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Methadone Maintenance Treatment Participant Retention and Behavioural Effectiveness in China: A Systematic Review and Meta-Analysis

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Abstract

**Background:** Methadone maintenance treatment (MMT) has been scaled up by the Chinese government alongside persistent compulsory drug user detention, but the extent to which detention interferes with MMT is unknown. The study systematically reviews Chinese MMT retention rates, reasons for drop out, and behavioural changes.

**Method:** Chinese and English databases of literature are searched for studies reporting retention rates, drug use and sexual behaviours among MMT participants in China between 2004 and 2013. The estimates are summarized through a systematic review and meta-analysis.

**Results:** A total of 74 studies representing 43,263 individuals are included in this analysis. About a third of MMT participants drop out during the first three months of treatment (retention rate 69.0% (95% CI 57.7-78.4%)). Police arrest and detention in compulsory rehabilitation was the most common cause of drop out, accounting for 22.2% of all those not retained. Among retained participants, changing unsafe drug use behaviours was more effective than changing unsafe sexual behaviours. At 12 months following MMT initiation, 24.6% (15.7-33.5%) of MMT participants had a positive urine test, 9.3% (4.7-17.6%) injected drugs and only 1.1% (0.4-3.0%) sold sex for drugs. These correspond to 0.002 (<0.001-0.011), 0.045 (0.004-0.114) and 0.209 (0.076-0.580) times lower odds than baseline. However, MMT participants did not have substantial changes in condom use rates.

**Conclusion:** MMT is effective in drug users in China but participant retention is poor, substantially related to compulsory detention. Reforming the compulsory drug user detention system may improve MMT retention and effectiveness.

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Introduction

Since 1979 the illicit drug trade has prominently re-emerged in China [1], contributing to a substantial burden of drug-associated disease. The number of registered drug users in China increased 19-fold between 1990 and 2009 [1]. Intravenous injection is the most common means of drug use, with injecting drug users (IDUs) accounting for 59-85% of drug users in China [2,3,4,5,6,7,8]. The high injection frequency, sharing of contaminated needles and other risk behaviours [9,10,11] [12,13] among IDUs accelerate the spread of HIV infection. The cumulative number of diagnosed HIV/AIDS cases in China is now well over 200,000, among which over 60% are drug users [14,15], and new infections among IDUs accounts for 17% of new HIV cases in 2011 [16].

Responding to the growing IDU HIV epidemic in China, domestic and international programs launched harm reduction programs in 2003 [17,18,19]. A major component of harm reduction is methadone maintenance treatment (MMT), a substitution program known to reduce morbidity, a mortality...
serving 344,254 drug users by the end of 2011. Now MMT launched pilot MMT programs in 8 clinics serving 1,029 drug users in 2004 and subsequently expanded to 738 clinics serving 344,254 drug users by the end of 2011. Now MMT reaches approximately 30% of registered IDUs in China (personal communication with China CDC). MMT services focus on decreasing drug use and sexual risk behaviours, including counselling and HIV testing [23]. However, MMT services in China are closely monitored by the public security. Police raids and arrests near MMT sites are common, and MMT participants who have positive urine tests will be sent for compulsory detention and rehabilitation [23,24,25]. During and following detention and rehabilitation, access to MMT services is limited [24]. At places where the police is cooperative with the local CDC, participation and intervention outcomes in MMT participants are generally better [26].

While several studies have reported retention rates and behavioural outcomes in MMT participants [14,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99], these studies have not been systematically reviewed and integrated to provide an overall assessment of the effectiveness of MMT programs in China [100,101]. Drop-out rates in MMT clinics are perceived to be as high as approximately 50-70% participants terminate treatment within three month of their enrolment in China. Poor retention, administrative detention, and other structural factors may obscure the effect of MMT on durable behaviour change [102,103]. This study systematically investigates overall retention rates, reasons for dropout, drug use behaviour changes, and sexual behaviour changes at Chinese MMT clinics.

Methods

Search strategy

Two independent investigators (EPFC and XZ) conducted a systematic review of published peer-reviewed research articles by searching the following databases between January 2004 and April 2013: PubMed, Chinese Scientific Journals Fulltext Database (CQVIP), China National Knowledge Infrastructure (CNKI) and Wanfang Data. We performed two separate search strategies for (1) retention rates and reasons for dropout; and (2) behavioural changes attributable to MMT services. This review was reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement issued in 2009 [30] (Checklist S1). The search strategy was detailed in Supplementary Text S1.

Study selection

Studies were eligible for inclusion in this systematic review if they met all following criteria: (1) study published in Chinese or English language; (2) study reported the drug and sexual behavioural changes before and after entering MMT clinics; (3) study reported percentage of retention rate among the MMT participants; (4) study reported reasons for dropout; and (5) study reported study site, time period and sample size. Intervention studies were selected, but only the control groups among MMT participants were included. Exclusion criteria were: (1) review papers; (2) non peer-reviewed local/government reports; (3) conference abstracts and presentations; (4) dissertations; (5) studies reported baseline or follow-up data only. If the same study data were published in both English and Chinese sources, the articles published in Chinese language journals were excluded from this study. A MMT participant was considered as ‘drop-out’ if he/she failed to attend the enrolled MMT clinic for seven consecutive days without providing a reason. All MMT clinics in China were under the supervision of China CDC and adapted the same definition of retention.

