Effect of community-based extension clinics of methadone maintenance therapy for opiate-dependent clients

A prospective cohort study in Dehong Prefecture, Yunnan Province of China

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Abstract

Methadone maintenance therapy (MMT) is effective in treatment of opiate dependents. However, there is a gap between the coverage of standard MMT clinics and the need of opiate dependents. Establishment of extension clinics of methadone maintenance therapy (EMMT) will increase the coverage and improve MMT accessibility. We implemented a prospective cohort study to understand the effects of establishment of community-based EMMT clinics comparing with MMT clinics in Yunnan Province.

A total of 462 opiate-dependent clients were interviewed from the community-based EMMT clinics and standard MMT clinics located in 5 counties of Mangshi, Ruili, Longchuan, Yingjiang, and Lianghe in Yunnan Province. The information on the demographic characteristics, drug risk behaviors, quality of life (QOL), and urine testing results for morphine of the clients was collected and compared between the EMMT and MMT clinics. A survival analysis method was utilized to know the retention situation of the newly enrolled clients with Kaplan–Meier method during 9 months treatment.

Among the EMMT clients, 96.9% were male; 31.4% were Han; 61.4% were married; 39.0% had primary school education; 95.5% lived with their family or relatives; 96.9% who arrived the clinic less than 15 min; 52.9% had used drugs for more than 10 years; and 16.7% injected drug. After 9 months therapy, there was no difference in the changes of life quality such as physical and psychological features, social relationships, environmental function, and total QOL and well-being between those of EMMT and MMT clinics. The positive detection rate of urine-morphine testing among newly enrolled clients of EMMT clinics decreased as the period of treatment lengthened. The average time of retention for newly enrolled EMMT clients who are still receiving the treatment was 175 days. And the average time from initiations to drop-out of treatment for newly enrolled EMMT clients was 122 days. The 9-month retention rates of the clients were 52.1% and 60.9% at EMMT and MMT clinics, respectively.

The effect on EMMT retention was the same as that of MMT. Establishment of EMMT clinics was an effective strategy to expand the coverage of MMT and increase the retention of opiate dependents in the rural areas of the counties.

Abbreviations: CDC = Centers for Disease Control and Prevention, EMMT = extension of methadone maintenance therapy, IDUs = injecting drug users, MMT = methadone maintenance therapy, QOL = quality of life, SPSS = Statistical Package for the Social Sciences.

Keywords: life quality, methadone maintenance therapy, opiate dependent, retention
1. Introduction

High-risk behaviors among injecting drug users (IDUs), such as sharing syringe and contacting with multiple sexual partners, made the high rate of HIV infection.\(^{[11-13]}\) By the end of 2014, there were 301,000 reported cases of people living with HIV/AIDS and 159,000 deaths had been reported in China. The national HIV/AIDS epidemic maintained a low level, with higher prevalence in some areas and among some high-risk behavior groups. The percentage of IDUs infected with HIV was 6.0% in 2014.\(^{[4]}\) HIV/AIDS epidemic was more serious in Yunnan than in other parts of China,\(^{[5,6]}\) especially in the border region of Yunnan, called “golden triangle.” AIDS cases were initially reported among native IDUs in 5 counties, including Mangshi, Ruili, Yingjiang, Longchuan, and Lianghe, Yunnan in 1989, representing the first wave of HIV epidemic in China.\(^{[7]}\) Owing to the special geographical position and frequent migration of people at the border with Myanmar, drug abuse was popular and harmful to the life and health of local people. Drug abuse resulted in the high incidence of HIV/AIDS in the whole province and made Yunnan as one of the most stricken HIV/AIDS epidemic areas in China.\(^{[8,9]}\)

By the end of 2014, the cumulative number of drug addicts registered by the Ministry of Public Security was 2.955 million, including 480,000 newly registered in 2014. According to data from China National Drug Abuse Surveillance Center, HIV infection rate among heroin abuse users was 3.5%,\(^{[10]}\) which was much higher than that of other groups because of syringe sharing and commercial sexual activities with multiple sexual partners.

