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Review

Drug abuse treatment as an HIV prevention strategy: a review

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Abstract

We review drug abuse treatment as a means of preventing infection with HIV. Thirty-three studies, with an aggregate of over seventeen thousand subjects, were published in peer-reviewed journals from 1988–1998. Research on the utility of drug abuse treatment as an HIV prevention strategy has focused primarily on methadone maintenance treatment (MMT) rather than other modalities such as residential or outpatient drug-free treatment. Recent research provides clear evidence that MMT reduces HIV risk behaviors, particularly needle-use, and strong evidence that MMT prevents HIV infection. There is less definitive evidence that MMT reduces needle-sharing and unsafe sexual behavior, or that other treatment modalities prevent HIV infection. Future research should take into account patient self-selection processes and investigate other treatment modalities for heroin and stimulant abuse to determine their effects on HIV risk behaviors and HIV infection.

Keywords: HIV/AIDS prevention; Treatment; Methadone maintenance; Risk behavior

1. Introduction

In the United States as of the end of December 1998, 32% of the 679,739 adult/adolescent cases of AIDS have been linked to drug injection — either as the sole risk factor (20% of cases), concomitantly with male-to-male sexual contact (5% of cases), through heterosexual contact with an injecting drug user (5% of cases) or multiple exposure categories that include drug injection (2% of cases) (Centers for Disease Control and Prevention [CDC], 1998; Table 18, p. 28). The proportion of male AIDS cases attributable to the CDC-definition of 'men who have sex with men' has declined considerably in the last decade, while the proportion assigned to injection drug use has risen (Normand et al., 1995). Moreover, crack-cocaine users, who transmit HIV through their sexual behaviors, account for an increasing proportion of AIDS cases (Cohen et al., 1994). Choosing among the intervention strategies purported to prevent HIV in drug abusers is one of the most urgent questions facing health policy makers.

Drug abuse treatment is one approach that may have a strong impact on preventing HIV infection. Treatment has the potential to restrict the spread of HIV by reducing needle-use, a primary vector of HIV infection. If drug abuse treatment programs reduce injection practices that transmit HIV, they will have a direct effect in reducing the spread of HIV/AIDS. Many large-magnitude studies have shown that patients participating in methadone maintenance treatment (MMT), therapeutic communities, and outpatient drug-free programs decrease their drug use significantly (Simpson et al., 1979; Hubbard et al., 1989; Simpson, 1993), yet there is a need to examine the association between treatment and HIV risk behaviors such as sharing and re-use of needles.

Drug abuse treatment programs can also interrupt HIV transmission by decreasing risk behaviors related to sexual transmission of HIV, such as not using condoms. Drug abuse treatment programs see many people engaging in high risk sexual behaviors, including work-

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ers in the sex industry. If these programs are able to decrease high risk sexual practices among patients, they will also have a direct effect in reducing the spread of HIV/AIDS.

Drug treatment also has the potential to interrupt HIV transmission by promoting rehabilitation and serving as a platform for services such as HIV education and medical care. As early as 1986, policy groups called for all drug treatment programs to provide HIV transmission information (Inciardi, 1990). Federal regulations now require that the treatment admission process include HIV education (Drugs Used for Treatment of Narcotic Addicts, 1998). However, there have been mixed results in controlled trials of information and skills training (Auerbach et al., 1994). Other services can also be useful: For example, many programs have begun to offer primary medical care in drug abuse treatment (Selwyn et al., 1989; O'Connor et al., 1994). The recent development of HIV protease inhibitors adds optimism that HIV-infected people can postpone disease by adding protease inhibitors to their HIV treatment regimens (DeNoon, 1996). Offering medical care on-site at drug treatment programs helps patients receive appropriate medical treatment (Umbricht-Schneiter et al., 1994). Providing appropriate medical treatment can decrease patients' viral load and possibly their infectivity to others.

Thus, it is plausible that drug abuse treatment can have these powerful effects in preventing transmission of HIV, but how strong is the evidence that these preventive effects actually occur? Many reports have called for increasing the availability of drug abuse treatment in the United States to slow the spread of HIV (Public Health Service, 1988; Turner et al., 1989; Sisk et al., 1990). This expansion, however, has not occurred during the AIDS epidemic. To the contrary, the quality of treatment programs may actually be decreasing (D'Aunno and Vaughn, 1995; Etheridge et al., 1995). Further, there is debate about the conditions under which expanding drug abuse treatment is a cost-effective deterrent to the expanding HIV epidemic (Lampinen, 1991). This paper reviews recently published research evaluating the effect of drug abuse treatment in preventing HIV infection. Two earlier reviews have addressed this issue, though less methodically than the present study. Des Jarlais and colleagues reviewed the 'hard data' studies as of 1989 (Des Jarlais et al., 1990). They concluded that 'bringing IV drug users into drug abuse treatment programs should be an effective method of protecting some of them from HIV infection' (p. 51), and they sounded several qualifications about the necessity of having drug users enter treatment early in the expansion of HIV in a community and about the importance of retaining patients in treatment. Metzger et al. (1998) reviewed a variety of articles, published as early as 1984, concluding that drug users who are in treatment practice significantly lower rates of HIV risk behaviors, and 'these self-reported behavioral differences are consistent with seroprevalence and seroincidence data' (p. 102). In addition, Marsch (1998) published a meta-analysis on the efficacy of MMT as a pharmacotherapeutic agent in reducing drug use, HIV risks, and criminality. The present review extends these works by systematically reviewing the literature to understand how strong the evidence is that drug abuse treatment prevents HIV infection.

2. The experimental evidence

2.1. Search strategy and limitations

We conducted a search of the relevant English-language literature from 1988–1998 utilizing the databases MEDLINE and Psych/INFO, pairing keywords for modalities (*drug abuse treatment*, *methadone*, *therapeutic community*, *detoxification*, *ambulatory care and drug abuse* [*outpatient drug-free* is not a medical subject heading in MEDLINE]*;* with *AIDS* or *HIV*. We also searched both databases for articles by ten authors known to have conducted research in this area. In addition, our colleague, Michael Prendergast of UCLA, who was conducting a meta-analysis on a related topic, contributed references to our review. MEDLINE and PsychINFO are only two of over 100 computerized databases but they comprise two of the major databases for publication of research in the drug abuse and HIV area, with over 5.5 million and 1.5 million references in their respective databases. This search strategy yielded over 400 total references. We limited the present review to include only articles describing empirical research, published in peer reviewed journals, which provided new quantitative information about the relationship between drug abuse treatment and HIV risk behaviors or HIV seroconversion. We excluded policy descriptions about issues as well as such sources as conference presentations, letters to the editor, book chapters, books, and doctoral dissertations. Limiting the review to empirical research published in journal articles limits our conclusions about the utility of drug abuse treatment — particularly treatments that do not involve methadone. We believe, however, that the editorial review process is an important part of quality control.