Validity assessment

The quality of studies was assessed using a validated quality assessment tool [31]. The following eight items were assessed to calculate a total quality score: (1) clear definition of the target population; (2) representativeness of probability sampling; (3) sample characteristics matching the overall population; (4) adequate response rate; (5) standardised data collection methods; (6) reliability of survey measures/instruments; (7) validity of survey measures/instruments; (8) appropriate statistical methods. Answers were scored 0 and 1 for ‘No’ and ‘Yes’, respectively. The total quality score varied between 0 and 8 for each study.

Data abstraction

We extracted the following information from all eligible studies: published year, study location, study period, age and sex composition of the sample, percentage married, level of education, study design, methods of recruitment and sample size at recruitment as the demographic indicators. We extracted the following behavioural change data for the pre-MMT and post-MMT periods: injecting drug in the past month, sharing needles in the past month, percentage who sell sex for drugs in the past three months, and the rate of consistent condom use during any sexual intercourse in the past month. Additionally, we extracted data on the retention rate of the MMT participants at several follow-up points, and the reasons for drop out. An individual was considered ‘dropped-out’ if they did not attend an MMT clinic for seven consecutive days.

Statistical analysis

Meta-analyses were carried out with the Comprehensive Meta-Analysis software (V 2.0, Biostat, Englewood, New Jersey) [104]. The principal summary measures, including the effect rates of pooled prevalence estimates, odd ratios and their 95% confidence intervals (CIs) were determined based on random effect models. Random effect models were applied when heterogeneity across subgroups were found to be significant [105]. Heterogeneity tests were performed using the Cochran Q-test (p<0.10 represents statistically significant heterogeneity) and the I² statistic [106,107,108]. We investigated the factors that are associated with heterogeneities in the stratified meta-analyses using meta-regression [109]. Meta-regression was performed in STATA statistical software package (Version 10, StataCorp, College Station, TX, USA).
Results

A total of 495 and 650 potentially relevant studies on MMT retention and behavioural changes, respectively, among drug users after MMT intervention were identified. A total of 56 [14,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81] studies (Figure S2) were subsequently eligible and selected for analyses, respectively.

Retention in MMT

Twenty-seven studies reported retention rate among MMT participants (Table S1). The retention rates at one, three, six, 12, and 24 months after enrolment were 89.4% (95% CI, 85.6-92.3%), 69.0% (57.7-78.4%), 62.9 (55.3-69.9%), 55.2 (48.5-61.7%) and 43.0 (34.7-51.7%) (Figure 1). Notably, most drop outs occur in the first three months. MMT retention rates decrease less than 10% in the following 21 month period. Forty-three studies (20,873 studies participants) reported reasons for drop out from MMT in China (Table S2). Among the drop-outs, about one-fourth of the participants (22.2%) were arrested by police and sent to detention centres due to relapse in drug use (positive urine test) during the course of MMT, 19.1% self-withdrew and 13.3% were due to relocation to another city outside the clinic coverage. Other drop out reasons such as criminal activities (7.6%), unregistered by the MMT clinics (6.3%), death and sickness (6.3%) and dosage issues (0.1%) were also reported (Figure 2).

Drug using behaviours among MMT participants

Nineteen studies reported changes in injecting behaviours among MMT entrants after receiving MMT. Our analysis showed that 82.3% (75.2-87.7%) of the MMT entrants injected drugs in the past month at baseline and this significantly reduced to 9.1% (4.5-17.6%) after six months of entry and slightly increased to 9.3% (4.7-17.8%) after twelve months of MMT intervention (Figure S3a). These correspond to 0.012 (0.004-0.033) and 0.045 (0.017-0.114) times lower odds of injecting drug at six and twelve months after treatment respectively (Figure 3a). However, MMT did not change drug sharing behaviours among MMT participants (aOR = 0.531 [0.174-1.627] and 0.298 [0.017-5.100] for six and twelve months intervention) (Figure 3b). An estimated 10.8% (6.3-17.8%) of MMT participants shared syringes in the past month, whereas 7.6% (2.8-18.9%) and 1.8% (0.2-12.7%) of the MMT participants shared syringes after six and twelve months intervention (Figure S3b).

Six studies reported proportion of positive urine tests among MMT participants. At baseline, 92.6% (90.1-95.2%) of participants had positive drug urine tests. The proportion significantly dropped to 60.9% (53.5-68.3%), 50.8% (53.5-68.3%) and 24.6 (15.7-33.5%) at three, six and twelve months after enrolment in MMT (Table S3). These correspond to 0.47 (0.03-8.29), 0.05 (0.01-0.24) and 0.002 (<0.001-0.011) lower odds of positive urine testing compared with baseline.

Sexual behaviours among MMT participants

Six studies reported the changes in sexual behaviours among MMT participants (Figure 3c). The consistent condom use in past one month increased from 24.6% (20.2-29.5%) at baseline level to 40.9% (18.7-67.6%) after 6 months of intervention, although the increase was not significant (aOR = 2.036 [0.696-5.957]) (Figure S3c).