Evidence showed that opiate substitution treatment was associated with reduction of injecting frequency, sharing injection equipment, and drug-related HIV infection risk scores.\(^{[11-13]}\) To prevent HIV/AIDS spreading among IDUs, and to reduce social problems with drug use and HIV transmission,\(^{[14]}\) the first group of 8 Methadone Maintenance Therapy (MMT) clinics was setup at city level in 5 provinces (or autonomous regions), including Yunnan, Guizhou, Sichuan, Guangxi, Zhejiang in 2004.\(^{[15]}\) With the development of MMT and accumulating experiences of MMT clinics in China,\(^{[16]}\) the effects of MMT were gradually apparent in reducing drug use behavior, decreasing infection of HIV, hepatitis C, and other blood-borne diseases,\(^{[17,18]}\) recovering social and family function of the clients, improving the quality of life (QOL) of the clients, and reducing the crimes related to drug addiction.\(^{[16,19-23]}\)

MMT coverage and accessibility was insufficient in some rural regions of Yunnan, Sichuan Provinces and other Southwest of China, where only 6% to 12% of drug injectors received it.\(^{[24-26]}\) Low attendance of clients to MMT clinics due to difficulties in transportation, long distance to clinics, and limited treatment hours negatively impacted the coverage and effect of MMT services. To expand the coverage of MMT services, the joint MMT working group at Yunnan provincial level including provincial public security bureau, Yunnan provincial center for disease control and prevention, Yunnan provincial food and drug administration, decided to pilot the program of establishing extension MMT (EMMT) clinics based on community healthcare agencies in the areas where opiate dependents were relatively concentrated since June, 2008.\(^{[16]}\) EMMT clinics were established mainly in village clinics, rural township hospitals, or community healthcare centers in Dehong Prefecture, which situated in the western part of Yunnan Province and bordered Myanmar on 3 sides with about 500km border. The original intentions of establishing EMMT clinics were to solve the difficulty of transportation and provide the services like MMT clinics; besides to meet the needs of increasing clients. EMMT clinics were setup and scaled up quickly in all 5 counties of Dehong Prefecture, and in pilot phase. There was no research on the characteristics of the clients and effectiveness of EMMT clinics. In order to assess the effectiveness of EMMT clinics, we analyzed the characteristics, retention rate, and the life quality of clients of EMMT clinics, which were compared to that of MMT clinics. The results of study will provide the evidence for the expansion of the EMMT clinics in similar rural areas of other parts of China in the next step.

2. Methods

2.1. Study sites

We selected 5 counties of Dehong Dai and Jingpo Autonomous Prefecture of Yunnan Province as the study sites, including Mangshi, Ruili, Yingjiang, Longchuan, and Lianghe. These sites were those of the worst stricken regions by HIV/AIDS epidemic and the first batch of EMMT clinics setup in China with complete information of the MMT clients. The ethnic minorities accounted for 51.68% of the total population of 5 counties, and 85% of the areas were mountainous. Due to the special geographical location, adjacent to the well-known “golden triangle,” opiate dependents in the areas were living widely in the remote townships and villages along the border and they were at high risk of HIV infection.

Originally, the standard MMT clinics were required to establish in the urban areas with more than 500 registered drug users,\(^{[27]}\) normally with one MMT in one county managed by the local institutions of disease control and prevention or medical institutions to undertake harm reduction services for opiate dependents.

2.2. Participants

Participants were selected according to the criteria of drug users eligible for MMT services in China,\(^{[28]}\) including those with repeated relapse from detoxification; with 2 times of failure in compulsory drug addiction rehabilitation; over 20 years of age; of local residents with a fixed residence or temporary residents, and with a complete civil capacity. The opiate dependents infected with HIV were eligible for the MMT services if they met only the fourth and fifth items of the above criteria for reducing HIV transmission among opiate dependents and, benefiting and covering more opiate dependents. The opiate dependents would be expelled from MMT clinics, if they had, consecutive 30 days away from MMT during the past 3 months of receiving the treatment; 3 times of positive results of urine morphine testing in the past 6 months or the methadone taken out of MMT clinics; behaviors interfering with the clinics’ routine work, and discontinuing the treatment because of complications; and not insisted on the treatment by self-report.\(^{[16]}\) All participants enrolled in the study got written informed consent before interviewing according to the requirements of Work Plan of Community Maintenance Treatment for Opioid Addicts.\(^{[29]}\)

