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The Impact of Methadone Maintenance Treatment on HIV Risk Behaviors among High-Risk Injection Drug Users: A Systematic Review

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Abstract

Injection drug users (IDUs) are at high risk of acquiring HIV infection through preventable drug- and sex-related HIV risk behaviors. In recent decade, there has been a growing evidence that methadone maintenance treatment (MMT) is associated with a significant decrease in both drug- and sex-related risk behaviors among this high-risk population. The better understanding of the relationship between MMT and HIV-related risk behaviors will help to better inform future HIV prevention strategies, which may have policy implications as well. In this systematic review, we therefore aimed to explore the relevant literature to more clearly examine the possible impact of MMT on HIV risks behaviors among high-risk IDUs. The findings thus far suggest that MMT is associated with a significant decrease in injecting drug use and sharing of injecting equipment. Evidence on sex-related risk behavior is limited, but suggest that MMT is associated with a lower incidence of multiple sex partners and unprotected sex. The literature also suggests that the most significant factor in reducing HIV risks was treatment adherence. As such, more attention needs to be given in future studies to ensure the higher rates of access to MMT as well as to improve the adherence to MMT.

Keywords

Methadone maintenance treatment; HIV risk reduction; injection drug users; HIV/AIDS; behavioral interventions; opioid-dependence; systematic review

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Conflicting interest

The authors have declared that no competing interests exist.

Author Contributions

Conceived and designed the study: PK, THM, and MC. Analyzed the data: RK, RS, THM, and MC. Wrote the paper: RK, RS, THM, and MC. Proof read the paper: RK, RS, THM, and MC. Final approval: RK, RS, THM, and MC.

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Introduction

Globally, approximately 78 million people have been infected with the HIV and about 39 million people have died of HIV, since the beginning of the HIV/AIDS epidemic.[1] In the United States alone, approximately 600,000 people have died of AIDS-related illnesses. Despite a wide array of primary and secondary HIV prevention approaches, the US is still facing a major ongoing HIV epidemic with around 50,000 new infections per year.[2] Although new HIV infections attributed to drug injection have been decreasing in the United States since the late 1980s, rates continue to be high among specific sub-populations of IDUs, including racial/ethnic minority groups.[2]

Injection drug use has been inextricably linked with HIV/AIDS since the beginning of the epidemic.[3, 4] Behaviors related with drug use that are specific for HIV transmission include shared use of injection equipment and other paraphernalia and unprotected sexual intercourse with injecting drug users (IDU),[5–9] both of which are influenced by wider structural and environmental factors such as patterns of drug use, commercial sex work, and the availability and nature of interventions aimed at reducing harm.

Despite advances in scientific understanding of HIV, its prevention and treatment, previous research has found that drug users engage in high-risk sexual behaviors and most people living with HIV or at risk for HIV do not have access to prevention and treatment. However, effective treatment with antiretroviral drugs can control the virus so that people with HIV can enjoy healthy lives and reduce the risk of transmitting the virus to others.[10–12]

In a recent decade, treatment programs, such as methadone maintenance treatment (MMT), have been shown to be effective in reducing drug use and injection related risk behaviors.[13–15] Studies have indicated that MMT is associated with a significant decrease in both drug-related and sex-related risk behaviors and emphasize the benefits of methadone programs for public health and HIV prevention.[13–15] Indeed, the studies have shown that the higher rate of retaining IDUs in MMT is positively associated to their treatment success rate and can affect many aspects of the participant's life in a positive way, including reduction of HIV risk.[16, 17] Likewise, studies have found that low-threshold MMT programs can reduce the risk of HIV without the enforcement of abstinence–based policies.[18] Understanding the effectiveness of MMT on high-risk population, some studies points to the need for further study of MMT access in this setting as a means of informing efforts aimed at maximizing initiation of MMT among the target population.

The better understanding of the relationship between MMT and HIV-related risk behaviors will help to better inform future HIV prevention strategies, which may also have policy implications as well. Thus, understanding the relationship between injection drug use, methadone maintenance program, and HIV risk factors is crucial to successfully intervening against a range of risk behaviors among IDUs. This systematic review is aimed at exploring the relevant research literature to more clearly examine the possible impact of MMT on HIV risks behaviors among high-risk IDUs. The outcome of this study could potentially provide general evidence about the influence of methadone maintenance treatment on HIV related risk behaviors among high-risk injection drug users.

