Human Immunodeficiency Virus Prevention and the Potential of Drug Abuse Treatment

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Since first recognition of the scope of the acquired immunodeficiency syndrome epidemic among the drug-using community, substance abuse treatment has been viewed as playing an important role in preventing new infections. In the past 20 years, many studies have documented significantly lower rates of drug use, drug-related risk behaviors, and human immunodeficiency virus (HIV) infections among drug users who remain in treatment programs. There is also growing evidence that drug detoxification alone is insufficient to provide protection from HIV infection. These findings have important implications for users of cocaine and noninjection drugs, as well as heroin injectors. Despite strong evidence of effectiveness and widespread support for the important public health role of drug treatment, its impact has been compromised by limited availability and acceptability. The available data clearly establish drug abuse treatment as HIV prevention, yet without expansion of existing treatment programs and the continued development of treatments for addiction to cocaine and other widely used stimulants, its public health potential cannot be realized.

The AIDS epidemic among injection drug users (IDUs) in the United States was first recognized in the early 1980s. Since then a variety of prevention interventions have been targeted at IDUs [1–3]. No intervention, however, has been as widely endorsed as substance abuse treatment [4–7].

Here we review the research that has examined the relationship between treatment participation and HIV risk reduction. Of importance, most of the published research has evaluated the impact of methadone treatment, a modality that serves opiate-dependent drug users. During the first 15 years of the AIDS epidemic, the majority of IDUs at risk for HIV infection injected heroin or combinations of heroin and cocaine. As a consequence, most studies have focused on heroin injectors and their predominant treatment modality, methadone treatment.

There is now a growing body of evidence supporting the fact that sexual transmission (both heterosexual and between men who have sex with men) among both IDUs and users of noninjection drugs plays a significant role in fueling the spread of HIV infection, particularly among women [8]. Still, only a few studies to date have evaluated treatments for users of noninjection drugs and the impact of that treatment on sexual risk [9]. Although injection drug use may be seen as characterizing responses to the epidemic among drug users during the past 20 years, sexual risks associated with drug use may well define the prevention research agenda of the future.

REDUCTION IN DRUG USE AND TREATMENT PARTICIPATION

In considering the role of drug treatment as prevention for HIV infection, some fundamental questions regarding treatment effectiveness are raised. The most important of these is: “Does treatment work?” The association between treatment participation and reductions in frequency of drug use has been repeatedly documented in the literature [10–12]. Perhaps the most consistent finding has been the association between par-
participation in a methadone treatment program and lower rates of injection. For example, in a classic study by Ball and colleagues [13, 14], 506 male patients were recruited from 6 methadone maintenance treatment programs in New York City, Philadelphia, and Baltimore. The impact of treatment on injection frequency was dramatic—71% of the subjects did not inject during the month prior to treatment, and 60% had no injections during the prior year. Equally dramatic was the rapid return to injection drug use among those who left treatment programs. More than 80% of those who left treatment programs returned to injecting drugs within 12 months.

Similar reductions in drug use were observed among 2973 out-of-treatment drug users recruited in 15 cities in the United States as part of the National Institute on Drug Abuse’s cooperative agreement studies [15]. Once enrolled, all subjects were assessed and randomly assigned to either a 2-session standard intervention of HIV testing and counseling or an enhanced intervention offering additional risk reduction counseling and service referrals. The study provided the opportunity to compare changes in drug use among those from both study groups who had entered drug treatment between the baseline and six month assessments. Compared with those who had not entered treatment during the 6-month follow-up interval, subjects who continued to receive treatment for ≥90 days (n = 250) reported significantly lower rates of injection of heroin, cocaine, and “speedball” (a mixture of cocaine and heroin) and crack cocaine use. Additionally, they were 3 times more likely to have stopped drug use and nearly 4 times more likely to provide a urine specimen in which no drugs were detected.