To expand the coverage of MMT services, 17 EMMT clinics were setup at the community healthcare centers. Two medical staff members were employed at least at each EMMT clinic, including 1 doctor who delivered physical check and counseling and prescribed the methadone, and 1 nurse who dispensed the methadone and observed them to take in. The EMMT clinics were affiliated with MMT clinics which were responsible for the daily management, personnel training, and technical supports for the EMMT clinics.
From December 20, 2010 to March 19, 2011, 345 clients receiving MMT services more than 3 months were selected with stratified random sampling method from 5 MMT clinics and 17 EMMT clinics in 5 counties, with 193 cases from MMT clinics and 152 cases from EMMT clinics, respectively. During this period, 117 clients were newly enrolled to receive the services, with 46 from MMT clinics, and 71 from EMMT clinics. A total of 462 clients were recruited in the study, with the group of 239 cases from MMT clinics, and the one of 223 cases from EMMT clinics (Fig. 1).

Ethical approval (No:X140617338) for this study was obtained from the Institutional Review Board of the National Center for AIDS/STD Control and Prevention (NCAIDS), Chinese Center for Disease Control and Prevention (China CDC). Permission to access MMT registers and database was given by the Dehong Prefecture Center for Disease Control and Prevention that was responsible to MMT services for opiate-dependent clients in 5 counties of Dehong.

2.3. Data collection

The prospective cohort study was designed for opiate dependents receiving the treatment for more than 3 months and newly enrolled from MMT and EMMT clinics. Both groups were followed up for 9 months with their QOL, urine testing results for morphine, and retention situation compared with those of baseline.

The entry date of treatment was counted as the first follow-up visit, and the follow-up deadline was January 20, 2012. If a client did not visit the EMMT or MMT clinic for consecutive 30 days, the date of last visit was recorded as the date of the outcome. If a client still survived and received the treatment through the deadline, the client was defined as a censored one with January 20, 2012 as his/her date of censorship.

2.4. Measures

The health workers of MMT and EMMT clinics interviewed the clients and filled in the community MMT baseline questionnaire in the first week of the research, with the data of life quality and daily record of urine morphine testing collected and analyzed, including basic demographic features, maintenance treatment, life quality, the testing results of urine morphine of the clients. The questionnaire was attached to Chinese Methadone Maintenance Therapy Clinic Data Management System, which was developed, tested, and validated by NCAIDS in 2004. After 9 months of treatment, the results of newly enrolled EMMT clients were compared with those of newly enrolled MMT clients, and then, the treatment effectiveness of MMT clinics and EMMT clinics was assessed.
The community MMT baseline questionnaire was completed as the baseline in the first week of enrollment by Chinese Methadone Maintenance Therapy Clinic Data Management System. The interviewers collected the basic demographic information of the clients, including age, sex, ethnicity, educational level, current marital status, and living conditions, such as income, dwelling status, the distance between inhabitance and the clinic (less than 15 min, more than 30 min, between 16 and 30 min), drug risk behaviors before the treatment entry.

The QOL scale brief form (QOL-BREF) Chinese version was utilized\(^{29}\) and completed by the interviewers at the baseline and 9 months of treatment to understand the clients’ QOL in the domains of physical, psychological, social relationships, and environment in the past month. The form included 24 items on the individual’s QOL, and 2 items reflecting the overall QOL and health. Each item had a scale from 1 to 5 points, with the higher the score, the better the QOL.

The incidence of urine morphine positive was calculated among the clients with randomized sampling and testing monthly. Urine morphine test with the colloidal gold morphine detection kit (ABON Biopharm Co., Ltd., Hangzhou, China) was a qualitative screening conducted irregularly in MMT and EMMT clinics. The test could not determine the content of morphine in urine, but could tell whether clients took opiates substance in the past 7 days therefore could assess indirectly the effectiveness of MMT.

