

•ORIGINAL RESEARCH ARTICLE•

Status Investigation of Outpatients Receiving Methadone Maintenance Treatment (MMT) in Shanghai from 2005 to 2016

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Background: Methadone maintenance treatment (MMT) is an effective measure to control drug abuse, prevent AIDS, and improve family and social functions among those with heroin addiction. Relevant surveys in recent years show that the number of outpatients receiving MMT has a downward trend.

Aims: To understand variation in maintenance treatment rates and causes of withdrawal for outpatients receiving MMT in Shanghai since initiation of this program.

Method: This study was a retrospective investigation, with data from the AIDS Comprehensive Prevention and Control Data Information Management System of the China AIDS Prevention and Control Center. Descriptive statistics were used to describe demographic data, treatment maintenance rate, and number of new outpatients receiving MMT in Shanghai From May 2005 to June 2016. The causes of withdrawal were summarized and analyzed.

Results: From May 2005 to June 2016, there were a total of 7181 outpatients receiving MMT in Shanghai. These patients were primarily male (male to female ratio around 3:1), young adults (more than 90% of these patients were 25 to 54 years old), with junior high school education level and below (65.4%), single (total of unmarried, divorced and widowed: 63.1%), and unemployed or underemployed (81.5%). The daily dose of methadone in MMT patients showed an upward trend since 2008, and gradually declined after reaching its peak in 2013. The mean (sd) dose of methadone taken in the years studied was 56 (2.75) ml/d. The number of new outpatients increased sharply in 2007 and 2008 (more than 1500), and then decreased year by year. The number of outpatients had increased continuously from 2005 to 2011, with the peak in 2011 (3840 patients), and then decreased gradually. The maintenance rate was stable at over 80% since 2010. The main causes of withdrawal: 1) arrested due to unrelated criminal causes (19.89%), 2) sent to compulsory isolated rehabilitation center due to occasional drug use, and 3) physical reasons (disease/pregnancy/death, 11.80%).

Conclusion: The maintenance rate has been kept at a relatively good level since the initiation of the MMT outpatient clinic service in Shanghai. The number of patients receiving treatment showed an increase-then-decrease trend. The main causes of patients' withdrawal were mainly related to "crime" and "relapse". In order to make MMT outpatient service better, subsequent studies need to carry out related investigations to understand the causes of these changes and patients reasons for withdrawal.

Key words: Methadone maintenance treatment, heroin dependence, maintenance rate

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1. Background

Methadone as a replacement therapy drug for those with heroin addiction was put forward by Dole and Nyswander in 1965. Afterwards, western countries began to use MMT as the foremost treatment for opioid addiction, and gradually popularize the application.^[1] MMT has now become one of the most effective measures to control drug abuse and prevent AIDS among heroin users.^[2-3] Since 2004, MMT pilot clinics have gradually been established in China. As of May 2016, a total of 788 MMT clinics have been set up in 29 provinces.^[4] Evaluation of the therapeutic efficacy administered by the first batch of 8 MMT pilot clinics^[5] and the MMT clinic in Urumqi^[6] showed positive functions of MMT in reducing drug use, preventing drug-related high-risk sexual activities, unlawful acts and crimes, and improving patients' family and social functions. However, relevant surveys in recent years showed that the number of outpatients receiving MMT and the number of new outpatients showed a downward trend year by year, respectively.^[7,8]

The first Shanghai MMT clinic was officially launched in Changning District in May 2005. As of now, there are 14 MMT clinics in Shanghai. In this paper, data from patients receiving MMT since 2005 in Shanghai were analyzed to understand the variations in patient numbers, maintenance treatment rate, and causes of drop out for outpatients receiving MMT, in order to provide data support for the improvement of MMT clinics in the future.

2 Subjects and methods

2.1 Subjects

The subjects of this study included a total of 7181 patients, who received maintenance treatment at each MMT clinic in Shanghai from May 2005 to June 2016, according to the Community Drug Maintenance Treatment Program for Opioids-Abuse Addicts in Shanghai. Referral MMT patients from out of Shanghai were not included, without other exclusion criteria. All

the subjects' data were from the AIDS Comprehensive Prevention and Control Data Information Management System of the China AIDS Prevention and Control Center. These data are open for use in scientific research, after application to the China CDC. This study has been approved by the ethical review committee of Shanghai Municipal Center for Disease Control and Prevention.