The dependent variables in these studies were diverse and differed in importance with respect to preventing HIV infection. Some studies included only unsubstantiated self-report of HIV knowledge, attitudes, or behavioral intentions. Others focused on self-reported risk behaviors, some examining whether drug use and sexual activities decreased, others examining whether the methods of drug use and sexual activities changed (e.g. using sterilized needles or condoms a greater proportion of the time). Others included more objective mea-

sures, such as urine assays of recent drug use. A few studies assessed seroconversion to HIV, which is the most conservative yet also the most convincing dependent variable. The variety of dependent variables, coupled with the variety of experimental designs, prohibits making quantitative cross-study comparisons, much less conducting a meta-analysis.

We organized the review into three sections representing increasingly convincing categories of evidence that drug abuse treatment might prevent HIV infection: (1) longitudinal studies conducted with in-treatment samples examining the relation between drug abuse treatment and changes in HIV risk behaviors; (2) comparative studies contrasting patients in drug abuse treatment with control patients on changes in HIV risk behaviors; and (3) comparative studies contrasting these groups on rates of HIV seroconversion. If articles provided more than one category of evidence they were included in more than one section.

2.2. Longitudinal studies with in-treatment samples

A number of longitudinal studies have examined changes in HIV risk behaviors for patients currently in treatment. Most have found that longer retention in treatment, as well as completion of treatment, are correlated with reduction in HIV risk behaviors or an increase in protective behaviors. Twenty published studies are reviewed here and summarized in Table 1, organized by date of publication. These studies indicate that drug abuse treatment, especially MMT, is associated with decreased injection and sex-related HIV risk behaviors.

The changes are most apparent in drug use, where 16 of the 17 studies examining drug use found that treatment was associated with less HIV risk (generally evidenced by less injection or needle-sharing). The exception was a study by Calsyn et al. (1991) which studied needle-use patterns among injection drug users (IDUs) in treatment in Seattle (where needle purchase is legal and HIV seroprevalence rates comparatively low) to determine whether the availability of legal injection equipment was associated with decreased needle-sharing. The authors conducted analyses using participants who had been in treatment 6 months or less and found that, although this sub-sample engaged in more high-risk HIV transmission behaviors than the sample as a whole, the trends in the data regarding needle-sharing, needle-obtainment, and places of drug use were very similar. Unfortunately for the purposes of this review, the sub-sample was not compared with the sample of only those participants who had been in treatment for a longer period of time. It is likely that there would have been significant differences between these groups, given they differed from the sample as a whole.

Sexual behavior was addressed in twelve of these studies, and eleven of them found that treatment was associated with less sexual HIV risk behavior (measured with self-report of a variety of behaviors including number of sexual partners, condom use, involvement in prostitution, and having sex with an IDU). The exception was the cross-sectional study of Magura et al. (1990) in which those with less time in treatment (recently entering) reported higher rates of condom use. Further studies are needed to clarify what factors contribute to the reduction of sex-related risk behaviors and needle-sharing. For example, Longshore et al. (1994) surprisingly found that positive changes in sex-related risk behaviors (i.e. reductions in past-year sex partners) were not related to the AIDS education component included in the study.

Seventeen of the 20 studies included MMT, and 11 of them focused solely on MMT. It is unclear whether patients in other treatment modalities (e.g. therapeutic community, outpatient drug-free) experience the same magnitude of changes as patients in MMT because so little research examines them. The studies that did include other modalities (Calsyn et al., 1991; Saxon et al., 1994; Avins et al., 1997; Hubbard et al., 1997; Gottheil et al., 1998; Longshore and Hsieh, 1998; Magura et al., 1998; McCusker et al., 1998) did not conduct treatment modality by HIV risk behavior change analyses to clarify this issue. It is possible, therefore, that the behavior changes observed in the Calsyn et al. (1991) and the Saxon et al. (1994) studies are mainly due to the MMT programs, given that three-quarters of the patients were receiving methadone treatment. The Avins et al. (1997) study, however, examining patients in residential and outpatient treatment, suggests that other treatment modalities for alcoholic patients may also be associated with reduced risk behaviors. Even though alcohol was the substance targeted in treatment, the patients in the study exhibited positive behavior changes both in injection drug use and sex-related risk behaviors. The Drug Abuse Treatment Outcome Study (DATOS, Hubbard et al., 1997; Longshore and Hsieh, 1998) provides the most convincing evidence that not only methadone, but long-term residential, outpatient drug-free, and short-term inpatient programs are associated with significant reductions in both drug- and HIV sexual-risk behaviors.

The investigations included in this section of the present review were all longitudinal studies conducted with in-treatment samples, and all have in common a significant weakness of the lack of comparison groups for the in-treatment samples. For example, Avins et al., (1997) acknowledge this limitation and refer to their study as a 'Natural History' study. Bellis (1993) also acknowledges that this limitation makes it impossible todetermine how much change would occur without treatment. Avins et al. (1997) did somewhat strengthen

Table 1
Decreased HIV risk behaviors in substance abuse treatment: longitudinal studies with in-treatment samples