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Methods

Search methods for identification of studies

The literature review for this review paper was restricted to peer-reviewed research articles and dissertations on the effects of MMT on HIV risk behaviors among high-risk IDUs. To build the systemic review, we searched for relevant English-language papers published between 2005 through November 2015 (present date). Studies were identified using PubMed database with the following search terms: [(Methadone maintenance program) OR (MMP) OR (methadone maintenance treatment) OR (MMT) OR (opiate replacement therapy) OR (ORT)] AND [(HIV risk behaviors) OR (sexual risk behavior) OR (substance abuse risk behavior) OR (condom use) OR (injection drug use) OR (IDU) OR (multiple sex partner)] AND [(high-risk injection drug users) OR (injection drug users) OR (IDU)]. A secondary search was conducted, which involved checking the reference sections of relevant review papers for articles that may have missed in the initial computerized search.

Study selection and inclusion/exclusion criteria

In conducting the systematic review, we included peer-reviewed studies that met all of the following criteria: (1) participants were high-risk injection drug users; (2) participants enrolled in MMT; (3) assessed substance- or sexual-related HIV risk behavior outcome(s); and (d) were published in English. The search was not limited to any particular geographic area or region and there were no restrictions imposed on the age of subject populations. Studies were excluded if they focused on sexual and drug use transmission risk but not on impacts of MMT on HIV risk behaviors. We also excluded the studies with medically and psychologically unstable participants and pharmaceutical studies.

A total of 360 articles were retrieved as of October 25, 2015. After 3 additional articles were found in the reference section of the relevant journal articles, we had 363 articles for preliminary review. Of these, 190 were subsequently excluded because they were non-human studies (30), non-English articles (14), and outside time frame (146), thus leaving 173 records for further review. After inspecting study titles and abstracts, we found that 113 records were not directly relevant to the study objectives, 2 described ongoing studies with no data published, and 29 lacked the stated outcomes of interest, leaving 29 records for further, more detailed, review. A full-text copy of these subset of studies were obtained and assessed for inclusion. Seventeen full-text records were excluded because they did not investigate an association between the variables of interest and behavioral outcomes that constitute HIV risk behaviors. Finally, a total of 12 studies were included for this review. A flowchart of the study population selection process is shown in Figure 1.

Data extraction and management

Studies found relevant and rigorous were eligible for the review. Data concerning study characteristics, participant characteristics, study design characteristics, and outcome characteristics were independently abstracted from relevant studies by two reviewers (PK and RS). Any discrepancies were resolved by discussion or by contacting additional authors (THM and MC).

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A standardized form was utilized for data extraction process. *Article characteristics* included such information as (1) authors, (2) publication year, (3) study duration, (4) location of study, (5) sample size, and (6) a theoretical framework guiding the intervention. *Participant characteristics* included (1) age, (2) gender distribution, and (3) sample type. *Study design characteristics* included (1) type of study design, (2) methadone dose, and (3) years in methadone treatment program. *Outcome characteristics* included influence of MMT on HIV risk behaviors, including (1) self-reported condom use (male or female condoms), (2) self-reported number of sexual partners, (3) self-reported injection drug use pattern, and (4) self-efficacy (assessing self-confidence related to condom application skills, sexual practices, and needle cleaning skills after intervention).

Results

Description of studies

A total of 12 studies met the review inclusion criteria (Table 1). Studies were conducted between 2005 and 2015, with almost two-forth (41%; k = 5) of the studies taking place within the last 5 years. Study locations included 4 countries: China (41.7%), Canada (33.3%), the United States (16.7%) and Iran (8.3%). In terms of methods, over half of the studies (58.3%) were longitudinal, 33.3% cross-sectional, and 8.3% were randomized controlled trial. Studies collected data through face-to-face interviews (66.6%), self-administered surveys (33.3%). Sex-related risk behaviors among samples were assessed in 8 studies (66.7%), whereas, drug-related risk behaviors were assessed in all the studies (k = 12). However, no studies looked at the self-efficacy related to HIV risk reduction skills.

