table 1. Of the 500 participants, 78.2% were males. There were 266 (53.2%) participants recruited from the 11 clinics in Hubei Province, and

the rest 234 (46.8%) were recruited from the 9 clinics in Shaanxi Province. The mean age (result not shown) of the participants was 40.1 years. They earned an average monthly household income of 3145 Yuan (about 500\$). There were 186 (37.2%) single participants who did not have a regular sex partner. Another 56 (11.6%) participants had a concordant drug-using regular partner. The majority of the participants (51.6%) were living with a regular sex partner who had never used drugs. There were 283 (56.6%) first-time MMT patients and the rest 217(43.4%) re-enrolled for MMT during the recruitment period. The participants received an average daily methadone dose of 56.7ml. They had undergone an average of 5.9 (non-methadone) detoxification attempts prior to the first MMT enrollment (result not shown). There were 413 participants who remained in treatment after 3-months and among them, 320 were also retained after 6-months. Among them, a total of 80 participants tested positive for illicit drug uses at 3-months and 49 tested positive at 6-months.

Univariate analysis showed that (Table 1), participants who were 40 years or younger ( $p=0.0049$ ), participants whose household monthly income was more than 2000 Yuan ( $p=0.0346$ ) and participants who had a drug-free regular sex partner ( $p=0.0187$ ) were more likely to continue using substances while taking methadone 3-months after enrollment. Six month after the baseline survey, for the participants who had remained in treatment after 3-months, those from Shaanxi Province ( $p=0.0036$ ) were more likely to continue to use substances and those who were enrolled to MMT for the first time were more likely to be retained in treatment at 6-month follow-up ( $p=0.0076$ ).

By considering the variables together and adjusting for intra-clinic correlations (Table 2), participants who had a drug-using regular sex partner were less likely (AOR=0.84, CL [0.720, 0.972]) to continue to use substance at 3-months. But for those who were maintained at 3-months,

having a drug-using partner was no longer a protective factor for continued drug abuse at 6-months.

Table 3 presented the predictors for treatment adherence. Participants who had more (non-methadone) detoxification failures prior to their methadone enrollment were less likely to stay in treatment at 3-months (AOR=0.92, CL [0.843, 0.995]). But for those who were maintained at 3-months, more previous detoxification attempts were not predicting retention at 6-months. Surprisingly, participants who received a higher dose of methadone were less likely to be retained at 3-months (AOR=0.96, CL [0.930, 0.999]). But among those who were maintained at 3-months, dosage was not predicting retention at 6-months. For the participants who remained in treatment at 3-months, those who had a concordant drug-using regular partner were less likely to stay in treatment at 6 months after enrollment (AOR=0.94, CL [0.896, 0.993]). After 6-months, first-time MMT patients were better retained compared with those who previously enrolled (AOR=1.04, CL [1.007, 1.071]).

## **Discussion**

Our study has been focusing on examining the association between partnership status (whether living with a drug-using partner) and treatment retention and/or odds of continued substance use. About 63% of our participants were living with a regular sex partner, among whom 11.2% were living with a concordant drug-using partner. These participants were found to be less likely to be involved in substance abuse 3-months after methadone enrollment. But among those who remained in treatment at 3-months, the participants living with a drug-user partner were more likely to drop-out by 6-months. The decreased odds to continue to use drugs at 3 months after enrollment may be explained by the couple's determination to quit. There were 43 (77%) drug-using partners of the participant who also enrolled for MMT (result not shown in tables) at the

same time. However, after a slightly longer course in MMT the negative effect of having a drug-using partner would then dominate. It has been documented that drug-using social relationships promote continued drug injection (Gogineni, Stein & Friedmann, 2001; Wasserman, Duva & Stewart, 1999). Drug-using couples have greater opportunities to be exposed to the drug-sharing circle compared to a sole user. As long as one of them fails to resist the temptation of drugs, it would be difficult for the other to stay clear. Relapse to drug use then promotes drop-outs of these concordant drug-using couples. Staff at MMT clinics should pay special attention to concordant drug-using couples as they are at greater risk to relapse and drop out in the long run. Special counseling for couples should be helpful if available.