Eight studies examined the likelihood of selling sex for drugs among MMT participants. Approximately 5.2% (2.5-10.3%) of MMT participants had sold sex for drugs in the past three months before receiving MMT intervention. This percentage dropped to 1.1% (0.5-2.3%) and 1.1% (0.4-3.0%) after six-month and 12-month post-intervention, respectively (Figure S3d). MMT had a significant impact on reducing commercial sex activities among drug users, as the odds of selling-sex in the past three months reduced to 0.248 (0.111-0.553) and 0.209 (0.076-0.580) six and 12 months after intervention (Figure 3d).

Heterogeneities and publication biases

Heterogeneities were observed in several sub-group meta-analyses. In the meta-analyses of retention rate among MMT participants, high and significant heterogeneities were detected at 1 month (I²=96.3%, p<0.001), 3 months (I²=99.0%, p<0.001), 6 months (I²=98.4%, p<0.001), 12 months (I²=98.0%, p<0.001) and 24 months (I²=98.6%, p<0.001) post-registration (Figure 1). Additionally, significant heterogeneities were also observed in measuring the OR of the percentage of who injected after six months (I²=97.2%, p<0.001) and twelve months (I²=94.1%, p<0.001) of follow-up (Figure 3a); the OR of the percentage who shared needles at six months follow-up (I²=87.8%, p=0.002) (Figure 3b); the consistent condom use rate in the past one month (I²=96.1%, p<0.001) after six-month follow-up (Figure 2c); and the OR of the percentage of MMT participants who sold sex for drug (I²=72.3%, p=0.013) after twelve months follow-up (Figure 2d). Subsequent meta-regression suggested that sampling size, publication language, study design, period and location are not contributing factors to the observed high heterogeneities. No publications biases were observed in all meta-analyses performed. Of the full quality score of eight points, the selected studies have a median score of 4 (Interquartile range: 3-5) (Table S1-2, 4).

Discussion

MMT is a key harm reduction strategy for improving the health and well-being of drug users worldwide. To our knowledge, this is the first systematic review of MMT effectiveness in a nation with common detention practices. Our analysis indicates that drop-out rates are high within the first three months of enrolment, as more than one-third of the participants discontinue their treatment. Retention increases substantially in the next 21 months, with over half of the participants remaining on treatment after 24 months. This...
### Figure 1. Retention of participants of MMT clinics in China.

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Figure 2. Major reasons of dropping-out from MMT clinics among 20,873 participants.

Figure 3. Changes in injecting behaviours among retained MMT participants. (a) Likelihood of injecting drug use in the past one month of Chinese MMT participants at six and twelve months follow-up. (b) Likelihood of sharing injection equipment in the past one month among Chinese MMT-participating IDUs at six and twelve months follow-up. (c) Likelihood of having consistent condom use during all sexual intercourses in the past one month among Chinese MMT participants at 6 months follow-up. (d) Likelihood of selling sex for drugs in the past three months among Chinese MMT participants at six and twelve months follow-up.

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demonstrates that participants who sustained the first three months are likely to remain on treatment. The phenomenon of early drop-out is consistent with findings in international settings [112,113]. In comparison, the 12-month MMT retention rate in China is substantially lower than programs in other developed (60-85% [22,114,115,116]) and developing countries settings (62-82% [117,118]).

The leading cause of MMT dropout (22.2%) was related to relapse in drug use and compulsory police detention. Our quantitative analysis extends previous qualitative literature suggesting interference between detention and MMT in Asia [102,103,119]. A recent 12 United Nation Joint Agency Statement called for an end to compulsory detention, as mandatory detention centres do not provide an effective environment for treatment of drug dependence and constantly violate internationally recognised human right standards [120].

Our results suggest that relapse and detention, self-withdrawal, and mobility are major barriers to durable MMT participant retention. The major reason for drop out is relapse and compulsory detention. In China, the police are entitled to request random urine tests for any suspected drug users. During times to meet arrest quotas, police will act aggressively toward drug users, especially those registered with MMT program [25]. Relapsed drug users are sent to detention centres. Detention centre confinement does not reduce unsafe drug use behaviours [121,122,123] and as many as 95% of IDUs relapse within one year of release from detention [124].

Access to general health care and harm reduction programs is extremely limited in Chinese detention centres [24]. Our results indicate that police arrest and forced detention of relapsing drug users may be a major obstacle for MMT program in China reaching its full potential in providing sustaining quality care for its participants. Second, more than one-fifth of the drop-outs choose to self-withdraw from the treatment. The self-perception of substantial improvement of physical conditions and alleviation of addictive symptoms during the early phase of MMT may lead to a misconception about maintaining drug abstinence without completing the course of treatment [125,126]. The high self-withdraw highlights the need for improving necessary counselling services and peer support to eliminate these misconceptions [48,52,125]. Third, high mobility of MMT participants, reflected by their frequent relocations, also significantly contributes to the interruption of their treatment. This poses a great challenge to the current fragmented administrative model of MMT, in which MMT clinics in different administrative jurisdictions do not share the medical and treatment records of their participants [38,125,127,128].

Addressing these structural issues is important for retaining mobile drug users within the MMT system.

Our study found large reductions in drug-related risk behaviours among retained MMT participants in China. These findings are comparable to international research [129,130,131,132,133], indicating that the MMT has been effective in its core objective of reducing drug related risk. Nevertheless, these results need to be interpreted with caution. Individuals who relapse in China are more likely to be expelled from MMT and detained, decreasing their future chance of entering the MMT system. It may undermine the effectiveness of the program as relapsing individuals represent a subgroup with higher risks and needing the treatment the most. Notably, among continuing IDUs, the sharing rate of injection equipment did not change over the course of treatment, contradicting findings in other international contexts [129,130,131,134,135,136]. Further integration of MMT and syringe exchange programs is needed to reap the full benefits of harm reduction. The fact that MMT in China does not reduce unprotected sexual acts is consistent with international findings [137].