First author (year)	Sample size and background [a]	Treatment modality	Results/conclusions
Ball (1988)	506 male IDUs in treatment in 6 programs in New York, Baltimore, and Philadelphia. In treatment ≥1 year, most for 2+ years. Little other information about patient demographics and treatment program variables.	Methadone maintenance treatment (MMT)	71% of those who remained in MMT 4+ years ceased injection, compared with 18% of those who left treatment.
Magura (1990)	211 IDUs enrolled in treatment. 37% women; 32% minority; most 30–39 years. 31% reported more than one sexual partner in past year, and 33% reported sexual partners who were IDUs. 41% reported injection in past month, and 42% injectors reported sharing needles. 68% reported not using condoms in the prior month, and only 11% used condoms in a consistent manner.	MMT	Recent entry into MMT associated with condom use.
Calsyn (1991)	313 IDUs in treatment; 28% women; 27% minority; 73% opiates primary drug; 12% cocaine primary drug.	73% MMT; 18% inpatient; 9% outpatient drug-free.	Subsample of newly admitted (in treatment ≤6 months) did not differ from entire sample on needle-sharing, needle-obtainment, and places of drug use.
Williams (1992)	98 IDUs in treatment; 37% women; 17% minority; most in their mid to late 30's, and men (63%); methadone doses averaged 70 mg.	MMT	Those in continuous treatment reported less needle-sharing, fewer needle-sharing partners, fewer sexual partners, and more likely to be women.
Bellis (1993)	41 heroin-addicted female prostitutes. 50% Hispanic, 33% Caucasian, 13% African–American, 4% Native American; mean age 32.	MMT	Reduced prostitution; reduced drug-positive urinalysis.
Gottheil (1993)	229 IDUs in MMT	MMT	Opiate use decreased significantly by time in treatment; 35% opiate-free at 3 months, 71% at 4+ years, 85% at 10+ years.
Longshore (1994)	372 IDUs (129 currently in MMT). 52% women; 40% Anglo, 34% Hispanic, 26% African–American; 21–71 years, mean 38 years; in MMT a mean of 3.4 years.	MMT	Number of past-year sex partners negatively related to time in treatment.
McCusker (1994)	402 drug users in treatment. 68% men; 83% White non-Hispanic, >half 25–34 years.	Short-term residential.	Decreased injection, risky injection, number of sex partners, borrowing/lending injection equipment, number of sharing partners; increased use of bleach.
Saxon (1994)	220 IDUs in treatment. 72% men; 73% Caucasian, 24% African–American, 7% Hispanic/other; 52% in treatment <7 months and 25% in treatment >24 months; primary drug problems were opiates (73%) and cocaine (12%).	MMT; drug-free outpatient; inpatient; naltrexone therapy.	Decreases in injection, sharing; ongoing HIV risk associated with less time in drug treatment.
Camacho (1996)	326 IDUs entering treatment. 68% men; 45% Hispanic, 36% Caucasian, 16% African–American; mean age 37.	MMT	Reductions in both injection and sex-related HIV risks.
Shore (1996)	277 IDUs in and out of treatment. 77% men; 36% Hispanic, 31% Caucasian, 29% African–American; most 30–49 years; 36% shared needles in past six months; 14% used shooting gallery monthly.	MMT	Injection frequency decreased with consistent MMT enrollment.

Table 1

First author (year)	Sample size and background [a]	Treatment modality	Results/conclusions
Avins (1997)	700 alcoholics entering alcohol treatment. 72% men; 53% African–American, 33% Caucasian, 9% Latino.	Residential (63%) and outpatient (37%) alcohol treatment.	Reductions in having sex with an IDU and injecting drugs; improvement in condom use.
Hubbard (1997)	2966 drug users in DATOS: followed through 1 year of treatment. Proportion of men from 69% in LTR to 66% in ODF; proportion of African–Americans or Hispanics from 52% in LTR to 66% in ODF; and proportion over 30 years from 50% in LTR to 82% in MMT.	MMT; long-term residential; outpatient drug-free; short-term inpatient.	Reductions in cocaine, heroin, and other drugs in the 12 months post-treatment; significant reductions in sexual behavior HIV-risk.
Abbott (1998)	227 IDUs admitted to MMT; 73% male; 81% Hispanic, 17% Caucasian; mean age 37.	MMT; community reinforcement approach and standard intervention.	Significant reductions in injection drug use and risky sexual behavior at 6, 12 and 18 months from admission; no differences related to treatment type.
Gottheil (1998)	447 cocaine dependent patients entering treatment; 61% male; 94% African–American; mean age 32; mean length of use 7 years; mean prior treatment episodes 1.1.	Outpatient: individual counseling 1 ×/week group; or intensive 3 h 3 ×/week.	Significant reductions in HIV risk behaviors over 9-month period subsequent to admission; no differences related to treatment type.
Iguchi (1998)	51 IDUs admitted to MMT; 73% male; 75% Caucasian, 25% non-Caucasian; median age 32; median lifetime opiate use 108 months.	MMT 90-day detoxification.	Significant reductions in opiate use rate and amount; also significant reduction in opiate use with strangers and acquaintances (vs. alone or with friends/family).
Longshore (1998)	Intake data from DATOS: 6620 drug users; 66% male; 47% African–American, 38% non-Hispanic Caucasian; mean age 32.6 years; 72% reported weekly cocaine use and 29% weekly heroin use in prior year.	MMT, long-term residential; outpatient drug-free; short-term inpatient.	Greater lifetime exposure to drug abuse treatment associated with less risky sexual behavior among drug users.
Magura (1998)	207 cocaine-using MMT patients; 59% male; 53% Hispanic, 36% African–American, 11% Caucasian; mean age 38.5; mean methadone dose 67 mg; mean time in treatment 27.8 months	MMT and experimental supplementary therapies for cocaine use.	Most needle-related and all sexually-related risk behaviors significantly decreased.
McCusker (1998)	1994 drug users entering treatment; 66% male; 77% Caucasian, 14% Hispanic, 8% African–American.	Detoxification, long-term residential, outpatient.	Injection risk behavior decreased for those in long-term residential and outpatient; risky sexual behavior decreased in males.
Rhoades (1998)	123 IDUs; 71% male; 52% Caucasian, 29% Hispanic, 19% African–American; mean age 38.3.	MMT	HIV risk behaviors decreased over time in MMT as a function of dose and visit frequency.

[a] Note: *N* is the number of subjects included in the outcome analysis. Some results in this table were calculated from data reported in the published article.

their conclusions by conducting a second cross-sectional study in the same clinic the year after their follow up interview. No differences were found in rates of reported HIV-related behaviors in the new sample compared with the previous baseline. Changes were therefore likely not temporal trends and were more likely to be the effects of treatment. Most of the studies, however, were not this creative in addressing the issue and therefore, in the absence of a comparison group, must be interpreted cautiously.

Changes in HIV risk behaviors are common findings in cohort studies with drug users, representing either true behavior change or increased desire to present a socially desirable impression (Latkin et al., 1993). Pre-post studies have found decreased risk behaviors associated with participation in brief outreach interventions (Neaigus et al., 1990), educational interventions (Stephens et al., 1991), and even in non-intervention longitudinal studies (Celentano et al., 1994). These differences generally diminish under more strenuous experimental controls (see Calsyn et al., 1992). Thus, there is a question as to whether treatment programs produce the changes observed, or whether the changes would have occurred anyway. Studies with comparison conditions can provide a higher level of evidence about the degree to which drug abuse treatment decreases HIV risk behaviors.

2.3. Studies comparing treatment patients with other samples

A number of cross-sectional studies have compared HIV risk behaviors among patients in drug abuse treatment with out-of-treatment samples. Most studies focused on IDUs in MMT. Overall, these studies demonstrate that patients in treatment engage in less risk behavior than their out-of-treatment counterparts. Nine published studies are reviewed in this section and summarized in Table 2.