A number of large, multisite longitudinal studies of drug treatment have reached similar conclusions—drug use after treatment is significantly lower than drug use prior to treatment. In the most recent of these, the Drug Abuse Treatment Outcomes Study, 3000 randomly selected subjects were interviewed 1 year after leaving treatment [16]. Drug use was found to have been reduced (relative to pretreatment levels) by >50% for each of the 4 most common forms of treatment in the United States—outpatient drug-free programs, short-term inpatient programs, outpatient methadone programs, and long-term residential programs. Thus, there are substantial data to support the conclusion that drug users who participate in treatment significantly reduce their rate of drug use. Do these reductions in drug use lead to reduction in the risk behaviors that transmit HIV?

REDUCTIONS IN HIV TRANSMISSION RISK BEHAVIOR AND TREATMENT PARTICIPATION

In addition to reductions in the frequency of drug use, many studies have documented lower rates of HIV transmission risk behaviors among drug users who enter and remain in treatment programs. Most studies have examined IDUs in and out of methadone treatment programs, and most have reported on reductions in syringe sharing. For example, in a large community-based survey in Sydney, Australia, 1200 IDUs were interviewed regarding their injection practices and treatment participation [17]. Analyses of these data revealed 2 important findings. First, IDUs in methadone treatment programs were 50% less likely to report syringe sharing. Second, the protective effects of treatment disappeared when those who had stopped injecting were removed from the analyses. In-treatment drug users who continued to inject were as likely as those not in treatment to report syringe sharing, suggesting that it is the reduction in drug use that accounts for the protective effects of treatment.

These authors also summarized findings from 8 other studies that compared rates of syringe sharing of IDUs receiving methadone treatment with their untreated counterparts from the same communities [17]. These studies were conducted in Australia, Europe, and the United States between 1985 and 1995. With a single exception, these studies documented a significantly lower rate of syringe sharing among those in methadone treatment programs, one-third to one-half the rate of the out-of-treatment subjects.

Similar findings have been reported by a number of other investigators. Abdul-Quader et al. [18] found that both injection frequency and the practice of injecting in “shooting galleries” (i.e., in a place where IDUs gather to inject drugs—a common practice early in the epidemic that is associated with increased risk of HIV infection) were significantly reduced proportionate to the amount of time spent in a methadone maintenance treatment program.

Avants et al. [19] conducted a comprehensive examination of HIV risk among drug users participating in a clinical trial of 2 models of methadone treatment. Although there was no difference in outcomes between the 2 forms of treatment delivery, subjects in both groups showed significant declines in drug-related risk behaviors during the 6-month follow-up interval.

Gossop et al. [20] reported on the changes in HIV transmission risk behaviors between entry into a treatment program and a 1-year follow-up evaluation among subjects admitted to 54 programs (8 inpatient, 15 residential, 16 methadone maintenance, and 15 methadone reduction programs) in the United Kingdom. Of the clients, 753 (72% of the original sample) completed follow-up assessments 1 year after entering the treatment program. The results “...showed marked and statistically significant reductions in injection risk and sex risk behaviours among clients in both residential and methadone programmes” [20, p. 81]. Sharing of injection equipment dropped by two-thirds and condom use increased significantly in both treatment modalities.

Although most of the past work has been focused on IDUs and methadone treatment, there are now data emerging from
studies of noninjection drug use (e.g., crack smoking and alcohol abuse). These studies also suggest a strong association between treatment participation and reductions in risky sexual behaviors.

A study of change in HIV transmission risk behavior among 700 persons being treated for alcohol dependence was reported by Avins et al. [21]. Significant reductions in both sexual and drug-related risks were observed at follow-up. These included a 58% reduction in injection drug use, a 15% reduction in reports of multiple sex partners, a 26% reduction in the number of sex partners who were IDUs, and a 77% increase in the use of condoms with all secondary sex partners.

Shoptaw et al. [22] in Los Angeles found significant reductions in risk behaviors among 232 cocaine-abusing or cocaine-dependent persons who received up to 6 months of weekly drug counseling. Although no formal HIV prevention interventions were delivered, those who completed treatment showed significant decreases in sexual risk behavior, primarily the result of a reduction in the number of sex partners. Among subjects who demonstrated a treatment effect, significant reductions in cocaine use (as monitored by urinalysis) were accompanied by reduced rates of sexual risk behaviors.