Several limitations in this study should be noted. First, our data covers only 19 provinces that are disproportionately in the south and south-western part of China. However, these regions have a larger number of IDUs with greater HIV disease burden. Although we systematically incorporated all available operational data, there remain a large number of governmental documents, community-level reports and other unpublished data that have never been archived in any of the public literature databases. For some indicators, the numbers of available publications are quite limited and this may potentially reduce the statistical power and accuracy of subsequent meta-analysis. Second, many studies report a high drop-out rate without indicating specific reasons (12.9% on average). Many contributing factors to treatment drop-out, such as attitudes of staff, under-dosing, costs of treatment, family support and commitments, stigma of being on methadone, poor psychosocial services, and ability for drop-out individuals to re-enter treatment, are not reported in the published literature and hence cannot be investigated. Third, only 0.1% of the drop-outs report insufficient methadone dosage as one of the reasons for leaving treatment [138]. International literature indicates that adequate methadone dosage should be above 60mg/day to be effective [128] and insufficient methadone dosage results in lower retention rates [138]. Daily dosage among Chinese MMT participants is substantially lower than this level and may have a strong effect on retention rates [38,125].

Our review provides pooled evidence that MMT has been effective in reducing drug-related risk behaviours among Chinese drug users. It informs policies to further expand the coverage and scope of MMT to provide better and more comprehensive treatment services for its participants. However, despite the 2008 revised Law on Drug Control allowing drug users in China access to community-based rehabilitation prior to compulsory detention [23], punitive incarceration of drug users in China remains common [139,140] and substantially impacts on participants’ retention. Our research adds quantitative public evidence for ending compulsory drug use detention, amplifying the recent UN joint statement [120] calling for an end to compulsory drug user detention. A recent pronouncement from the Chinese government stated that the re-education through labour system responsible for detaining drug users is likely to be reformed in the coming year [141]. Implementation of community-based rehabilitation in China and other states could substantially improve the effectiveness of MMT.
Supporting Information

Table S1. Summary of the demographic characteristics of the studies reported retention rates in MMT clinics. Remove this caption text. (DOCX)

Table S2. Major reasons of participants dropping-out from MMT clinics. Remove this caption text. (DOCX)

Table S3. Percentage and likelihood of positive urine tests at baseline, 3, 6 and 12 months of follow-up. Remove this caption text. (DOCX)

Table S4. Summary of the demographic characteristics of the studies that reported the changes in risk behaviours. Remove this caption text. (DOCX)

Figure S1. Flow chart of study selection for retention among MMT participants. Remove this caption text. (DOCX)

Figure S2. Flow chart of study selection for behavioural changes after MMT intervention. Remove this caption text. (DOCX)

Table S5. Checklist S1. PRISMA Checklist. (DOCX)

Text S1. Search strategy. (DOCX)

Author Contributions

Conceived and designed the experiments: LZ DPW. Performed the experiments: EPFC LZ YL YW LL CT. Analyzed the data: EPFC LZ. Contributed reagents/materials/analysis tools: XZ YL WJ. Wrote the manuscript: EPFC LZ JDT DPW.