Overall, 16,195 IDUs were enrolled across the study. Study sample sizes ranged from 160 to 5305, with the average number of 1,350 per study. The average age across samples was 35.4 years (range = 31.0 – 39.2; k = 8). Study participants were predominantly recruited from venues that served active drug users, including substance abuse treatment clinics, service organizations, or defined communities. Half (k = 6) of the studies paid incentives to individuals for participation in the study. A complete summary of the outcome measures generated from each citation appears in Table 1.

MMT and HIV risk behaviors

All studies reviewed in the present study found a significant association between MMT and reduction of sex- and drug-related HIV risk behaviors among IDUs. For example, a recent study by Wang et al. (2014) on long-term effects of MMT among 2662 patients in China found that the use of illicit drug and related risk behavior among the participants with MMT was significantly lower.[19] Similarly, Chen, Xia, Hong, Hall and Ling (2013) showed that the HIV-risk behaviors among drugs users decreased over the course of MMT, especially in the first 6 months, indicating positive effects of MMT on HIV prevention.[20] Likewise, Wang et al. (2014) examined the associations of MMT and voluntary counselling and testing (VCT) with HIV risk behaviors among 2530 IDUs in China. The findings showed that the prevalence of unprotected sex and drug use risk behavior was significantly more common among those receiving VCT-only than those receiving both MMT and VCT.[21]

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In a prospective study that sought to longitudinally investigate MMT use among HIV positive IDUs in Canada, Pettes, Wood, Guillemi, Mmath, Montaner and Kerr (2010) showed that MMT use was associated with a reduced likelihood of frequent heroin injection, syringe borrowing, non-fatal overdose, and public injection.[22] Likewise, Corsi, Lehman and Booth (2009) found that spending more time in MMT was a significant predictor of positive outcomes on drug use and HIV risk behaviors.[23] The results underscore the importance of retaining IDUs in MMT in order to maximize their treatment success.

In addition, Willner-Reid, Belendiuk, Epstein, Schmittner and Preston (2008) examined the impact of MMT on risk behaviors for transmission of blood-borne disease in poly drug users. The study found that HCV-positive participants were engaged in more HIV risk behaviors than HCV-negative participants. Interestingly, this difference was specific to injection-related behaviors and decreased significantly within the first few weeks of MMT.[24] In a cohort study of HIV/HCV co-infected IDUs in Canada, Palepu et al (2006) found that enrollment in MMT was associated with reduced heroin use, and improved adherence, HIV-1 RNA suppression and CD4 cell count response.[25] These findings demonstrate that both drug- and sex-related risk behaviors decrease during MMT, and emphasize the benefits of MMT for public health and HIV/HCV prevention.

A cross-sectional study conducted by Qian et al. (2008) revealed that opioid addicted individuals in MMT were less likely to use or inject drugs, share needles, have multiple sexual partners or have unprotected sex as compared to their counterparts.[26] Similarly, Pang eta al. (2007) demonstrated that the MMT contributed to a reduction in drug use, drug injecting behaviors, drug-related criminal behaviors, and HIV infections.[27] Furthermore, Millson et al. (2007) assessed injection–related HIV risk behavioral changes among opioid users 6 months after enrollment in low-threshold MMT programs in Canada. Results found that the proportion of participants injecting drugs, sharing needles, sharing drug equipment, indirectly sharing and using shooting galleries declined with follow–up for the whole cohort.[18] These findings suggest that low-threshold MMT programs can reduce the risk of HIV risk behaviors.

Moreover, Kerr, marsh, Li, Montaner and Wood (2005) evaluated the correlates of MMT use within a prospectively followed cohort of 1587 IDUs in Vancouver, Canada. The study demonstrated that the use of MMT was associated with reductions in heroin use and HIV risk behavior.[28]

Discussion

We reviewed studies that included data on the influence of MMT on HIV risk behaviors among high-risk injection drug users. Consistent with our hypotheses, we found both direct and indirect associations between use of MMT and risk behaviors. The studies identified in this review, whether controlled trials or other types of study, provide evidence that MMT in IDU is associated with significant reductions in HIV risk behaviors. The studies consistently revealed a decrease in the proportion of participants reporting injecting use, the frequency of injection, the sharing of injecting equipment, and drug-related HIV risk scores. The data from the studies included in this review suggests that substantial reductions in injecting drug

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use occur in the first six months. Similarly, data also suggest that MMT is associated with a lower likelihood of multiple sex partners or unprotected sex.