2.5. MMT and EMMT services

The EMMT clinics were setup in public medical institutions, usually located in primary healthcare institutions according to the requirements of Ministry of Public Security, Yunnan Health Bureau, and China Food and Drug Administration. The health workers of the EMMT clinics, from community healthcare centers got trained on diagnosis of heroin dependence, treatment, policy support for and management of MMT program, counseling and communication skills, and emergency response to the clients.\(^{30}\)

The following services were delivered to the clients to the MMT and EMMT clinics, including directly observed treatment, testing for antibody of HIV, hepatitis B virus, hepatitis C virus, testing for urine morphine, counseling, physical check, transfer treatment for sexually transmitted infections, antiretroviral therapy, opportunistic infections, support of family members, health education on HIV prevention, MMT, and psychological counseling. EMMT clinics were more flexible in services delivery than MMT clinics located in urban areas. For example, comparing to MMT clinics’ routine and regular working time from 8:00 AM to 4:00 PM every day, EMMT clinics could have longer and flexible working hours, like from 9:30 AM to 18:30 PM or from 10:00 AM to 19:00 PM. Because EMMT clinics were community-based, staff of EMMT clinics would spend more time on visiting the family of the clients and seeking the family supports to help the clients keeping in the treatment.

Before the field investigation, all the interviewers from local CDC, MMT and EMMT clinics were trained to understand the research protocol, especially to know the procedures of data collection such as how to get informed consent and how to fill in the questionnaires, and to master the communication skills for the interview. The interviewers collected monthly relevant information of the clients after the entry month.

2.6. Data analysis

The database of the study was setup via EpiData 3.0 for Windows (The EpiData Association, Odense, Denmark) and transferred and analyzed via SPSS version 17.0 (SPSS Inc., Chicago, IL). \(\chi^2\) analysis was carried out to study the difference of demographic information, the living conditions, and drug risk behaviors between MMT and EMMT clinics, and the difference of urine morphine positive of the clients between MMT clinics and EMMT clinics monthly in 9 months. The mean scores of each of the 4 domains of QOL of newly enrolled clients were calculated with \(t\) test analysis at baseline and after 9 months follow-up, respectively, between MMT clinics and EMMT clinics. Median retention time receiving MMT services was calculated by Kaplan–Meier survival analyses as a point where 50% of the clients were still receiving MMT services. Retention time after initiating MMT services was calculated by different newly enrolled clients of MMT clinics and EMMT clinics, and differences in retention time between 2 types of MMT clinics were examined by using the log-rank test of Kaplan–Meier survival analyses. With \(P < .05\) for the difference was statistically significant. All the tests were two-tailed, and the type 1 error rate was set at 5%.

3. Results

3.1. Study population

A total of 462 clients were recruited, with 239 enrolled in MMT clinics, and 223 in EMMT clinics, or with 345 clients receiving services more than 3 months and 117 clients newly enrolled. By January 20, 2012, 26.2% (121/462) dropped out of the treatment among the 462 clients receiving MMT services, from 3 MMT (45 clients) clinics and 17 EMMT (76 clients) clinics. Follow-up rates were 81.2% (194/239) among the clients of MMT clinics and 65.9% (147/223) among the clients of EMMT clinics. In total, 84.0% (163/194) of those with follow-up was the clients of receiving MMT services more than 3 months before the study. In total, 76.9% (113/147) of those with follow-up was the clients of receiving EMMT services more than 3 months before the study (Fig. 1).

3.2. Baseline characteristics

The mean age at entry of the clients of EMMT clinics firstly was 38.9 (SD = 9.6) years old, with a range from 22.7 to 72.3 years old. The mean age of drug use initiation was 25.8 (SD = 7.8) years old, with a range from 12.5 to 50.0 years old. The mean time spending on the way from the inhabitance to the clinic was 14.3 min (SD = 12.7), with a range from 3 to 40 min. The mean duration of drug use was 11.7 (SD = 7.5) years, with a range from 0.5 to 38 years.

In total, 96.9% of EMMT clients were male, 31.4% Han nationality, and 61.4% married, 39.0% received primary school education, and 95.5% lived with their family or relatives. At the treatment initiation, 75.3% was supported financially by their family members, 96.9% arrived the clinic less than 15 min, 55.2% never saw their drug-using friends in the past week, 96.4% initiated drug use more than 15 years old, 52.9% used drug over 10 years, 16.7% injected drug last month, 92.8% had good or better relation with their family members.