References

1. Yan Ping, B., Zh Min L (2009) Current situation and trends of drug abuse and HIV/AIDS in China. HIV Therapy 3: 237-240. doi:10.2217/hiv.09.4.
2. China Ministry of Health and UN Theme Group on HIV/AIDS (2003) China (2003) A Joint Assessment of HIV/AIDS Prevention, Treatment and Care in China. Beijing.
3. Zhu QY, Liu W, Chen J, Liang FX, Guo NZ et al. (2006) Analysis of data AIDS sentinel surveillance from 1996 to 2003 in Guangxi province. Chin J AIDS STDS 12: 290-432.
4. State Council AIDS Working Committee Office UN Theme Group on AIDS in China (2007). A Jt Assess HIV/AIDS Poretreat Care China; 2007: Beijing.
5. Chen J, Wang D, Jin T, Zhang Y, Zhi Q et al. (2007) Analysis of data AIDS sentinel surveillance in Xinjiang province 2005 Endemic Disease Bulletin 22: 55-56.
6. Li Q, Chen R, Huang L, Teng X, Yuan K (2008) Analysis of HIV prevalence from 1997 to 2006 in Anshun City. Chin J AIDS STDS 12: 270-271.
7. Yang L, Li J, Zhang Y, Li H, Zhang W et al. (2008) Societal perception and support for methadone maintenance treatment in a Chinese province with high HIV prevalence. Am J Drug Alcohol Abuse 34: 5-16. doi:10.1080/00952990701653836.
8. Chow EP, Wilson DP, Zhang L (2010) The next era of HIV in China: rapidly spreading epidemics among men who have sex with men. J Acquir Immune Defic Syndr 55: e32-e33; author reply e33-34. doi:10.1097/QAI.0b013e3181591578. PubMed: 20151991.
9. Qian HZ, Vermund SH, Wang N (2005) Risk of HIV/AIDS in China: subpopulations of special importance. Sex Transm Infect 81: 442-447. doi:10.1136/sti.2004.014258. PubMed: 16326842.
10. Chen J, Wang D, Jin T, Zhang Y, Zhi Q et al. (2007) Analysis of data AIDS sentinel surveillance in Xinjiang province 2005 Endemic Disease Bulletin 22: 55-56.
11. Xie X, Lu L, Tee KK, Zhao W, Wu J et al. (2008) The unique HCV genotypic distribution and the discovery of a novel subtype 6u among IDUs co-infected with HIV-1 in Yunnan, China. J Med Virol 80: 1142-1152. doi:10.1002/jmv.21204. PubMed: 18461611.
12. Bao YP, Liu ZM (2009) Systematic review of HIV and HCV infection among drug users in China. Int J STD AIDS 20: 399-405. doi:10.1258/ijsa.2008.008362. PubMed: 19451325.
13. Li H, Goggins W, Lee SS (2009) Multilevel analysis of HIV related risk behaviors among heroin users in a low prevalence community. BMC Public Health 9: 137. doi:10.1186/1471-2458-9-137. PubMed: 19435512.
14. Wang ZC, Zhong HJ, Wang L, Huang GY, Li SC et al. (2007) Qualitative study of factors contributed to retention in a community-based methadone maintenance treatment among heroin users. J Public Health Prev Med 18: 10-12.
15. Fang YX, Wang YB, Shi J, Liu ZM, Lu L (2006) Recent trends in drug abuse in China. Acta Pharmacol Sin 27: 140-144. doi:10.1111/j.1745-725X.2006.00270.x. PubMed: 16412261.
16. China Mohtpsr (2012) 2012 China AIDS Progress Report. Beijing: Ministry of Health the People’s Republic China.
17. Pang L, Hoo Y, Mi G, Wang C, Luo W et al. (2007) Effectiveness of first eight methadone maintenance treatment clinics in China. AIDS 21: S103-S107. doi:10.1097/01.aids.0000304074.71917.64. PubMed: 18172377.
18. Wu Z, Luo W, Sullivan SG, Rou K, Lin P et al. (2007) Evaluation of a needle social marketing strategy to control HIV among injecting drug users in China. AIDS 21: S115-S122. doi:10.1097/01.aids.0000304076.79541.ef. PubMed: 18172379.
19. Lau JTF, Zhang L, Zhang Y, Wang N, Lau M et al. (2008) Changes in the prevalence of HIV-related behaviors and perceptions among 1802 injecting drug users in Sichuan, China. Sex Transm Dis 35: 325-335. doi:10.1097/OLQ.0b013e3181613464. PubMed: 18277942.
20. Amato L, Davoli M, Perucci CA, Ferrl M, Faggiano F et al. (2005) An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. J Subst Abus Treat 28: 321-329. doi:10.1016/j.jsat.2005.02.007.
21. Yoast R, Williams MA, Deitchman SD, Champion HC (2001) Report of the Council on Scientific Affairs: methadone maintenance and needle-exchange programs to reduce the medical and public health
consequences of drug abuse. Addict Dis 20: 15-40. doi:10.1300/ 
J098v20n02_03. PubMed: 11318395.

22. Mattick RP, Breen C, Kimber J, Davoli M (2009) Methadone 
maintenance therapy versus no opioid replacement therapy for 
opioid dependence. Cochrane Database Syst Rev 3: CD002209. PubMed: 
19325167.

23. Yin W, Hao Y, Sun X, Gong X, Li F, Li et al. (2010) Scaling up the national 
methadone maintenance treatment program in China: achievements 
and challenges. Int J Epidemiol 39 Suppl 2: i29-i37. doi:10.1093/ije/ 
dyq210. PubMed: 2113034.

24. Cohen JE, Amon JJ (2008) Health and human rights concerns of drug 
users in detention in Guangxi Province, China. PLOS Med 5: e234. doi: 
10.1371/journal.pmed.0050234. PubMed: 19071964.

25. Wu F, Peng CY, Jiang H, Zhang R, Zhao M et al. (2012) Methadone 
maintenance treatment in China: perceived challenges from the 
perspectives of service providers and patients. J Public Health (Oxf). 
35: 206–12. PubMed: 22997278.

26. Bao YG, Li YZ, Duo L, Zhao XR, Xue HM (2008) Analysis of the survey 
on police-based knowledge on HIV/AIDS and attitude and behavior 
toward harm reduction of drug use and the risk of professional 
exposure of HIV in Yunnan. Soft Science Health 22: 87-88.

27. Che Y, Aasanangkornchai S, McNeil E, Chongsuvivatwong V, Li J et al. 
(2009) The impact of AIDS-related stigma on drug treatment patients 
and retention situation. Acta Univ Med Nanjing (Soc 
Science) 8: 230-233.

28. Hao C, Wu JL, Ruan YH, Yao HM, Yang XG et al. (2007) Factors 
associated with retention in a community-based methadone 
maintenance treatment among heroin addicts. Zhonghua Yu Fang Yi 
Xue Za Zhi 41: 250-253. PubMed: 17959041.

29. Chen A, Wang X, Yang HT, Qian X, Xu GY, Zhu YF et al. (2008) 
Effectiveness evaluation of six-month community-based methadone 
maintenance treatment in Jiangsu province. Chin J AIDS STDs: 590-593.