Surprisingly, the participants in our study who received a higher dose of methadone at baseline were more likely to drop out of treatment 3-months after enrollment. The finding contradicts what most authors report that higher dosage is usually associated with lower probability of substance use and better retention. We should note that more than half (55.7%, see Table 1) of our participants received a dose lower than 60ml which is recommended as the lowest adequate dosage. The inadequate dose could be a possible explanation of the contradicting finding. Besides, higher dose is usually associated with more symptoms of side effects, especially for new patients. Another possible explanation could be the low level of acceptance of long-term treatment adherence to MMT among Chinese patients. In a recently published study, Xu and the team (2012) reported that two thirds of 300 first-time MMT patients in Guangdong Province believed that one could be completely detoxified and quit using methadone after 2–3 months. A recent study in Zhejiang and Jiangxi Province interviewing 28 service providers of MMT clinics found that the overwhelming majority of their clients did not want to stay in a life-long maintenance program. Many of the clients then attempted voluntarily to reduce their methadone

dosage in a gradual manner to 0 mg to quit treatment (Lin & Detels, 2011). Under such circumstance, the patients who received a higher methadone dose than what they preferred would have a motivation to quit prematurely as they may perceive the high dosage as an undesirable treatment outcome. The finding that dosage only predicts adherence for 3-months, but not for a longer term at 6-month for those who survive the first 3-months confirms our conclusion. The finding also implies the first few months after enrollment are the key time for interventions. The propaganda that methadone should be taken for years or even for a life-time could hinder potential patients from enrolling at all. The best possible time to educate the patients could be 1-2 months after enrollment which allows some time for the benefits of MMT to be perceived. Once a patient is retained for the first 3 months, we can be more optimistic about their longer term retention. Making the patients understand and accept the long-term maintenance nature of MMT shortly after initial enrollment is a key to long-term adherence. One thing to be noted that is our participants are new patients who have been in treatment for less than a month. It takes some time for the dose to reach a stabilized level for newly enrolled patients, especially the 283 participants (see Table 1) who get enrolled for the first time. As the information about dose was collected at only one time-point at baseline but not collected at each follow-up, we could not have observed the changes in doses received by each participant and confirmed that whether the dose at baseline was the stabilized dose. This should be considered a limitation of our study.

There are some limitations of the study that should be noted. The data were collected from a region with moderate drug-use problems. MMT patients in this area might differ from their counterparts in more heavily drug-affected regions of China, limiting the generalizability of the results. The study has adopted a prospective design which is considered the best way to study treatment adherence. But due to logistic limitations, the participants were not really revisited at



3-month and 6-month follow-up. The treatment status and urine test result of each participant was obtained by contacting the clinics with the consent of the participants. As mentioned previously, if the study had re-contacted the participants at 3 and 6 months, more relevant information could have been collected. Nonetheless, the findings of the study highlight the impact of a drug-using regular sex partner's on a new MMT patient's treatment adherence and outcome. As drug-using couples are more vulnerable to continued substance use and premature treatment termination compared to sole users, special effort needs to be made to keep them in treatment. Education about the importance of long-term treatment adherence is another key to improve treatment adherence in the long-run. Patients who have had more (non-methadone) detoxification failures prior to their methadone enrollment were less likely to be retained after 3-months. The first few months in MMT for newly enrolled patients therefore are considered the key period for intervention to keep patients in the long term. Education of new patients should start early after their initial enrollment to prevent future drop-out. Special attention should be paid to the patients who have had many prior detoxification failures. Reenrolled patients who have a history to drop-out of MMT and show no significant difference regarding retention during their first 3-months in treatment but are more likely to drop-out after 6-months as compared to the first time enrollers. This group of patients therefore needs to be monitored especially closely.

Table 1: Sample Description and Continued Substance Use and Treatment Retention at 3 and 6-months after baseline survey by demographic characteristics, partner drug use and treatment-related factors (N=413 for 3-months analysis and N=320 for 6-months analysis).