Our results support the notion that the use of MMT may influence the degree to which IDUs engage in risky behaviors. Importantly, some studies showed that reduction in drug-related risk behaviors were observed after participating in the MMT, so that the changes in behavior were less likely to be caused by factors other than the MMT.[19–22] Also, one study found the cumulative effect of VCT and MMT on reducing the HIV-related risk behaviors among people who inject drugs.[21] It could be that the psychological counseling, health education, group activities, social support and skills training that were provided along with MMT had some impact for better outcome. Thus, the finding from this review highlights that more attention needs to be given for measures to promote adherence among MMT clients.

Some of the limitations of this systematic review should be acknowledged. First, the review was restricted to peer-reviewed journal articles published in English, which likely biased our collection toward primarily English-speaking countries. The search itself was restricted to one database, although this is unlikely to have been a major limitation as PubMed Central (PMC) is the largest repository research article in the world. In addition, only abstracts were screened for this review to determine whether the study investigated the impact of MMT on HIV risk behavior. Thus, any secondary findings and analyses relevant to our topics of interest not mentioned within the abstracts may have been excluded from this review. Many behaviors were self-reported, thus, recall or social desirability biases might be present. In some studies participants were not randomly allocated to each of the treatment groups as a result of conditional limitations of the participating clinics and related ethical issues.

Although randomized allocation was not carried out, comparisons of drug use and demographic characteristics, such as age, and gender, were found to be not significantly different among groups. In addition, there were significant differences in methadone dosages in the different treatment groups. Some studies reported monthly urine tests instead of weekly tests, which could potentially lower the rate of positive urine tests obtained. Similarly, we included only a limited number of outcome and independent variables in the survey; other important psychosocial measures, such as mental health status as well as structural factors such as social support and social networks were not included. These variables might explain more about the relationship between continued HIV-risk behaviors and MMT characteristics.

Conclusions

The findings of this study indicate that the majority of the available research has shown a close and direct association between the uses of MMT and reduced HIV risk behaviors. There is evidence that MMT is associated with a significant decrease in injecting drug use, sharing of injecting equipment. Evidence on sex-related risk behavior is limited, but suggest that MMT is associated with a lower incidence of multiple sex partners and unprotected sex.[21, 26] The literature also suggests that the most significant factor in reducing HIV risks was treatment adherence. As such, more attention needs to be given in future studies to ensure the higher rates of access to MMT as well as to improve the adherence to MMT.