Klee et al. (1991) examined the risk behavior of IDU opiate users. They assessed details of needle-exchanging, involvement in treatment, and its relation to needle-sharing. Although more non-treatment IDUs shared injection equipment than MMT patients, those in methadone over 6 months were older, and time using drugs was correlated with age and with receiving treatment. After controlling for age, differences were found only in the older age group. IDUs in treatment were more likely to use needle exchanges and less likely to give their used equipment to others. Overall, there were important differences between the treatment and non-treatment groups in the sharing of equipment. This study also suggests, however, that IDUs entering treatment may be less predisposed to share equipment due to other factors such as demographics, and that short-term treatment is unlikely to facilitate significant behavior change.

Longshore et al. (1993) investigated whether reduced needle-sharing was merely the result of reduced injection while in treatment or whether it was attributable to the actual treatment process (e.g. HIV education). Fewer patients shared needles in the past year than non-treatment participants. Further, among those who reported sharing needles, those in treatment shared significantly less frequently than those not in treatment, even when background characteristics were controlled. This relationship was not due to the negative correlation between treatment and injection frequency. These researchers extended prior investigations by isolating a significant relationship between MMT and the likelihood of needle-sharing after controls were introduced for injection frequency and drug-user background traits.

In a related study, Longshore et al. (1994) investigated whether the relationship between sex-related HIV risk behavior and drug abuse treatment was due to treatment or to drug-user background characteristics. They interviewed IDUs in MMT and not in treatment. IDUs in treatment reported fewer sex partners in the past year, and among those in treatment there was a negative correlation between treatment duration and number of past-year sex partners. Controlling for background differences, treatment status was still associated with fewer partners. Results examining mediating variables suggested that treatment influences disengagement from paid sex and raises patient self-efficacy for risk reduction.

Meandzija et al. (1994) examined relationships between HIV status, ethnicity, MMT, active substance use, and sexual risk behaviors among IDUs. Treatment participants were excluded if they had been in treatment more than a year. They found that current MMT patients engaged significantly less frequently in giving sex for drugs or money in the last 30 days before the interview and reported 50–65% lower injection frequency than those not in treatment. These findings are impressive given the exclusion of longer-term methadone patients. The authors conclude that MMT is a potentially important AIDS prevention strategy.

Baker et al. (1995) compared injecting behavior with sexual risk-taking behavior among current, previous, and never-in-MMT patients. They hypothesized that those currently in treatment would engage in less injection and sexual risk-taking than the other two groups and that previous methadone participants would not differ in injection or sexual risk-taking from opiate users who had never been in MMT. They found that the current MMT group injected less than the other groups, and those not injecting in the last month had been enrolled in MMT longer (95 vs. 59 weeks). Also, use of bleach was more common in the current MMT group, but reduced sharing behavior was not. There were no differences between the non-methadone and

the previous methadone groups, highlighting the tendency for injection practices to resume when patients leave MMT and the importance of retention in treatment. There was no indication of reduced sexual risk behaviors among those in treatment. The authors suggest that MMT provides added benefits of relapse prevention and clean injecting equipment.

Caplehorn and Ross (1995) tested the hypothesis that MMT reduced the likelihood of using contaminated needles and syringes by reducing their injection frequency, and that this effect was independent of knowledge of HIV/AIDS. They found that MMT patients were half as likely to report having injected with a used syringe in the previous 6 months as those not in treatment. This effect disappeared when methadone patients who had not injected in the month prior to the interview were excluded, suggesting that methadone patients had less HIV risk because they were less likely to inject drugs. Participants in MMT and those not in treatment were comparable in knowledge about HIV infection, and there was no measurable association between participants' beliefs and attitudes and their injecting behavior. These findings support the conclusion that MMT reduces HIV risk-taking by reducing needle-use (not due to educational efforts associated with methadone programs).

Greenfield et al. (1995) examined the validity of self-reported drug use among IDUs. They compared self-reported drug use with urine drug screen results at study intake, and months 2, 4 and 6. Urine samples were collected at the time of each interview. Changes in risk behavior were analyzed as a function of time and treatment group. The rates of self-reported risk behavior declined over time, and treatment participants reported lower rates of risk behavior — both fewer injections and less needle-sharing — than the commu-

Table 2
Lower HIV risk behaviors among patients in substance abuse treatment compared with non-treatment samples

First author (year)	Sample size and background [a]	Comparison groups	Results/conclusions
Klee (1991)	216 English IDUs from 16–35 years (45% under age 25); ethnicity and gender not reported.	74 IDUs in MMT > 6 months; 44 in MMT < 6 months; 98 not in treatment.	Longer-term treatment group was less likely to share injection equipment than those in MMT < 6 months or not in treatment.
Longshore (1993)	258 IDUs; 40% Caucasian, 32% Hispanic, 28% African–American; 52% women, 65% ≥ 36 years.	105 IDUs in MMT vs. 153 not in treatment.	63% in MMT shared needles in last year, compared with 79% of those not in MMT, significant after controlling for background differences and injection.
Longshore (1994)	372 IDUs. Background in Table 1.	129 IDUs in MMT vs. 243 not in treatment.	MMT group reported fewer past-year sex partners.
Meandzija (1994)	424 IDUs. 70% men; 47% African–American; 40% were HIV positive.	107 IDUs in MMT vs. 317 not in treatment.	MMT group reported fewer drug injections. MMT group engaged less frequently in giving sex for drugs or money in past 30 days.
Baker (1995)	260 Australian IDUs. 70% men; mean age 30; mean dose of methadone 66 mg.; mean time in the MMT program 71 weeks.	95 IDUs in MMT; 52 previously MMT; 113 never in MMT.	Current MMT group reported less injecting and more cleaning, but no difference in sexual risk-taking or in needle-sharing.
Caplehorn (1995)	239 Australian IDUs.	109 IDUs in MMT vs. 130 not in treatment.	MMT group was half as likely as not-in-treatment group to inject with used syringe in prior 6 months.
Greenfield (1995)	281 IDUs. 70% men; 63% African–American; most age mid-30s; 5 months MMT experience in those not in treatment, 55 months in MMT group.	146 IDUs in MMT vs. 135 not in treatment.	MMT group reported fewer injections, less needle-sharing, and had fewer drug-positive urine tests.
McCusker (1995)	450 IDUs. 67% men; 82% White, 9% Black, 9% Hispanic; median age 30.	115 IDUs in drug treatment (85 residential; 30 outpatient); 335 not in treatment.	Residential group had lowest relapse rates; among those who relapsed, treatment groups did not report safer injection practices than those not in treatment.
Stark (1996)	612 German IDUs. Two-thirds men; median age 29; median duration of injection drug use 8 years; median duration in MMT 16 months.	61 IDUs in MMT vs. 551 not in treatment.	MMT group reported they had injected less and were less likely to borrow syringes; no difference in sexual risk behaviors.