2.2 Methods

This study was a retrospective investigation, with relevant data including demographic data (i.e. age, gender, ethnicity, education level, marital status, and employment status), dosage, outpatient number, number of new outpatients, causes of withdrawal, and treatment maintenance rate. According to the National Center for Disease Control and Prevention, outpatient maintenance rate = number of patients treated in the past month/(number of patients being treated–number of dropouts due to special reasons in the past year)*100%. 'Special reasons' refer to death, contraction of a rare disease, pregnancy, unlawful acts and crimes not involving drug use.

2.3 Statistical methods

Descriptive statistics using SPSS 20.0 were employed to describe demographic data, treatment maintenance rates, and number of new outpatients receiving MMT. The causes of dropout were summarized and analyzed.

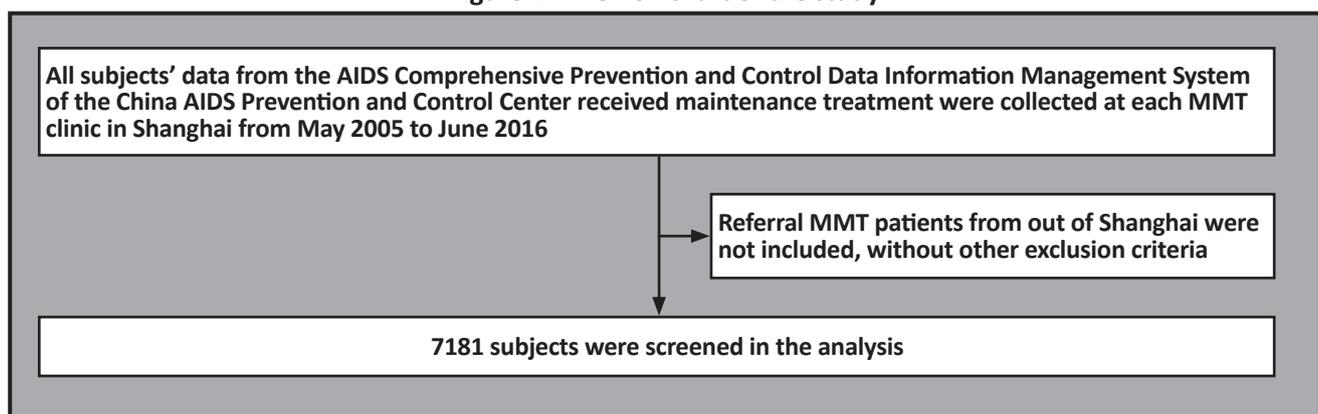
3. Results

3.1 Outpatient treatment

3.1.1 Number of patients

From May 2005 to June 2016, there were a total of 7181 outpatients receiving MMT in Shanghai. There was an increase in the number of new patients from 2007–2009, with average new patient numbers exceeding 1000. After peaking in 2008, the number of new patients decreased year by year. The number of patients

Figure 1. The flowchart of the study



increased continuously between 2005 and 2011, with the peak in 2011 (3840 patients), and then gradually decreased, see Figure 1.

3.1.2 Comparison of number of heroin-related arrests and the number of people treated by methadone treatment clinics in Shanghai (2009-2015)

From 2009-2015, the number of heroin-related arrests showed a slow downward trend in Shanghai. In 2012, the number of arrests considerably increased. Afterwards, the number continued to decrease year by year. The number of new treatments in methadone clinics was 1141 in 2009. Afterwards and until 2015, the number was <1000 each year, showing a downward trend year by year, see Figure 2.

3.1.3 Maintenance treatment rate

The maintenance treatment rate at methadone clinics in Shanghai increased year by year, from 66.1% (2008) to 84.3% (2010). Although with a slight decline in the subsequent four years, the maintenance treatment rate was stable above 80%. In 2015, the outpatient maintenance rate was 87.7%, showing good maintenance treatment effects. See Figure 3.

3.2 Patient conditions

3.2.1 Demographic characteristics

MMT clinic patients in Shanghai were primarily male (77.9%), predominantly young adults 25 to 54 years old, with below-average education, i.e. junior high school education level and below (65.4%), single (total

of unmarried, divorced and widowed: 63.1%), and unemployed or underemployed (81.5%), see Table 1.

3.2.2 Dosage

Between 2008 and June 2016, the daily average number of people taking medication through Shanghai MMT clinics was 1687. In 2012, the number of people taking medication peaked, followed by a downward trend. The average daily dosage of methadone per patient was 56ml. The daily average number of MMT medication users and daily average dosage per patient in each year are shown in table 2.