30. Qiao Q, Cheng H, Ding L, Qian XC, Wang B (2008) Study on 
characteristics of social network among methadone maintenance 
treatment patients and retention situation. Acta Univ Med Nanjing (Soc 
Science) 8: 230-233.

31. Huang YJ, Huang JG, Lv K, Zhou MX, Xia CL et al. (2012) An outcome 
assessment on methadone maintenance treatment in Youjiang 
prefecture of Yunnan. Zhonghua Liu Xing Bing Xue Za Zhi 28: 41-44. 
doi:10.1007/s11432-008-0195-z. PubMed: 17959041.

32. Huang YK, Hu JL, Huang JP, Feng XX, Kong HQ (2010) Effect on 
psychological and behavior intervention among drug users in 
community-based methadone maintenance treatment programs in 
Guangdong, China, and their impact on patient quality of life. Subst 
Use Misuse 46: 749-757. doi:10.1080/10826084.2010.534124. 
PubMed: 21114401.

33. He Q, Qian YH (2008) Effect of Methadone Maintenance Therapy on Drug 
Users in Wuxi. Zhonghua Liu Xing Bing Xue Za Zhi 30: 1-4. PubMed: 
18172377.

34. Kong HQ (2011) Reasons for dropout of methadone maintenance 
treatment clinics of Anhui. Harm Reduct Prev Treat 3: 103-109. 
PubMed: 21993758.

35. Liu YJ, Deng PX, Xiong XY, Shuai YL, Wu W (2007) Effective 
evaluation on methadone maintenance treatment in Chaoyang District, 
Beijing. Chin J Drugs Depend 16: 306-309. PubMed: 18172377.

36. Qian YH (2008) Effect of Methadone Maintenance Therapy on Drug 
Users addicts in Wuxi. Jilin Medical Journal 31: 153-154.

37. Li XL, Tan HZ, Ou QY, Chen MS, Zhang H (2011) Methadone 
maintenance treatment among HIV positive and HIV 
negative heroin addicts. Chin J Drugs Depend 20: 362-366.

38. Wang P, Zhu JH, Yan J, Ou YS, Liu CF et al. (2009) Analysis of 
patients’ dropout from methadone maintenance treatment. Chin J 
Drugs Abuse Prev Treat 15: 1-3.

39. Liu JB, Di LXTHP, Li F, Zhang F, Mo LR, et al. (2007) The Effective 
Evaluation of the Methadone Maintenance Treatment of Heroin 
Addicts. Chin J Drugs Abuse Prev Treat 13: 10-13.

40. Lu ML, Li XG, Hu LY, Li F, Luo LH (2010) Influencing factors for 
dropout of 138 drug users on methadone maintenance treatment. 
Chin J Drugs Abuse Prev Treat 14: 253-256.

41. Mu FK (2011) A study on 180 drug addicts on methadone 
maintenance treatment. China Med Pharm 01: 117-118.

42. Pu YC, Long YC, Duan QX, Mo HP, Lu ZQ et al. (2012) Adherence 
and determinants of methadone maintenance treatment among heroin 
addicts in Longchuan County, Yunnan Province. Chin J AIDS STDs 18: 
815-817.

43. Wang J, Li F, Mo LR, Li L, Guan YS et al. (2007) Factors associated 
with retention in a community-based methadone maintenance 
treatment among drug users in Urumqi, Xinjiang Uigur Autonomous 
Region. Zhonghua Liu Xing Bing Xue Za Zhi 28: 37-41. PubMed: 
17575929.

44. Wei XL, Li HK, Ma CF, Liu JF (2008) Effective evaluation of methadone 
maintenance treatment for heroin dependent patients in Xi’an city. Chin J 
Drugs Depend 17: 197-201.

45. Xiang LF, Liu P, Gao J, Yang YC, Ye RH et al. (2011) Evaluation of 
effectiveness of methadone maintenance treatment in Dehong 
prefecture of Yunnan. Chin J AIDS STDs 17: 425-429.

46. Xu JS, Chen GH, Li L, Huan XP, Yang HT et al. (2009) Retention 
and related factors of methadone treatment among drug users. Zhonghua 
Liu Xing Bing Xue Za Zhi 35: 206–12. PubMed: 22993758.