[a] Note: *N* is the number of subjects included in the outcome analysis. Some results in this table were calculated from data reported in the published article.

nity participants. Urine tests for cocaine and opioids corroborated the self-report data of significantly greater drug use in the community group at each time point. In contrast to the self-reported changes in risk behavior, however, the rates of positive urine specimens were relatively stable for each group, with no significant changes over time. The study raises questions about the validity of reported reductions in high-risk drug use behaviors.

McCusker et al. (1995) studied patients in a 21-day inpatient drug detoxification program that attempted to connect patients with longer-term treatment. They investigated outcomes including length of stay, transfer to further treatment, and HIV risk behavior. In this review we are focusing only on the participants who were successfully followed. Relapse rates to either any drug use or drug injection were lower among participants transferred to residential treatment than either patients transferred to outpatient programs or those with no further treatment. Among participants who continued to inject drugs at follow-up, no reduction in HIV risk behaviors was found regardless of further treatment. Overall, this study indicates that there are beneficial outcomes of detoxification among patients who stay long enough to be transferred to further treatment, particularly to residential drug-free treatment.

Stark et al. (1996) sought to determine whether MMT was effective in reducing the levels of HIV risk-taking behavior (borrowing and lending of injection equipment, irregular condom use) among IDUs and to identify independent predictors of the borrowing of used syringes. They found that patients in MMT tended to be older, have a longer injection history, were more likely to be HIV positive, had injected less frequently in the previous 6 months, and were less likely to have borrowed or passed on used syringes recently. In logistic regression analyses MMT was protective against the borrowing of syringes but not against the lending of syringes. Sex behaviors did not differ significantly in relation to treatment status. After adjusting for confounding factors, IDUs who had received MMT during the entire 6 months before the interview were less than half as likely to have borrowed used syringes during this time period. The study supports the conclusion that methadone may play a significant role in reducing levels of drug use and borrowing of syringes but does not affect risky sexual behaviors.

Overall, the studies reviewed in this section provide support for the generalization that, compared with IDUs who are not in drug abuse treatment, patients in MMT and perhaps other drug abuse treatments demonstrate lower HIV risk behaviors, suggesting that drug abuse treatment is an effective strategy for HIV prevention. Eight of the nine studies compared MMT patients with IDUs out of treatment, and non-methadone treatment was addressed in only one (McCusker et al., 1995). The data are convincing for the reduction of risky injection behavior but less robust for the reduction of risky sexual behavior among IDUs. All eight of the studies addressing drug use risk found differences between the in-treatment and out-of-treatment samples, while the findings were mixed regarding sexual behaviors. For example, in the Baker et al. (1995), Stark et al. (1996) articles, patients in MMT engaged in significantly less injection risk behaviors, but showed no difference in sexual risk behavior from their out of treatment counterparts. Two other studies, (Longshore et al., 1994; Meandzija et al., 1994) did find less sexual risk behavior among those IDUs in treatment. Longshore et al. (1994) suggest that in the cases where MMT is successful in reducing sexual risk behaviors it is by facilitating disengagement from prostitution and enhancing patient self-efficacy for risk reduction. These data suggest that substance abuse treatment is an effective platform for informing patients about risky sexual behavior in addition to reducing injection behavior, to prevent HIV transmission.

Despite the compelling evidence these studies provide for the protective influence of drug abuse treatment, a critical question remains: Do people who enter and remain in MMT differ in other ways from those out of treatment that could account for the observed differences in risk behavior? For example, Klee et al. (1991) found that age accounted for the relationship between MMT and reduced injection risk behavior. Many other studies noted demographic differences between the treatment and non-treatment groups. For example, those in treatment tended to be older, and several studies found that ethnic minorities were over-represented in the out-of-treatment groups. Many of the studies reviewed (e.g. Longshore et al., 1993), however, addressed this issue by statistically controlling for background and drug user characteristics, and found that the association between treatment and reduced risk behavior remained.

The mechanism by which treatment influences reductions in risk behavior has been addressed in several articles (e.g. Longshore et al., 1993, 1994). These studies have focused on the question: Is reduced injection merely a result of being in treatment (for example, reduced drug use leads to reductions in HIV risk behavior) or is it due to what is learned in treatment (e.g. HIV education leads to reductions in HIV risk behavior)? The data appear mixed as to whether the association is due to more than simply being in treatment.

A common significant weakness of the studies in this section, with the exception of Greenfield et al. (1995), is dependence on self-report, and therefore the validity of the data is subject to the same pitfalls reviewed inSection 1. Indeed, another finding in the Greenfield et al. (1995) study in using biological indicators such as urinalysis, was that IDUs tended to under-report their

Table 3
Low seroconversion to HIV in methadone maintenance treatment (MMT) patients

First author (year)	Sample size and background	Results/conclusions
Novick (1990)	58 IDUs in long-term MMT; 81% men; mean age 46; on methadone a mean of 17 years; at mean dose of 60 mg.	Zero seroprevalence found in sample.
Williams (1992)	98 IDUs in MMT; background in Table 1.	Seroconversion was 2% for those continuously in treatment, 19% for those whose MMT was interrupted (ns).
Metzger (1993)	255 IDUs in or out of treatment. 76% men; 67% African–American; most age 38–50.	Seroconversion was 3.5% for those who stayed in MMT vs. 22% for those who remained out of MMT.
Serpelloni (1994)	80 Italian IDUs. 78% men; mean age 27; mean duration of drug use 8 years.	Time out of MMT was the most important risk factor, also daily dosage of methadone. HIV risk increased 1.5 times for every 3 months spent out of treatment.
Moss (1994)	681 heterosexual IDUs in MMT or methadone detox. 53% men; 56% Caucasian, 21% African–American, 15% Hispanic; 60% ≥age 35.	Stable attendance in MMT was 'highly protective' (hazard ratio 2.7, $P = 0.02$).
Hartel (1998)	622 IDUs in MMT; 51% male; 24% African–American, 50% Latino, 24% Caucasian; mean time in treatment 5.5 years; mean methadone dose 64 mg.	Longer duration in MMT and higher methadone dose (≥ 80 mg/day) associated with lower rates of HIV.

drug use. To reduce demand effects, the majority of studies did employ research interviewers who were independent of the treatment programs, yet much more convincing proof would be provided by measures that do not rely on self-reports.

2.4. Studies examining seroconversion to HIV

A small number of studies have examined the relationship between HIV seroconversion and substance abuse treatment, which provides the most stringent test of the relationship between treatment and HIV prevention. We identified six such studies, which are reviewed below and summarized in Table 3. As we have indicated in the other sections, studies of MMT provide the most compelling evidence that substance abuse treatment can prevent HIV infection.