In each year, the daily average number of MMT medication users exceeded 100 in Pudong New Area, Hongkou District, Xuhui District, Yangpu District, Zhabei District, Putuo District and Huangpu District, respectively. The average daily dosage of methadone per patient exceeded the Shanghai average 56ml/d in Hongkou District, Putuo District, Huangpu District, Baoshan District and Qingpu District, respectively. The average number of daily MMT medication users and average daily dose per person in each district are shown in Figure 4.

In year 2008-2015, there was a significant correlation between the maintenance rate and the average daily dosage in the methadone clinics in Shanghai ($r=0.199, p<0.001$).

3.2.3 Causes of dropout

Statistical data showed that, the main causes for the withdrawal from outpatient services were not collected due to an inability to follow up, see Figure 5.

Figure 1. Number of patients in methadone maintenance clinics in Shanghai (2005-2016)

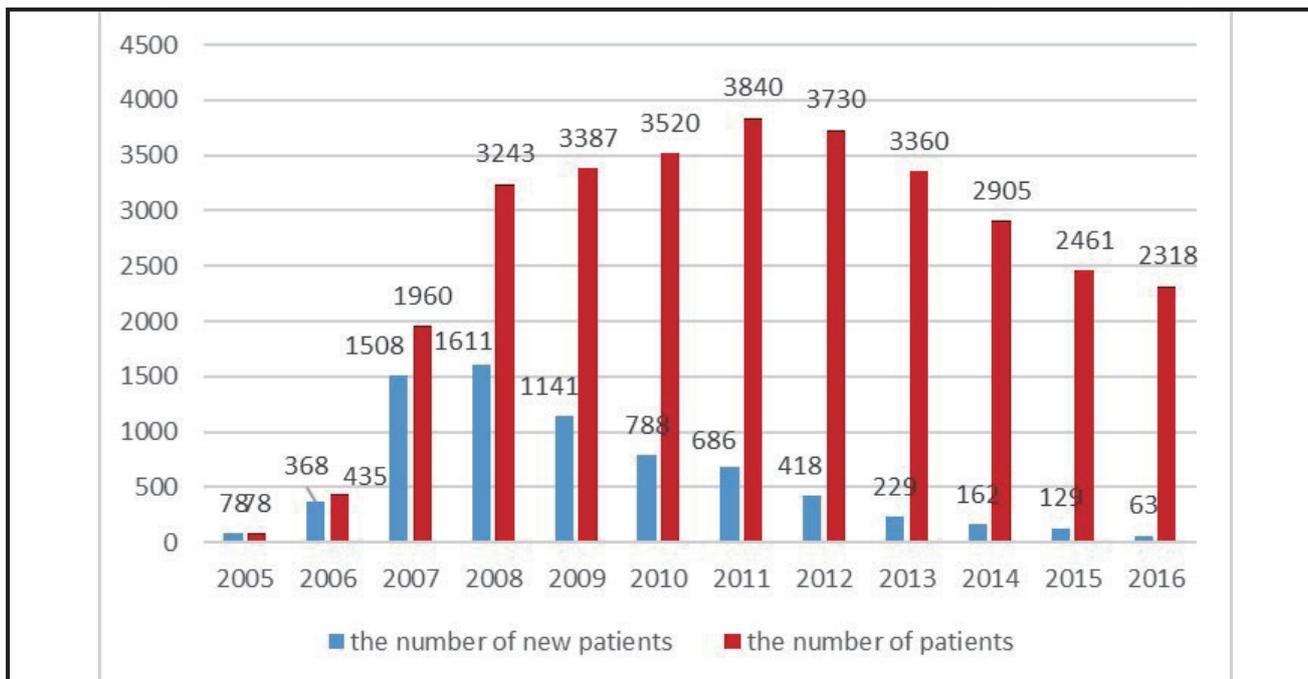


Figure 2. Comparison of number of heroin-related arrests and the number of people treated by methadone treatment in Shanghai (2009-2015)