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List of abbreviations

MMT	methadone maintenance treatment
IDU	injecting drug user

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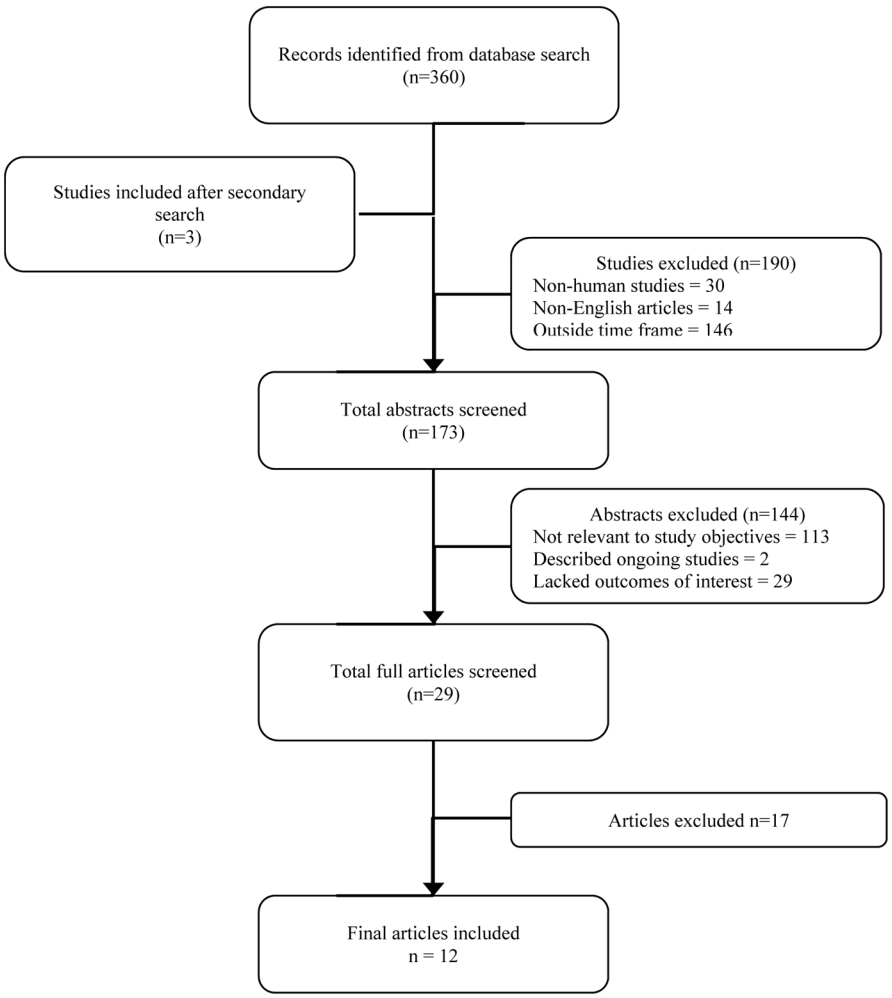

Figure 1.
Summary of study selection process

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Table 1

Summary of studies included in the review

Study (first author, date)	Study location	Study site	Sample size (N)	Age (Years)	Study design	Incentive	Sex-related Outcome	Drug-related Outcome	Summary of findings
Wang et al., 2014	China	Community-based	2530	31.0	Cross-sectional	No	Yes	Yes	MMT-only & combination of MMT and VCT associated with needle sharing and unprotected sexual behaviors
Wang et al., 2014	China	Clinics, Hospitals	2662	36.9	Randomized Controlled Trial	Yes	No	Yes	MMT supplemented with CP or CM reduce heroin use and related risk behaviors
Chen et al., 2013	China	Clinic-based	5305	38.7	Longitudinal	No	Yes	Yes	Positive effects of MMT on HIV prevention
Alavian et al., 2013	Iran	Clinic-based	259	33.0	Longitudinal	No	Yes	Yes	MMT shown to prevent transmission of STDs
Pettes et al., 2010	Canada	NR	353	NR	Longitudinal	No	No	Yes	MMT use associated with a reduced likelihood of drug use related risk behavior
Corsi et al., 2009	USA	Community-based	160	39.0	Cross-sectional	No	Yes	Yes	Retaining IDUs in MMT is needed in order to maximize the successful treatment
Qian et al., 2007	China	Clinics	557	NR	Cross-sectional	Yes	Yes	Yes	MMT participants less likely to use or inject drugs & share needles & less likely to have multiple sexual partners or have unprotected sex
Willner-Reid et al., 2008	USA	Clinic-based	659	38.0	Longitudinal	Yes	Yes	Yes	both drug- and sex-related risk behaviors decrease during MMT
Pang et al., 2007	China	Clinic-based	1662	32.9	Cross-sectional	No	Yes	Yes	MMT contributed to a reduction in drug use, drug injecting behaviors

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Study (first author, date)	Study location	Study site	Sample size (N)	Age (Years)	Study design	Incentive	Sex-related Outcome	Drug-related Outcome	Summary of findings
Millson et al., 2007	Canada	NR	183	NR	Longitudinal	Yes	No	Yes	Low-threshold MMT programs can reduce the risk of HIV
Palepu et al., 2006	Canada	NR	278	NR	Longitudinal	Yes	No	Yes	Among HIV/HCV co-infected IDUs on HAART, enrollment in MMT associated with reduced heroin use
Kerr et al., 2005	Canada	NR	1587	33.4	Longitudinal	Yes	Yes	No	MMT associated with reductions in heroin use and HIV risk behavior

Note: NR: Not reported | CP: Counseling psychology | CM: Contingency Management

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