Novick et al. (1990) conducted a cross-sectional study that assessed HIV and hepatitis B prevalence rates in 58 long-term MMT patients in New York City. The patients were involved in 'medical maintenance', a treatment designed for socially rehabilitated MMT patients who received both medical care and methadone from a primary care physician. None of the patients had antibody to HIV, and the authors infer that methadone can protect patients from HIV infection. Although this study is important because it was one of the first to examine this relationship, the highly selected sample, uncontrolled methodology, and absence of a comparison group make it difficult to draw meaningful conclusions regarding MMT and HIV seroconversion.

We reviewed Williams et al. (1992) in Section 1, because the study provided evidence for reduced HIV risk behaviors over the course of treatment. These investigators followed 98 patients in and out of MMT. The MMT program offered a range of services, including mental health, mandatory counseling, and primary health care, Fifty-seven percent of the patients remained in continuous treatment and were followed for a mean of 29 months. The other 43% were not in treatment at all, left treatment, or left and returned to treatment during the study period and were followed for a mean of 53 months. Results indicated that the patients who remained in MMT continually during the follow-up period were less likely to seroconvert than those who did not. Only one patient of 56 in continuous treatment seroconverted, while eight of the 42 in the interrupted treatment group seroconverted. For the continuous treatment group, the seroconversion rate was 0.7 per 100 person years, and for the interrupted treatment group the seroconversion rate was 4.3 per 100 person years. However, when the authors controlled for length of follow-up, which differed between the two groups, the difference in seroconversion rates was not statistically significant. These findings provide weak evidence that continuous MMT involvement decreases the likelihood of HIV seroconversion.

Metzger et al. (1993) conducted a prospective, longitudinal study seeking to identify HIV seroprevalence and seroconversion rates and related risk behavior rates among IDUs in and out of MMT treatment in Philadelphia. They followed participants for 18 months and conducted assessments at 6-month intervals, including HIV counseling and education. They studied 255 IDUs (152 in treatment and 103 out of treatment). The out-of-treatment sample tended to be younger, African–American, and male. This out-of-treatment group was also more likely to have higher incomes and to receive money from illegal activity. The in-treatment group had entered treatment more times (5.6 vs. 3.5),

and the average daily methadone dose was 44 mg. Seroprevalence rates at baseline were 11% in-treatment and 18% out-of-treatment. The investigators calculated prevalence rates only for participants who provided data for all four time points (91% of the in-treatment group and 85% of the out-of-treatment group). For those in treatment, prevalence rose from 11 to 15%, and for those out of treatment, from 18 to 33%. These differences were significant at 12 and 18 months. Overall incidence rates were three conversions per 100 person years of exposure for the treatment group, and 10.7 conversions per 100 person years for the out-of-treatment group. The authors further examined the relationship between treatment participation and seroconversion by examining patients who were initially seronegative and who had provided data at all time points (185), and grouped them according to treatment participation. Of those participants in treatment at all time points, 3.5 became HIV-positive by 18 months, 4.4% of intermittent treatment participants seroconverted, and 22% of the untreated sample seroconverted. The untreated sample was 7.6 times more likely to become HIV seropositive than those in treatment, and six times more likely to become seropositive than the intermittent treatment group. These findings remained significant even after controlling for ethnicity, gender, age, and needle-sharing. Further, although the odds of seroconverting relative to the treated group were somewhat lower with these variables in the equation, treatment status remained as the only significant factor. This study strongly suggests that treatment with MMT decreases the likelihood of HIV seroconversion.

Serpelloni et al. (1994) conducted a longitudinal, nested case-control study to evaluate the protective effect of methadone treatment on HIV seroconversion. The study was conducted in Verona, Italy and the participants were 80 IDUs (40 seroconverters and 40 controls matched on sex, age, duration of drug use, and follow-up time). All IDUs from a local drug dependency unit received serological testing, those who were seronegative were asked to return every three months for testing, and only those who returned at least once were included in the study. Drug and HIV counseling were provided to all participants, and all received one 'treatment cycle' of methadone (Unlike the United States, in Italy methadone tends to be used for limited periods, usually to prevent withdrawal.). The daily dose for HIV seronegative patients ranged from 0 to 74 mg., and for HIV seropositive patients the dose ranged from 0 to 40 mg. Time spent out of treatment in the last 12 months was greater for HIV seropositive patients (median = 365 days, range 12–365) than for HIV seronegative patients (median = 292 days, range 0–365). Participants were followed for 12 months and underwent a mean of 3.4 (seroconverters) and 3.6 (controls) tests. The median time interval between the last negative and first positive test was 6.8 months. All methadone treatment variables were significantly associated with HIV infection (treatment cycles, daily dose, and time out of treatment). Duration of treatment and methadone dose predicted a protective effect of methadone treatment: For every 3 months spent out of treatment the risk of acquiring HIV infection increased by 70%, and the higher the dose of methadone used, the lower the risk of HIV infection. This study strongly supports the hypothesis that methadone treatment, even when used in periodic detoxification rather than maintenance, can prevent HIV infection.

Moss et al. (1994) conducted an observational, longitudinal study to examine seroconversion rates, risk factors for seroconversion, and changes in risk behaviors over time in IDUs in San Francisco from 1985 to 1990. They identified 'repeaters' in MMT and 21-day methadone detoxification programs — individuals who were seronegative at their first visit to treatment and were seen at least twice at some such agency. Six hundred and eighty-one heterosexual IDUs were seronegative at first visit. HIV testing was conducted at nine MMT and methadone detoxification programs in San Francisco, with the majority of the samples recruited from MMT programs. Twenty-two of the 681 patients seroconverted (an estimated annual seroconversion rate of 1.9% per person year), and the conversion rate was significantly higher in African–Americans. When the authors examined separate 20-month time periods, seroconversion rates were 3.9% in the first period, 1.2% in the second, and 1.9% in the third (not a significant increase). Conversion rates were lower for those in MMT (1.4%) than for those in detoxification (3.1%). In addition, a lifetime history of more than 1 year in MMT programs was identified as a major protective factor against HIV seroconversion. Shorter times in MMT were less protective. This study provides evidence for the protective factor of MMT and, further, that MMT appears to provide superior protection over detoxification.