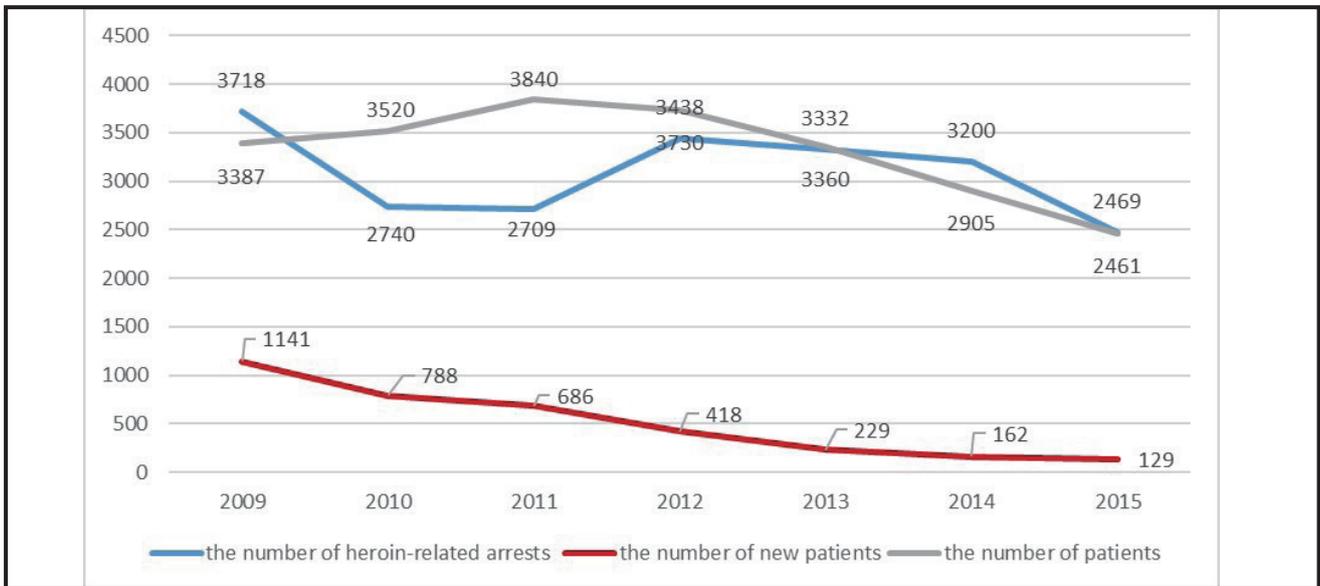
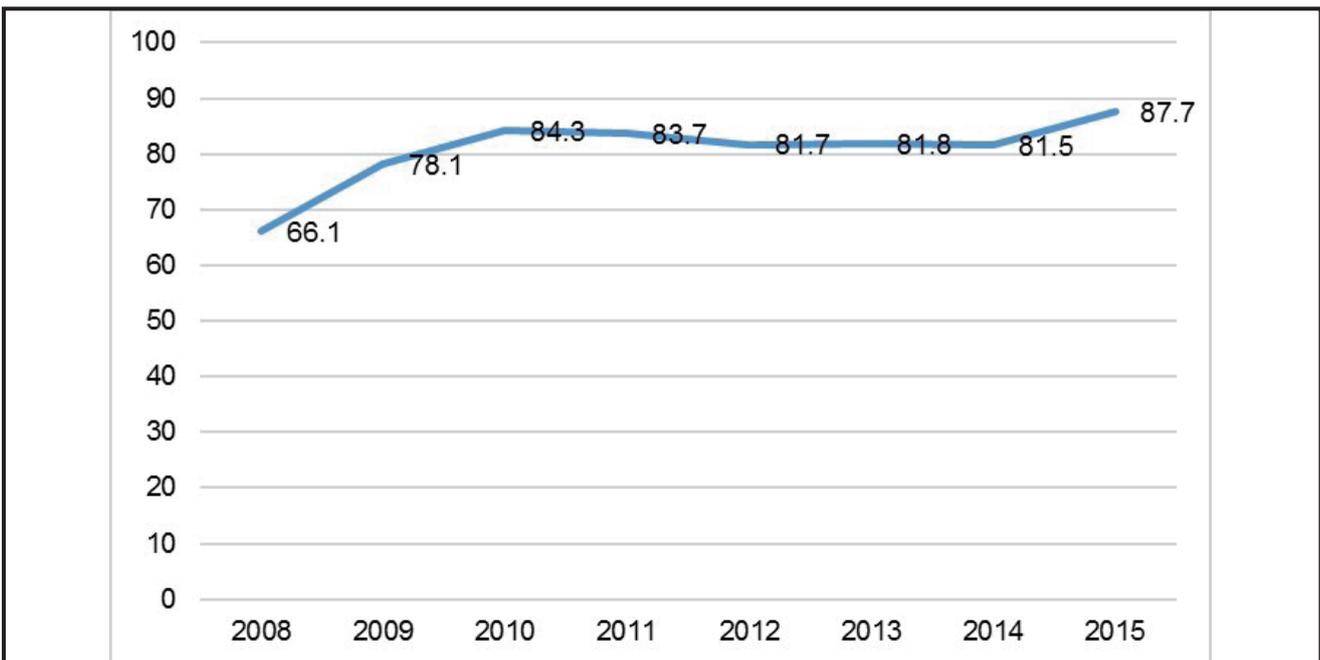