		N	%	Substance Use 3-Month		Substance Use 6-Month		Retention 3-Month		Retention 6-Month	
				Yes	P	Yes	P	Yes	P	Yes	P
Gender					0.6425		0.6788		0.1504		0.1342
	Male	391	78.2	65		39		328		249	
	Female	109	21.8	15		10		85		71	
Age					0.0049		0.7007		0.1374		0.4938
	<=40	234	46.8	48		21		187		142	
	>40	266	53.2	32		28		226		178	
Household Monthly Income					0.0346		0.5249		0.8882		0.9729
	<=2000	285	57.0	37		26		236		183	
	>2000	215	43.0	43		23		177		137	
Partnership Status					0.0187		0.3041		0.6341		0.9642
	Single	186	37.2	25		13		150		116	
	Drug-free partner	258	51.6	52		31		217		169	
	Drug-dependent partner	56	11.2	3		5		46		35	
Site					0.0788		0.0036		0.3797		0.6990
	Hubei	266	53.2	30		16		216		169	
	Shaanxi	234	46.8	50		33		197		151	
Detoxifications Attempts					0.2748		0.2484		0.1495		0.4544
	<=3 times	293	58.6	53		32		236		186	
	>3 times	207	41.4	27		17		177		134	
Dose					0.3935		0.0969		0.2412		0.4634
	<60 ml	278	55.7	51		33		235		179	
	>=60ml	221	44.3	29		16		178		141	
First MMT Enrollment					0.0718		0.1567		0.6756		0.0076
	Yes	283	56.6	38		25		232		191	
	No	217	43.4	42		24		181		129	
<b>Total</b>		<b>500</b>		<b>80</b>		<b>49</b>		<b>413</b>		<b>320</b>	

Table 2: Generalized Linear Mixed Regression on Continued Substance Use at 3-months (N=413) and 6-months (N=320) after baseline survey.

	Tested Positive for Drug 3-Month			Tested Positive for Drug 6-Month		
	AOR <sup>†</sup>	LCL	HCL	AOR <sup>†</sup>	LCL	HCL
Single	0.96	0.872	1.048	0.96	0.878	1.047
Drug-Dependent Partner	<b>0.84*</b>	<b>0.720</b>	<b>0.972</b>	0.97	0.850	1.106
Detoxification attempts (1/100)	1.00	0.641	1.569	1.00	0.645	1.558
Methadone Dose (1/100)	1.06	0.873	1.289	1.05	0.869	1.261
First-Time Enrollment	0.94	0.863	1.023	0.94	0.871	1.023

<sup>†</sup> Adjusted for gender, age, monthly household income (1/100) and study site (Hubei vs. Shannxi).

\* P<0.05.

Table 3: Generalized Linear Mixed Regression on Treatment Adherence at 3-months (N=413) and 6-months (N=320) after baseline survey.

	Retained at 3-Month			Retained at 6-Month		
	AOR <sup>†</sup>	LCL	HCL	AOR <sup>†</sup>	LCL	HCL
Single	0.99	0.975	1.009	1.03	0.996	1.066
Drug-Dependent Partner	0.98	0.957	1.012	<b>0.94*</b>	<b>0.896</b>	<b>0.993</b>
Detoxification attempts (1/100)	<b>0.92*</b>	<b>0.843</b>	<b>0.995</b>	1.18	0.998	1.403
Methadone Dose (1/100)	<b>0.96*</b>	<b>0.930</b>	<b>0.999</b>	0.99	0.927	1.070
First-Time Enrollment	1.01	0.998	1.029	<b>1.04*</b>	<b>1.007</b>	<b>1.071</b>

<sup>†</sup> Adjusted for gender, age, monthly household income (1/100), study site (Hubei vs. Shannxi) and result of the most recent urine test.

\* P<0.05.

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## CHAPTER V

### Summary

We concluded that the effectiveness of MMT was greatly appreciated by this group of newly enrolled patients and their partners. All patients claimed that MMT was the best detoxification experience they have had, which successfully suppressed the craving for substance with only minor side effects experienced. The patients returned to a close-to-normal life style with methadone. Couple began to make plans for their future as a family. However, the patients and their partners did not learn from past detoxification failures that one had to adhere to MMT for a long-term on a daily basis to continuously control their drug addiction. Rumors of the side effect of methadone were prevalent and should be countered as soon as a new patient is enrolled. Though the participants of our study showed an overall high level of satisfaction about the service provided, few of them discussed their concerns about MMT with the clinic staff. The majority of the patients perceived adherence to MMT as logistically manageable, which showed the feasibility of long-term adherence. Time management was more a burden than the financial cost for many patients, especially for those who had a full-time job. Some participants mentioned that they were not able to accept travelling assignments from work since MMT “tied” them locally.