Most recently Hartel and Schoenbaum (1998) conducted a study examining the protective role of MMT in preventing HIV infection in IDUs in the Bronx, New York. Participants were patients at the Montefiore Medical Center Methadone Treatment Program from 1985 to 1988. Patients were interviewed regarding their HIV risk behaviors, tested for HIV, and given urine screens for the subsequent 3 months, and historical information dating back to 1979 was obtained from clinic chart reviews. The overall HIV seroprevalence was 43%, with those patients on the highest doses of methadone (>80 mg/day) having the lowest prevalence. In addition, the relationship between methadone dose and HIV differed by treatment year. That is, among patients entering treatment in 1985 or later, there was a 53% prevalence rate, among patients ente-

ring treatment in 1980–1984, 44%, and among those entering treatment before or during 1979, 34%. Methadone doses of less than 80 mg/day were associated with HIV infection independent of other variables, including ethnicity, year of last cocaine injection, needle-sharing in galleries, income, and IDU sex partners. Counseling was unrelated to HIV infection. This study offers strong support for the protection against HIV infection provided by MMT. The data demonstrate that higher methadone dose and longer duration of involvement in MMT provide protection against HIV. However, the data is correlational and therefore cannot provide evidence for a causal role of MMT in protecting from HIV infection. Strengths of the study include the large number of patients for whom data was collected, the duration of the study, the use of historical information, and the urine drug screens conducted to verify reported use of both illicit drugs and methadone. This study is important because it provides specific information on what variables in MMT are important and provides suggestions for what treatment variables most greatly enhance the protective effects of MMT.

Overall, four of the six studies reviewed in this section provide firm evidence for the protective effect of MMT against HIV seroconversion. These findings are more convincing because they are based on biologically verified outcomes, rather than participant self-report which was problematic for the studies in Sections 1 and 2. Several of the studies have shown a protective effect for MMT even after controlling for demographic and drug use variables.

Even the most compelling studies of this section, however, have methodological problems. For example, nearly all the studies are inherently limited by a self-selected treatment sample. That is, the factors that enable some individuals to remain in MMT for an extended time may also allow them to better protect themselves from HIV infection — regardless of the treatment program with which they are involved. In most of the studies, the in-treatment and out-of-treatment groups differ on demographics, suggesting there may be other unidentified differences in these groups that may account for the differences found in HIV seroconversion. The Serpelloni et al. (1994) study, however, addresses this problem by using matched controls, and thereby provides more compelling evidence.

Several aspects of MMT were identified as important in providing this beneficial effect, including MMT versus detoxification, treatment duration, and methadone dose. The Moss et al. (1994) study suggested that MMT provides more benefit than does methadone detoxification. This study was also consistent with Metzger et al. (1993), Serpelloni et al. (1994) in identifying that shorter time spent in treatment was less protective. The findings regarding methadone dose are less clear. For example, although Serpelloni et al. (1994) found that higher doses were related to lower HIV infection risk, the Williams et al. (1992) study found only a nonsignificant trend for lower HIV seroconversion, while dispensing a relatively high mean dose of 70 mg. The issue of optimal methadone dose and other clinic variables (e.g. adjunctive counseling, medical care) need to be further investigated to clarify what factors contribute to lower HIV seroprevalence rates for MMT patients.

The findings from this section are consistent with the other two sections in implicating the strongest protective factor for MMT. Indeed, in this section the only empirical studies we were able to identify were for methadone treatment. This section, however, is also the one in which the fewest studies exist to demonstrate the important relationship between substance abuse treatment and HIV. These studies had relatively small samples and either short follow-up periods or high attrition rates. Studies with larger sample sizes, longer follow-up periods, and other treatment modalities are needed to clarify this important, yet complicated relationship between substance abuse treatment and HIV seroconversion.

3. Conclusions

This review has identified 33 studies, with an aggregate of 17,771 subjects, published in peer-reviewed journals from 1988 to 1999. Twenty-eight of the 33 studies included MMT as a treatment modality, usually the only treatment modality, and 26 of the 28 studies showed positive results in reducing HIV infection and risk behaviors, including four studies of HIV seroconversion. In our opinion, the accumulated research provides sufficient evidence to conclude that MMT is a powerful tool to protect IDUs against HIV seroconversion.

3.1. Modality predominantly methadone maintenance

What the field knows about the protective effect of drug abuse treatment against HIV infection is largely based on studies in MMT. There has been very little published on other kinds of treatments (e.g. therapeutic communities, traditional outpatient, or day treatment programs). The largest of these studies, DATOS, interviewed over 2200 patients in long- and short-term residential and outpatient drug-free programs and provides strong evidence that these treatment modalities prevent HIV infection, but the study did not have a comparison group, relied on subjects' self-report, and did not assess actual HIV serostatus.

Why has so little research been published with these other modalities when the HIV/AIDS epidemic has been identified for nearly 20 years? The authors believe one contributor is the perception the MMT is more

likely to produce measureable results. Studies that occur in MMT programs seem likely to find HIV prevention effects because: (1) virtually all patients are engaging in high-risk needle-use before they enter treatment; (2) the treatment directly affects high-risk needle-use; and (3) the treatment lasts long enough to have a measurable impact not only on high-risk behaviors but also on HIV seroconversion. In addition, MMT programs have a history of being more research-involved than other modalities such as therapeutic communities. Methadone treatment programs developed from ground-breaking research at a New York medical center (Dole and Nyswander, 1965). Therapeutic communities and outpatient drug-free programs, on the other hand, developed outside the traditional medical and scientific community (Lamb et al., 1998). These programs may be less involved with research because they did not develop from a research-oriented background. The research that occurs there may require more pre-study negotiations, be more high-risk for an investigator, and perhaps be less likely to be published in peer-reviewed journals because of these administrative factors rather than because the modalities are less effective in preventing HIV infection.

Because of these factors it is not surprising that the first generation of studies on the impact of drug abuse treatment on preventing HIV/AIDS were dominated by studies in MMT. There are additional research questions to be answered, such as the impact of MMT in preventing HIV infection in geographic areas with different HIV seroprevalence, patterns of needle-use, and availability of drug abuse treatment. There is a compelling need, however, for the next generation of studies to occur in outpatient drug-free and therapeutic community treatments, to understand the effect that these programs may have in preventing HIV/AIDS.

3.2. Complex relationships among background and outcome variables

In this review we identified the gender, ethnicity, and age of participants and any findings regarding differential risks or impact when these factors were described in the published reports. Men comprise the vast majority of study participants, and the evidence is mixed as to whether gender mediates the effectiveness of drug abuse treatment in preventing HIV/AIDS. Studies have reported that women are more likely to engage in high-risk drug use (e.g. Camacho et al., 1996), more likely to be in continuous MMT (Williams et al., 1992), and reduce risk behaviors less than men (e.g. Camacho et al., 1996). The larger problem is that few studies have assessed women's AIDS risk in drug abuse treatment programs, and there is a strong need for studies with enough women to detect gender effects.