Figure 3. The maintenance treatment rate at methadone clinics in Shanghai (2008-2015)



4. Discussion

4.1 Main findings

China began to establish MMT pilot clinics in multiple provinces and cities starting in 2004. In early years, the number of outpatients increased rapidly. In recent years, the number of MMT outpatients nationwide showed a downward trend, from 209,000 in 2012 down to 165,000 in 2016 (*the National HIV AIDS Epidemic Situation and Progress of Prevention and Control Work*). This study for the first time carried out

descriptive analysis on the treatment work over the years for MMT clinics in Shanghai. It was found that, since the beginning of the MMT clinics in Shanghai, the clinic maintenance rate was fairly high. The number of outpatients increased initially and then decreased subsequently, which is similar to the overall trends in the country. The main causes for patient dropout were related to crime and relapse. In the meantime, it was also found in the study that there were differences in patient number and dosage of medication among the districts in Shanghai. The details are as follows.

Table 1. Demographic characteristics of outpatients receiving MMT in Shanghai

Demographic characteristics	Number of patients	Percentage (%)
Gender		
Male	5593	77.9
Age		
15-24	175	2.4
25-34	1617	22.5
35-44	2489	34.7
45-54	2593	36.1
55-74	307	4.2
Education level		
Junior high and below	4696	65.4
Senior high or technical school	2290	31.9
College and higher	195	2.7
Marriage status		
Single	2791	38.9
Married or cohabitating	2648	36.9
Divorced or widowed	1730	24.1
Other	12	0.2
Occupation		
Unemployed	5850	81.5

Table 2. Patients' dosages at MMT clinics in Shanghai

Year	Daily average patient number taking medication	Daily average dosage per patient (ml)
2008	1339	52
2009	1689	53
2010	1911	56
2011	2103	58
2012	2064	59
2013	1812	61
2014	1575	58
2015	1382	56
2016.1-6	1311	57
Average	1687	56

First, the results showed that the number of MMT patients in Shanghai increased initially and then decreased subsequently, which was similar to the situation at MMT clinics in Wenzhou.^[7] The reason may be that, at the beginning stage of clinical treatment, MMT as an effective alternative therapeutic method supported by relevant national policy was heavily publicized and promoted. The degree of acceptance of medical institutions and patients was high fairly, which led to the sharp increase in patient number during the early years of the MMT clinics between 2005 and 2008. Since 2011, MMT clinics in Shanghai showed a downward trend. The decline in patient number was possibly related to various factors. The daily cost of treatment increased the economic burden for heroin users. Convenience in access to MMT began to gradually come out.^[9] Some studies found that patients with a low level of methadone awareness and those who were worried about methadone's adverse reactions were not likely to accept MMT.^[10] Improving patient awareness of methadone, through strengthened public education, was beneficial to improving the coverage rate of MMT in previous studies.^[11] MMT outpatient service was an important way for patients to acquire relevant knowledge. However the staff of MMT outpatient services nationwide generally lacked psychological training, had high staff turnover^[12] and job burnout.^[12,13] These factors likely affect the users satisfaction with MMT clinics, and may reduce the number of those willing to seek MMT. In addition, changes in the drug abuse situation, from traditional drugs to synthetic drugs have contributed to the decline in patient numbers.

According to the national drug control report (2008-2015), among the nationwide total drug users, the percentage of heroin and other opioid users decreased significantly and showed a downward trend since 2008 (77.5%). In 2014, it was less than half of all users (49.3%). The number of synthetic drug users increased rapidly year after year, from 6.7% in 2005 to 57.1% of the total number of drug users by the end of 2015. It is worth noting that, although there was a nationwide decrease in the number of heroin and other opioid addicts since 2008, and the number of new MMT outpatients in Shanghai had been decreasing, the number of heroin related arrests in Shanghai did not show a corresponding downward trend, see Figure 2. This suggests that the situation of heroin abuse in Shanghai was still relatively serious, and the crackdown effort was high. Nevertheless, only a small portion of patients had accepted MMT, i.e., the outpatient admission rate of MMT clinics in Shanghai was low, e.g. 6.87%, 5%, 5.2% for 2013-2015 respectively (the ratio of number of new patients at MMT clinics to the number of captured heroin addicts each year in Shanghai).