47. Zhao YT, Xu HF, Fan LR (2009) Evaluation for the Community-Based 
Methadone Maintenance Treatment in Guangzhou City. J Trop Med: 
19588331280443012519570.
80. Sun QY, Zhang YF, Zhang J, Xu M, Chen GH (2011) Evaluation of the community methadone maintenance treatment in Lianyang city, Acta Univ Med Nanjing (Nat Science) 31: 1471-1475.
81. Tang RH, Duan S, Yang YC, Xiang LF, Ye RH et al. (2012) Analysis of social effects of methadone maintenance treatment in Dehong Prefecture, Yunnan Province, Chin J Dis Control Prevent 16: 1044-1048.
82. Tang XY, Hou SQ, Tang JH (2008) Hunan Beihu methadone maintenance treatment in socio-economic evaluation. Chin J Drugs Depend 17: 380-382.
83. Xue FY, Xu CL, Pan QC, Zhuang MH, Bi H et al. (2006) Evaluation of the Therapeutic Effect of Methadone Maintenance in 115 Cases of Heroin Addicts. Chin J Drugs Abuse Prev Treat 12: 255-257.
84. Zhang HF, Deng KW, Zhang YF, Tong HY, Long HY (2009) Effectivity evaluation on methadone maintenance treatment in Hanzhong, Shaanxi. Chin J Drugs Depend 18: 43-46.
85. Zheng WX, Chen G (2012) Evaluation on methadone maintenance treatment in Fujian province. Strait Journal of Preventive Medicine 18: 72-74.
86. Zhao XL, Liang Y, Chow EP, Wang Y, Wilson DP et al. (2012) HIV and HCV prevalence among entrants to methadone maintenance treatment clinics in China: a systematic review and meta-analysis. BMC Infect Dis 12: 130. doi:10.1186/1471-2334-12-130. PubMed: 22682091.
87. Zhao X, Wang Y, Chen RJ (2011) Analysis of risk factors associated with HIV/HCV infection among entrants in methadone maintenance treatment clinics in China: a systematic review and meta-analysis. Drugs Alcohol Depend 126: 286-295. doi:10.1016/j.drugalcdep.2012.05.028. PubMed: 2261254.
88. Lin C, Wu Z, Detels R (2011) Opiate users’ perceived barriers against attending methadone maintenance therapy: a qualitative study in China. Subst Use Misuse 46: 1190-1198. doi:10.1080/10826084.2011.531695. PubMed: 21417558.
89. Phibin MM, Zhang F (2010) Exploring stakeholder perceptions of facilitators and barriers to accessing methadone maintenance clinics in Yunnan Province, China. AIDS Care 22: 623-629. doi:10.1080/09540120931190139. PubMed: 20229075.
90. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009) Introduction to Meta-Analysis. John Wiley & Sons Ltd.
91. Fleiss JL (1993) The statistical basis of meta-analysis. Stat Methods Med Res 2: 121-145. doi:10.1177/096228029300200202. PubMed: 8261254.
92. Huedo-Medina TB, Sanchez-Meca J, Marin-Martinez F, Botella J (2006) Assessing heterogeneity in meta-analysis. Q Statist Or I? index? Psychol Methods 11: 193-206.
93. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21: 1539-1558. doi:10.1002/sim.1186. PubMed: 12111919.
94. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327: 557-560. doi:10.1136/bmj.327.7414.557. PubMed: 12958120.
95. Thompson SG, Higgins JP (2002) How should meta-regression analyses be undertaken and interpreted? Stat Med 21: 1559-1573. doi:10.1002/sim.1187. PubMed: 12111920.
96. Thornton A, Lee P (2000) Publication bias in meta-analysis: its causes and consequences. J Clin Epidemiol 53: 207-216. doi:10.1016/S0895-4356(99)00161-4. PubMed: 10728693.
97. Song F, Khan KS, Dinnes J, Sutton AJ (2003) Asymmetric funnel plots and publication bias in meta-analyses of diagnostic accuracy. Int J Epidemiol 31: 88-95. doi:10.1093/ije/31.1.88. PubMed: 11914301.
98. del Rio M, Aino Perneger TV (1997) Predictors of patient retention in a newly established methadone maintenance treatment programme. Addiction 92: 1353-1360. doi:10.1111/j.1360-0443.1997.tb02854.x. PubMed: 9489052.
99. Peles E, Schreiber S, Adelson M (2006) Factors predicting retention in treatment: 10-year experience of a newly established methadone treatment programme (MMT) clinic in Israel. Drugs Alcohol Depend 82: 211-217. doi:10.1016/j.drugalcdep.2005.09.004.
100. Gowing L, Farrell M, Bornemann R, Sullivan L, Ali R (2008) Substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database Syst Rev CD: 004155. PubMed: 1842598815490580.
101. Verthein U, Bonorden-Kleij K, Degkwitz P, Dilg C, Köhler WK et al. (2008) Long-term effects of heroin-assisted treatment in Germany. Addiction 103: 960-966. discussion 967-968. doi:10.1111/j.1360-0443.2008.01815.x. PubMed: 18422829.
102. Kelly SM, O’Grady KE, Mitchell SG, Brown BS, Schwartz RP (2011) Predictors of methadone maintenance treatment from a multi-site study: a survival analysis. Drugs Alcohol Depend 117: 170-175. doi:10.1016/j.drugalcdep.2011.01.008. PubMed: 21305652.
predict dropout and poor adherence prospectively among newly
acquired infections among individuals over fifty years of age in
maintenance treatment in Hanoi, Vietnam. Harm Reduct J 9: 26. doi:
transmitted infections among individuals over fifty years of age in
patterns among attendees of drug cessation programs in China. Subst
self-reported injecting drug use patterns among IDUs during treatment
randomized clinical trial of a manual-guided risk reduction intervention
strategies: changes during drug use treatment. Addict Dis 19: 65-83. doi:
the National Treatment Outcome Research Study, Drugs Alcohol
improvement after methadone treatment: 1 year follow-up results from
prevent and control drug use and HIV epidemics. Drugs Alcohol Depend 125:
retention in methadone maintenance by dose and dosing strategy. Addiction
of retention in methadone maintenance by dose and dosing strategy. Am J Drug Alcohol Abuse 35: 28-33. doi:10.1080/00952990802342899.
randomised controlled trial of methadone maintenance treatment
between wait list control and an Australian prison system. Drugs Alcohol
MMT Effectiveness in China