The participating partners cared about the treatment progress of the patients and many of them were actively involved in monitoring the patients’ adherence to treatment. All of them had a good experience with methadone by observing the improvement in both physical and psychological health of their partners who had enrolled. The financial burden brought by substance use was greatly relieved, too. The drug-using partners who had not yet enrolled for MMT themselves planned to enroll after seeing the improvement of their partners. On the other



hand, the attitude towards MMT of the partners was biased by rumors in the drug-using circle that methadone could bring great harms to the patients' health in the long-run. Some partners observed or suspected the patients' continued substance use and they had played their part in reducing its occurrences.

The participants who had a drug-using regular partner were found to be less likely to be involved in substance abuse 3-months after methadone enrollment. But among those who remained in treatment at 3-months, these participants were more likely to drop-out by 6-months. Surprisingly, the participants who received a higher dose of methadone were more likely to drop out of treatment 3-months after enrollment. The finding contradicts what most authors report that higher dosage is usually associated with lower probability of substance use and better retention. This finding could be explained by the low acceptance of long-term treatment adherence to MMT among Chinese patients besides the average dose received by the participants were below the recommended 60ml and the finding reported by many authors that higher dose is usually associated with more side effects.

We make the following recommendations for future interventions based on our findings.

(1) The best possible time to educate the patients and partners about the importance of the maintenance nature of MMT could be 1-2 months after enrollment which allows some time for the benefits of MMT to be perceived. The first few months in treatment are therefore vitally important for long-term adherence.

(2) Training of the clinic staff is necessary for them to better understand the nature of methadone and how it works then they could better educate their patients. It would also improve the professional image of the staff in the eyes of the patients and partners.

(3) The popular opinion leader approach could be considered to counter the rumors of methadone's bad side effect. Patients who have been in treatment for a relatively long time are good candidates to be opinion leaders. The opinion leaders could reach not only the patients in treatment but also those who are affected by the rumors and hesitate to enroll.

(4) The patients could be freed if temporary transfers could be made in case they need to travel for work or for leisure. Such transfers are feasible in the sense that all MMT patients in China have a unique identification number and all MMT clinics are connected online by the national surveillance system.

(5) We suggest the staff at MMT clinics work closely with the partners for improved treatment outcomes. The partners are the key contact person to be reached in case a patient starts being absent from treatment.

(6) The partners should then be included in the educational programs held at the clinics. The programs also provide the partners an opportunity to meet one another and exchange ideas for better support.

(7) We urge the staff at MMT clinics to pay special attention on the concordant drug-using couples as they are at greater risk for relapse and drop out in the long run. Special counseling for couples would be helpful.

There are some limitations of the study that should be noted. The data were collected from a region with moderate drug-use problems. MMT patients in this area might differ from their counterparts in more heavily drug-affected regions of China. As a qualitative study, the sample was not representative of all newly enrolled patients and their partners, limiting the generalizability of the results. Regular partners who care more about the drug users' treatment

outcome were more likely to participate in this study. Besides, we did not interview other significant others of the drug users like parents or siblings who could also greatly contribute to treatment support, especially for single drug users under MMT. The participants of our study are newly enrolled patients and their partners. For a longer course in treatment more factors including relapses or logistic burden could complicate the factors associated with treatment retention and substance use. The study has adopted a prospective design, but due to logistic limitations, the participants were not really revisited at 3-month and 6-month follow-up. The treatment status and urine test result of each participant was obtained by contacting the clinics with the consent of the participants. If the study had re-contacted the participants at 3 and 6 months, more relevant information including current doses could have been collected.

Nonetheless, the findings of the study highlight the benefit brought by MMT to the drug users' family as a whole and highlight the impact of a drug-using regular sex partner's on a new MMT patient's treatment adherence and outcome. As drug-using couples are more vulnerable to continued substance use and premature treatment termination compared to sole users, special effort needs to be made to keep them in treatment.