This study showed that the maintenance rate at MMT clinics in Shanghai was 66.1% in 2008, 78.1% in 2009, and had been greater than 80% since 2010. In 2015, the maintenance rate was close to 90% (87.7%). It

Figure 4. The average number of daily MMT medication users and average daily dose per person in each district

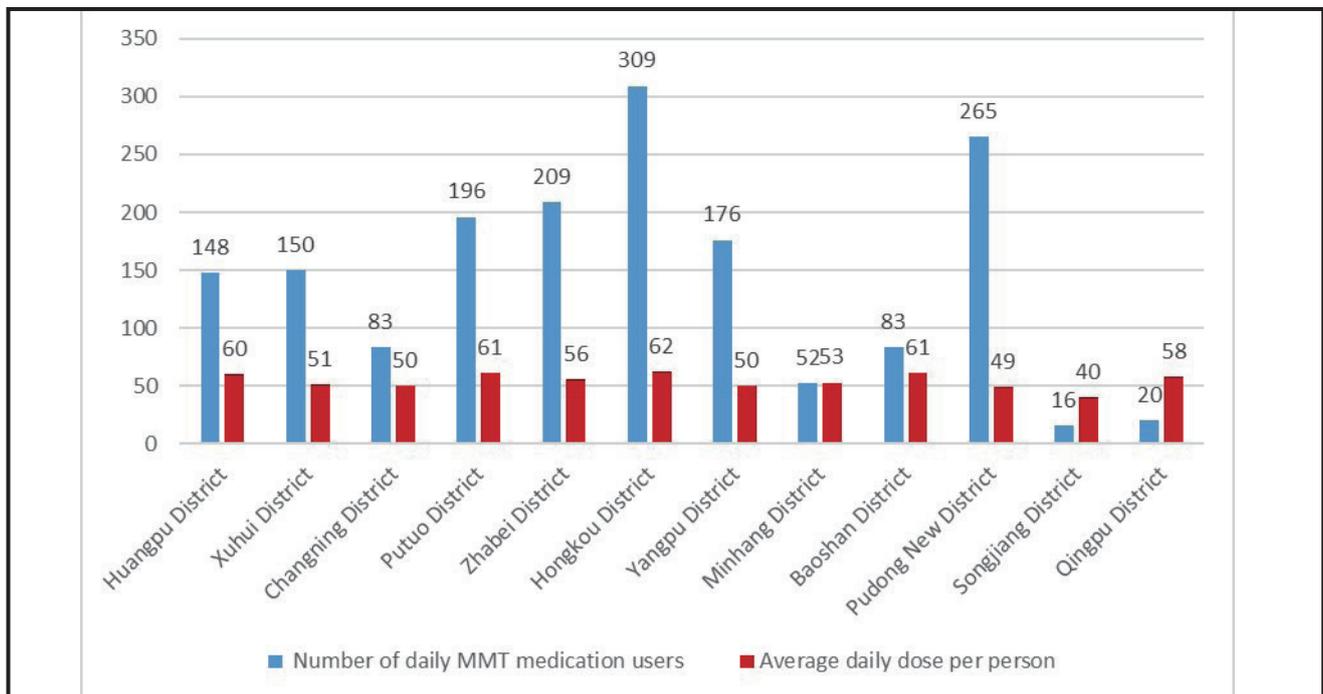
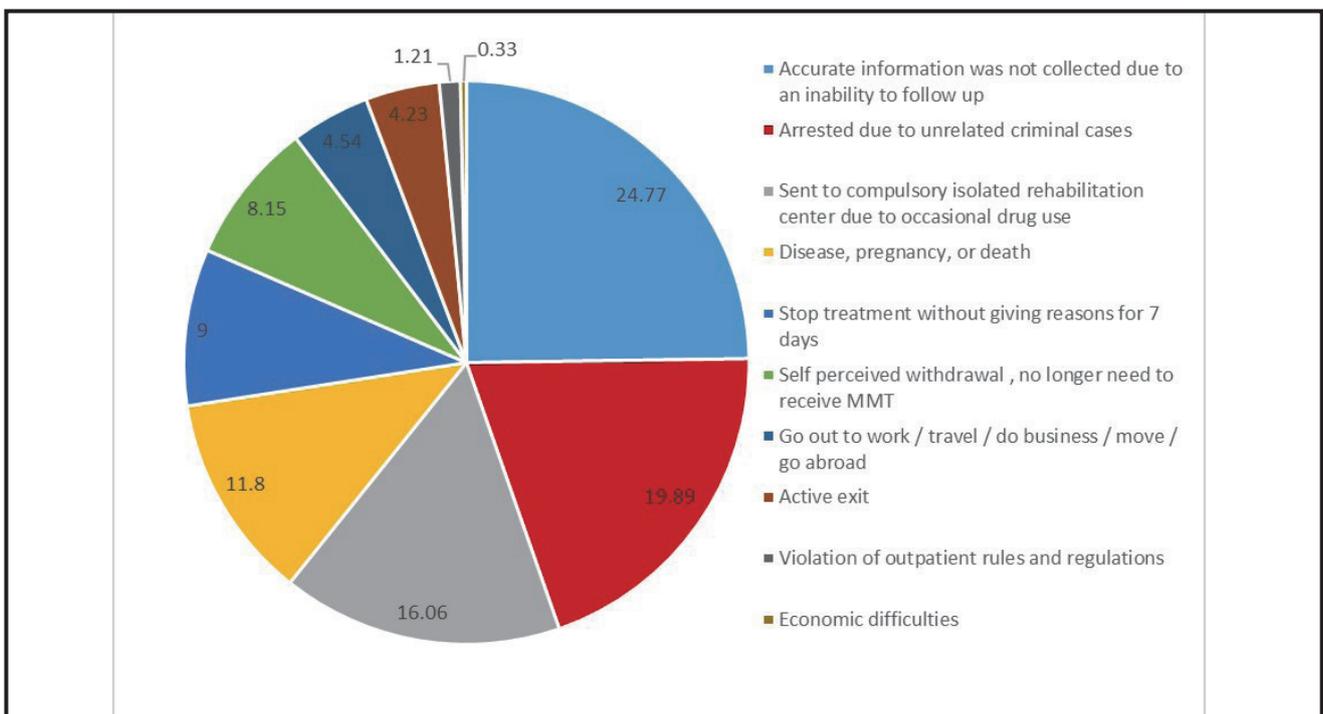