Table 1 showed the comparisons of the demographic characteristics, living conditions, and drug risk behaviors before treatment for the MMT and EMMT clients. There were no statistically significant differences between both groups with respect to sex, age, marital status, dwelling status, the mean time spending on the way from home to the clinic, age of drug use...
initiation, history of drug use, relationship with family members, and visiting drug-using friends at baseline. However, the differences were statistically significant between both groups of clients in the ethnicity, education, routes of drug use, sources of income, transportation mode to the clinic. More clients of MMT than those of EMMT were Han, high school educated or above, IDUs, and more clients of EMMT than those of MMT lived on family supporting, tripped on foot to the clinics.

Table 1
Characteristics of MMT clients and EMMT clients at baseline in 5 counties.

| Variable                                      | MMT clinic (n=239) | EMMT (n=223) | χ² | P value |
|-----------------------------------------------|--------------------|--------------|----|---------|
| Sex                                           |                    |              |    |         |
| Male                                          | 235                | 216          | 0.529 | .476    |
| Female                                        | 4                  | 7            | 3.1 |         |
| Age (years)                                   |                    |              |    |         |
| 18–29                                         | 56                 | 51           | 1.029 | .998    |
| 30–39                                         | 97                 | 82           | 36.8 |         |
| 40+                                           | 86                 | 90           | 40.3 |         |
| Ethnicity                                     |                    |              |    |         |
| Han                                           | 118                | 70           | 45.042 | <.001  |
| Others                                        | 121                | 153          | 68.6 |         |
| Marital status                                |                    |              |    |         |
| Unmarried                                     | 83                 | 62           | 2.571 | .277    |
| Married/cohabiting                            | 133                | 137          | 61.4 |         |
| Divorced/widowed                              | 23                 | 24           | 10.8 |         |
| Education                                     |                    |              |    |         |
| Illiteracy                                    | 22                 | 40           | 15.977 | .002  |
| Elementary                                    | 79                 | 87           | 39.0 |         |
| Junior high school                            | 97                 | 75           | 33.6 |         |
| High school or above                          | 41                 | 21           | 9.4 |         |
| Age of drug use initiation (years, N=458)     |                    |              |    |         |
| Less than 15                                  | 13                 | 8            | 4.512 | .105    |
| 16–30                                         | 188                | 167          | 74.9 |         |
| 30+                                           | 34                 | 48           | 21.5 |         |
| History of drug use (years)                   |                    |              |    |         |
| Less than 5                                   | 36                 | 39           | 1.335 | .277    |
| 5–10                                         | 82                 | 66           | 29.6 |         |
| 10+                                           | 121                | 118          | 52.9 |         |
| Routes of drug use (N=457)                    |                    |              |    |         |
| Intravenous injection                         | 70                 | 37           | 10.24 | <.001  |
| Others                                        | 165                | 185          | 83.3 |         |
| Sources of income                             |                    |              |    |         |
| Fixed salary                                  | 34                 | 24           | 10.8 |         |
| Temporary job salary                          | 58                 | 31           | 13.9 |         |
| Family supporting                             | 147                | 168          | 75.3 |         |
| Dwelling status (N=456)                       |                    |              |    |         |
| Living alone                                  | 11                 | 10           | 4.5 |         |
| Living with the family/relatives              | 222                | 213          | 95.5 |         |
| Relation with family members by self-report (N=459) |        |              |    |         |
| Bad                                           | 25                 | 16           | 7.2 |         |
| Good                                          | 149                | 139          | 62.3 |         |
| Better                                        | 62                 | 68           | 30.5 |         |
| Visiting drug-using friends (N=457)           |                    |              |    |         |
| Never                                         | 153                | 122          | 55.2 |         |
| Sometime                                      | 42                 | 46           | 20.8 |         |
| Often                                         | 41                 | 53           | 24.0 |         |
| Time spending on the way from the inhabitance to the clinic | |              |    |         |
| Less than 15 min                              | 224                | 216          | 3.443 | .717    |
| 16–30 min                                     | 10                 | 3            | 1.3 |         |
| More than 30 min                              | 5                  | 4            | 1.8 |         |
| Transport mode to the clinic                  |                    |              |    |         |
| On foot                                       | 31                 | 49           | 22.0 |         |
| By bus or car                                 | 23                 | 6            | 2.7 |         |
| Others∗                                       | 182                | 168          | 75.3 |         |

EMMT = extension of methadone maintenance therapy, MMT = methadone maintenance therapy.