111. Musa R, Abu BA, Ali KU (2012) Two-year outcomes of methadone
112. United Nations Drug Control Program (2000) China country profile. Bangkok: Regional Centre for East Asia and the Pacific.
113. the Joint United Nations Programme on HIV/AIDS, the United Nations International Drug Control Program (2000) Drug use and HIV vulnerability: Policy research study in Asia. Bangkok: Regional Centre for East Asia and the Pacific.
114. Liu H, Grusky O, Zhu Y, Li X (2006) Do drug users in China who frequently receive detoxification treatment change their risky drug use practices and sexual behavior? Drugs Alcohol Depend 84: 114-121. doi:10.1016/j.drugalcdep.2006.01.004. PubMed: 1644333
115. Pearlne RV, Tucker JD, Yuan LF, Bu J, Yin YP et al. (2010) Sexually transmitted infections among individuals over fifty years of age in China. AIDS Patient Care STDs 24: 345-347. doi:10.1089/apc.2009.0323. PubMed: 20515416.
116. Du Y, Zhang J, Xie Z, Hu JJ, Hao Y et al. (2012) Misconceptions prevalent in methadone maintenance treatment of injection drug users in Guangzhou, China. Addiction 107: 1641-1649. doi:10.1111/j.1600-0447.2012.03859.x. PubMed: 22360534.
117. Bao YP, Liu ZM, Epstein DH, Du C, Shi J et al. (2009) A meta-analysis of retention in methadone maintenance by dose and dosing strategy. Am J Drug Alcohol Abuse 35: 28-33. doi:10.1080/00952990802342899.
118. Faggiano F, Vigna-Taglianti F, Versino E, Lemma P (2003) Methadone maintenance at different dosages for opioid dependence. Cochrane Database Syst Rev CD: 002208. PubMed: 12917925.
119. Dolan KA, Shearer J, MacDonald M, Mattick RP, Hall W et al. (2003) A randomised controlled trial of methadone maintenance treatment versus wait list control in an Australian prison system. Drugs Alcohol Depend 72: 59-65. doi:10.1016/S0376-8716(03)00187-X.
120. Camacho LM, Bartholomew NG, Joe GW, Cloud MA, Simpson DD (1999) Gender, cocaine and during-treatment HIV risk reduction among injection opioid users in methadone maintenance. Drugs Alcohol Depend 41: 1-7. doi:10.1016/0376-8716(96)01235-5. PubMed: 8793304.
121. Chatham LR, Hiller ML, Rowan-Szal GA, Joe GW, Simpson DD (1999) Gender differences at admission and follow-up in a sample of methadone maintenance clients. Subst Use Misuse 34: 1137-1165. doi:10.1080/10826089909039401. PubMed: 10359226.
122. Kwiatkowski CF, Booth RE (2001) Methadone maintenance as HIV risk reduction with street-recruited injecting drug users. J Acquir Immune Defic Syndr 26: 483-489. doi:10.1097/00126334-200104150-00014. PubMed: 11291367.
123. Strang J, Marsden J, Cummings M, Farrell M, Finch E et al. (2000) Randomized trial of supervised injectable versus oral methadone maintenance: report of feasibility and 6-month outcome. Addiction 95: 1631-1645. doi:10.1046/j.1360-0443.2000.951116314.x. PubMed: 11053762.
124. Gossop M, Marsden J, Stewart D, Rolfe A (2000) Patterns of improvement after methadone treatment. 1 year follow-up results from the National Treatment Outcome Research Study. Drugs Alcohol Depend 60: 275-286. doi:10.1016/S0376-8716(00)00109-5. PubMed: 11053762.
125. King VL, Kidorf MS, Stoller KB, Brooner RK (2000) Influence of psychiatric comorbidity on HIV risk behaviors: changes during drug use treatment. Addict Dis 19: 65-83. doi:10.1300/J069v19n04_07. PubMed: 11100066.
126. Margolin A, Avants SK, Warburton LA, Hawkins KA, Shi J (2003) A randomized clinical trial of a manual-guided risk reduction intervention for HIV-positive injection drug users. Health Psychol 22: 223-228. doi:10.1037/0278-6133.22.2.223. PubMed: 12683743.
127. Sorensen JL, Copeland AL (2000) Drug abuse treatment as an HIV prevention strategy: a review. Drugs Alcohol Depend 59: 17-31. doi:10.1016/S0376-8716(99)00104-0. PubMed: 10706972.
128. Bao Y-p, Liu Z-m, Epstein DH, Du C, Shi J et al. (2009) A Meta-analysis of Retention in Methadone Maintenance by Dose and Dosing Strategy. Am J Drug Alcohol Abuse 35: 28-33. doi:10.1080/00952990802342899.
129. Tang YL, Hao W (2007) Improving drug addiction treatment in China. Addiction 102: 1057-1063. doi:10.1111/j.1360-0443.2007.01849.x. PubMed: 17567394.
130. Tang YL, Zhao D, Zhao C, Cubells JF (2006) Opiate addiction in China: current situation and treatments. Addiction 101: 657-665. doi:10.1111/j.1360-0443.2006.01367.x. PubMed: 16669899.
131. Human Rights Watch (2013) China: Fully Abolish Re-Education Through Labor. Human Rights Watch.