The sample was remarkably diverse in ethnicity. There was indication of African–Americans being less likely to be in drug abuse treatment (e.g. Metzger et al., 1993) and more likely to be HIV seropositive (Moss et al., 1994), yet there was no indication that treatment was differentially effective in affecting AIDS risk behaviors among separate ethnic groups. This perception is congruent with the research literature, which has shown that, although it is important to provide culturally sensitive drug abuse treatments (Perez-Arce et al., 1993; Finn, 1994), the relationship between ethnicity and treatment outcome is extraordinary complex, and ethnicity has not been a consistent predictor of patients' responsiveness to drug abuse treatment (John et al., 1997). Given that African–Americans and Hispanics have been affected disproportionately by HIV/AIDS, it is imperative that future research examine more closely the interplay between ethnicity and HIV infection.

Age may also be a significant variable influencing the effectiveness of drug abuse treatment in preventing HIV infection. Because the research has predominantly occurred in MMT programs, most of the participants studied have been middle-aged adults, with ages in the 30–49 year range. Several studies found that patients in MMT were older than those out of treatment (Klee et al., 1991; Longshore et al., 1994; Stark et al., 1996). It is important that future research examine a broader band of participants in both age and gender and that studies examine the interaction between background variables and treatment outcome.

3.3. Lowering drug use or sexual risk behaviors

In general, the studies with the stronger methodology — comparing treatment groups with other samples — have found more effectiveness for changing drug use than sexual risk behaviors. In this review both longitudinal studies of in-treatment samples (Section 2.2) and studies comparing treatment patients with other samples (Section 2.3) found very strong evidence that drug abuse treatment decreases the risk of HIV infection by decreasing needle-use. The evidence is less strong, but still substantial, that drug abuse treatment changes the needle-use patterns of participants (e.g. less needle-sharing, more use of sterile needles). Results of longitudinal studies described in Section 2.2 are more supportive than the comparative studies reviewed in Section 2.3 that drug abuse treatment decreases the risk of HIV infection by decreasing participants' incidence of risky sexual behaviors or increasing the use of condoms or safe-sex methods. Clearly, more research is warranted on the impact of drug abuse treatment on sexual behavior.

3.4. Methodological weaknesses of research

The studies to date have several methodological weaknesses, including reliance on self-report, high dropout rates that may eliminate the most high-risk patients, and the observation of considerable inter-program variability. First, most studies relied on participant self-report of undesirable behaviors (e.g prostitution, multiple sex partners, needle-sharing, injection drug use). Reliance on self-report presents problems based on both accuracy of participant recall and social desirability, which may limit the reliability and validity of data. Some studies (e.g. Calsyn et al., 1991) ensured that interviews were conducted by research (not clinical) staff at the treatment programs to increase the reliability of participant self-report. Having participants report to a computer rather than to a person is another option, and there is some evidence that computer-assisted self-interviews may lead to more open reporting of HIV risk behaviors (Des Jarlais et al., 1999). The alternatives to self-report are generally less sensitive, or they measure the behaviors of interest less directly. Alternatives to self-report include such measures as the account of significant others regarding sexual or needle-use behavior, physiological measures of alternative markers such as incidence of hepatitis B infection as a proxy for needle-use, or institutional records (such as arrests for prostitution). Other studies did include urine toxicology screens to corroborate self-reported drug use status (e.g. Bellis, 1993; Gottheil et al., 1993), although some indicated that patients were not observed consistently during this procedure (e.g. Bellis, 1993). Urinalysis results, however, are usually sensitive to drug use only in the last several days, while the period of interest in these studies is generally much longer. Others addressed participant accuracy of self-report by limiting the time period in which they were asked to reflect (e.g. only the past 90 days) (Avins et al., 1997). The study of Greenfield et al. (1995) raises serious questions about the validity of self-reported reductions in high-risk drug use and indicates the importance of using biological indicators of HIV risk behavior (such as urinalysis) whenever possible. At minimum, future studies should include biological tests to corroborate self-reported drug use and HIV status to enhance validity.

The studies in the present review often had high dropout and attrition rates. This is problematic because typically the most high-risk patients are the ones lost at follow-up periods (e.g. Saxon et al., 1994). In the Bellis (1993) study only 25 of the 41 women initially recruited into treatment remained after one year, but there were no analyses reported to determine if the 16 women lost to follow up significantly differed from the rest of the sample. Nine of the 16 were incarcerated during the follow-up period, which the authors state meant they had less opportunity to engage in high-risk behaviors. The fact that such a significant portion of these women were incarcerated may indicate they were overall higher-risk participants. A small number of studies, however, conducted analyses comparing those lost with those who were followed-up and found that the samples did not differ on significant variables. For example, Shore et al. (1996) found that those lost to follow up differed only on age (study participants were older). Still, this is a critical issue for future studies to address carefully.

A few of the studies identified intra-modality variation in MMT programs by clinic. Indeed, Ball et al., (1988) claimed that program characteristics predicted outcome better than patient characteristics. It is not surprising that treatment was most effective when methadone dosing was administered at recommended levels, there was a low rate of staff turnover, and patient attendance was consistent (although the fact that there were only six programs in the study limits the conclusions that can be drawn). Most studies found that longer retention in treatment was associated with better outcomes (Ball et al., 1988; Williams et al., 1992; Gottheil et al., 1993; Longshore et al., 1994; Saxon et al., 1994; Shore et al., 1996), and the remaining question is what treatment factors contribute to consistent patient attendance. New models are being developed for the delivery of drug treatment in combination with medical services (see O'Connor and Selwyn, 1997). These emerging treatment models highlight the need for future studies to examine both treatment program variables and patient variables that increase treatment retention and decrease HIV risk.

3.5. Limitations of the current methodology

This review no doubt missed important studies by virtue of its search criteria. Studies were not included that were published in journals not indexed in the databases searched, indexed under different topic areas, reports published in books, government reports, letters to the editor, unpublished work, articles in databases like *Current Contents* that may reach more popular-press types of publication outlets, and studies published after 1998. Nevertheless the number of articles reviewed here is larger than in comparable reviews by Des Jarlais et al. (1990), Metzger et al. (1998). It is our belief that, though not inclusive of the entire literature on the topic, these articles fairly represent the state of knowledge about the topic area.

Likewise this review did not conduct a meta-analysis, which would require reducing the diverse reports to a common scale (Bailar, 1997). A meta-analysis is being conducted on the overall effectiveness of drug abuse treatment programs (Prendergast et al., 1998), and the field soon may be ready for a meta-analysis addressing

some of the complex issues that remain, such as the influence of gender and ethnicity on the response to the effects of methadone maintenance treatment.

Despite these limitations, the literature reviewed here offers extremely powerful evidence that MMT prevents HIV infection. The evidence for other treatment modalities is consistent with the same conclusion, but more research is needed to provide policy makers with unambiguous evidence on which to make decisions about allocating resources.

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