Figure 5. Cause for the withdrawal of outpatients from Shanghai MMT clinics



was generally higher than the national average (74.9%). For example, the maintenance rate in Guizhou province between 2004 and 2012 was 74.1%.^[14] The maintenance rate in Dali city, Yunnan Province was lower than 80% in the first four years of the 2008-2012 survey.^[8] The

factors influencing effectiveness of MMT include drug dosage, support services, medication compliance, duration of medication, and personal characteristics of individual drug users.^[15] High average dosage was relevant to high maintenance rate of MMT.^[16] The

average dosage in China was 45ml-55ml/d.^[15] The average dosage for MMT patients in Shanghai was 56ml/d. Over the years between 2008 and 2016, 2013 was the only year that the average dosage for MMT patients in Shanghai was greater than 60ml/d. The dosage of MMT has been controversial. Although earlier studies have shown that appropriate dosage applied to individual patients was critical to the success of MMT,^[17] few patients could pass a urine test with negative results^[18] if the methadone dosage was below 60mg. International studies have shown that a methadone dosage of 100mg/d was more beneficial in reducing relapse during MMT. Including Shanghai, the nationwide average MMT dosage was generally below 60 ml/d.^[7, 20] Due to issues such as lower surface area of Chinese ethnic groups than that of Caucasians, the administered dosage generally does not exceed 80mg/d.^[20] However, the necessity of an individualized dosage with the 60 ml/d baseline according to the patients' individual status still needs further study. It is worth noting that the difference in daily average number of MMT outpatients in different districts in Shanghai could be related to various objective factors. For example, the number of MMT outpatients in Minhang, Songjiang, and Qingpu were less. It could be related to factors such as the convenience of transportation to MMT clinics. However, in this study, it was found that there were differences in average daily dosage per patient among the districts. In Hongkou District, the dosage was the highest (62 ml/d), whereas in Songjiang District, the dosage was the lowest (40 ml/d). The influencing factors and effects of average daily MMT dosage per patient have yet to be further investigated.