∗Other transport mode to the clinic included by bicycle, motorcycle, and tricycle.

The bold values means that the differences were statistically significant.
The urine morphine testing results among the newly enrolled MMT and EMMT clients by month in 5 counties, China.

| Month     | MMT clinics | EMMT clinics |
|-----------|-------------|--------------|
|           | No. of testing | Positive rate | No. of testing | Positive rate | $\chi^2$ value | $P$ value |
| 1st month | 9            | 100.00%       | 18           | 72.22%        | 0.137         | .711    |
| 2nd month | 24           | 75.00%        | 34           | 70.59%        | 0.013         | .905    |
| 3rd month | 38           | 57.89%        | 52           | 57.69%        | 0.001         | .965    |
| 4th month | 36           | 33.33%        | 52           | 28.85%        | 0.020         | .654    |
| 5th month | 30           | 36.67%        | 44           | 13.64%        | 5.347         | .021    |
| 6th month | 31           | 41.94%        | 29           | 13.79%        | 5.844         | .016    |
| 7th month | 29           | 31.05%        | 34           | 14.71%        | 2.414         | .120    |
| 8th month | 28           | 28.57%        | 35           | 17.14%        | 1.176         | .278    |
| 9th month | 28           | 25.00%        | 33           | 6.06%         | 4.320         | .038    |
The situation of drug addiction in Dehong. The results of the clinic were male, which was same as the result of the study on were setup in rural regions. The policy of establishment of EMMT was made and EMMT clinics were alleviated or removed. As the supplement and extension of MMT clinic, EMMT clinic can enlarge the coverage of services of harm reduction and improve the clients adhering to the treatment, especially in the villages of remote areas of drug users gathering. After 3 years of piloting EMMT clinics in Dehong of Yunnan from 2008. The study assessed the effect of MMT clinic, EMMT clinic can enlarge the coverage of services of harm reduction and improve the clients adhering to the treatment. The newly enrolled MMT clients could receive the quality and personalized counseling in the early months of the treatment entry. Counseling and rehabilitative services during the treatment were important, especially in the first month of enrollment. The life quality of the newly enrolled clients of EMMT clinics did not improve significantly in some domains after 9 months treatment. The reason for this may be the treatment time for the EMMT clients was short relatively, and the change of some domains of life quality such as social relations needed a long time to observe. However, there were no significant differences between the changes of life quality of the newly enrolled clients of MMT and EMMT clinics after receiving the treatment. The nature and contents of service be provided by EMMT clinics for the clients were same as those of MMT clinics, included mainly providing maintenance treatment and counseling.

One study on the first 8 of MMT clinics of China, established and piloted in 2004, found the average positive rate of urine test was low (1%–10%) during the follow-up period of 6 years. The positive rates of urine morphine test of the EMMT clients were above 50% during first 3 months follow-up, and fell to 28.85% at 4th month of the follow-up, to 6.06% at 9th month. There was a down trend of the positive rate of urine morphine test as time went on among the both of clients of MMT and EMMT clinics. This result was similar with the finding of the study implemented in Urumqi of China on evaluation of 6-month MMT effectiveness, in which positive rate of urine morphine test decreased from 100% at the entry treatment to 37.23% after 6-month of receiving the treatment. The positive rate of urine morphine test among the EMMT clients was lower than that of the MMT clients. The reason for this may be the health workers and the family members of EMMT clients were convenient to oversee and encourage the clients to receive and remain the treatment on the long-term, and reduce the opportunities of contacting with their former drug use friends and establish a new
should be strengthened in the remote areas. We also recommend local health authorities should cooperate with public security bureaus, community-based organizations, and other stakeholders on policy development and advocacy, financial and technical supports, and disseminations of knowledge of MMT.

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