MMT clinic patients in Shanghai were primarily male, young adults, with junior-high-school-and-below education level, single, and unemployed or underemployed. However, while investigating the marital status of MMT patients,^[7, 21] some studies reached different conclusions and found that married people accounted for the highest proportion of heroin users. Being married or not is one of the influencing factors affecting the quality of life for MMT patients.^[22] Family is an important social support system to prevent patients from relapse. Patients with a stable marriage had a significantly higher rate of medication than patients with unstable marriage or without marriage.^[23] This study showed that, except for the loss to follow-up cases, the main reasons for dropout at Shanghai's MMT clinics included "non-drug related arrests" "sent to compulsory rehabilitation center due to drug use", and "disease, pregnancy, or death", with the percentage from high to low. This result was broadly consistent with the investigation results by Chen Hong et al. in Chongqing.^[24] The withdrawal of patients from MMT medication involved many factors, such as the patient's personal condition, environment, treatment process, and so on. With regard to the patients themselves, male patients with low educational level and short drug

use time were more likely to withdraw from MMT.^[24] At the same time, marital status, relationship between patients and family members, and the attitude of family members towards MMT had significant impact on patient dropout.^[25]

4.2 Limitations

This study was a retrospective survey. Although descriptions were made regarding the causes of dropout and the trend of changes over the years at Shanghai's MMT clinics in number of patients and maintenance rate, in-depth explanation of the relevant factors leading to patients' withdrawal was lacking, due to the limitation of the available data.

Although differences in the number of patients at MMT clinics and average daily dosage per patient were found among different districts, this study had yet to find the cause of these differences. Therefore, follow-up qualitative study could be carried out, in order to explore the main reasons for the differences. In addition, this study takes Shanghai as an example. Shanghai has medical and healthcare services which are generally on a higher level than the rest of the country, so these results may not be generalizable.

4.3 Implications

MMT had positive functions^[5-6] in reducing relapse, controlling the spread of drug-related HIV and other STDs, improving patient's family and social functioning, and could effectively reduce social risks. Therefore, it is necessary to make a comprehensive analysis of the factors that affect treatment maintenance rate. This paper describes clinic and patient situations at MMT outpatient clinics since their establishment in Shanghai, and summarizes the development changes of Shanghai's MMT clinics. It provides reliable data support for the subsequent development of relevant MMT measures.

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Conflict of interest statement

The authors declare no conflict of interest related to this study

Ethical approval

This study has been approved by the ethical review committee of Shanghai Municipal Center for Disease Control and Prevention.

Authors' contributions

Jiayi Bao: data analysis and article writing

Lei Zhang : data analysis

Zhen Ning : data support and explanation

Min Zhao : article review and modification

Jiang Du : article review and modification

2005-2016 年上海市美沙酮维持治疗门诊状况调查

宝家怡, 张蕾, 宁镇, 傅洁, 赵敏, 杜江

背景: 美沙酮维持治疗是控制海洛因成瘾者滥用毒品、预防艾滋病, 以及改善家庭和社会功能的有效措施, 而近些年相关调查显示, 我国美沙酮维持门诊治疗人数呈现下降趋势。

目的: 了解自开诊以来, 上海市美沙酮维持治疗 (Methadone Maintenance Treatment, MMT) 门诊患者治疗维持率的变化趋势及脱失原因。

方法: 研究为回顾性调查, 数据来自中国疾病预防控制中心艾滋病综合防治数据信息管理系统, 采用描述性统计方法对 2005.5-2016.6 全市接受 MMT 患者的人口学资料、治疗维持率和新增人数进行描述, 并就脱失原因进行总结分析。

结果: 2005.5-2016.6 期间, 上海市接受 MMT 的患者共计 7181 人, 患者以男性 (男女比例约为 3:1)、青壮年 (25-54 岁占 90% 以上) 为主, 初中及以下文化水平居多 (65.4%)、单身 (未婚、离异或丧偶:

63.1%) 居多, 多为无业或待业 (81.5%)。MMT 患者日均服用美沙酮的剂量从 2008 年起呈上升趋势, 于 2013 年达到最高峰后逐渐下降, 历年平均服用美沙酮的剂量为 56(2.75)ml/d。新增治疗人数在 2007 和 2008 年急剧增加 (均超过 1500 人), 继而逐年降低。治疗人数在 2005-2011 年间不断增加, 于 2011 年达到峰值 (3840 人) 后逐渐下降。治疗维持率自 2010 年起稳定在 80% 以上。患者退出治疗的主要原因包括: (1) 因与毒品无关的刑事案件被逮捕 (19.89%), (2) 因偶吸被强制隔离戒毒 (16.06%), (3) 身体原因 (疾病/怀孕/死亡, 11.80%)。

结论: 上海市 MMT 门诊开展以来维持率较好, 在治患者人数呈现先增长后下降的变化趋势, 患者脱失原因主要与“犯罪”和“复吸”有关。后续研究需开展相关调查, 从不同层面深入了解影响上述变化和患者脱失的原因, 促使 MMT 门诊更好开展。

关键词: 美沙酮维持治疗; 海洛因依赖; 维持率

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