In a study of 447 cocaine-dependent persons entering outpatient treatment for the first time, Gotheil et al. [23] found significant reductions in AIDS risk behaviors at the 9-month follow-up point. The reduction in risk behavior was directly related to reductions in drug use and not to the duration or type of treatment. The authors emphasize the importance of treatment participation as the salient factor and not merely retention in a program.

HIV INFECTION AND DRUG TREATMENT PARTICIPATION

In one of the very first reports on the use of antibody testing for HIV infection among high-risk populations, participation in a methadone treatment program was found to be associated with lower prevalence of HIV infection [24]. In this descriptive 1984 report, antibody test results from 86 IDUs in New York City found 75 (87%) to be infected, whereas <10% (n = 3) of the samples from 35 patients receiving methadone treatment tested positive. All of the patients receiving methadone had been undergoing treatment for >3 years and, according to the authors, had "greatly reduced" their injection drug use [24].

Novick et al. [25] reported on findings from testing stored samples of blood that had been collected from IDUs between 1978 and 1983. Of the 48 subjects who were undergoing methadone treatment, 23% (n = 11) tested positive for HIV. The prevalence rate of HIV infection was found to be 17% (n = 6) among those who had been receiving treatment for >5 years.

Of those not receiving methadone treatment, 47% (n = 25) tested positive for HIV.

Among 360 IDUs studied in 1988, Brown et al. [26] noted that prevalence of HIV infection inversely varied by length of time receiving methadone treatment. Patients who had been receiving treatment for <1 year were 1.5 times more likely to test positive for HIV than were those who had received treatment for ≥1 year. Although, overall, the rate of infection was highest among African American subjects, the relationship between prevalence and duration of treatment was consistent across racial groups.

In 1988, 58 IDUs who had been receiving methadone treatment in New York City for an average of 17 years were tested and found not to be infected with HIV. During the time they were being treated, the prevalence of HIV infection among IDUs in New York had risen to >50% [27]. Similarly, Blix and Gronbladh [28] examined the HIV infection rate among patients receiving methadone in Uppsala, Sweden, in 1984. Only 2 (3%) infected patients were found in the group of 67 patients who had been admitted to a methadone treatment program before 1979. Yet, during the time of this study, HIV prevalence rates among IDUs in the community had risen to 38%.

Moss et al. [29] conducted an observational study of HIV incidence among 681 patients receiving methadone who had been tested at least twice while undergoing treatment in San Francisco between 1985 and 1990. The authors examined the characteristics that best distinguished those patients who seroconverted from those who remained uninfected. In all, 22 seroconverters were identified, yielding an average annual seroconversion rate of 1.9%. More than 3 times the rate of infection was found among those with <1 year of treatment compared with those with ≥1 year of methadone maintenance treatment.

Consistent with these findings, a prospective seroincidence study of patients receiving methadone in New Haven, Connecticut, identified substantially lower rates of new infections among subjects with continuous treatment experiences [30]. An overall incidence of 2.8 per 100 person-years was found among 98 patients who were receiving or had received methadone treatment. Among the 56 subjects with continuous treatment, 1 subject became infected (0.7 per 100 person-years); among the 42 subjects with interrupted treatment, 8 became infected (4.3 per 100 person-years). Although these findings were consistent with prior studies, these differences were not significant given the small sample size and the differential follow-up among the 2 groups.

In a study nested within a prospective evaluation of 952 seronegative IDUs, 40 incident cases were matched to 40 subjects who remained seronegative [31]. In analyses directed at identifying differences between infected and uninfected subjects, duration of methadone treatment and methadone dosage
were both found to have dramatic protective effects. For every 3 months spent out of treatment, the risk of getting infected with HIV increased by 70%. Further, the higher the methadone dosage, the lower the risk of infection. In multivariate analyses, these variables remained the most salient characteristics in explaining differences between case and control subjects.

A prospective longitudinal study of HIV infection and transmission risk behaviors among drug users participating in and not participating in a treatment program was initiated in 1989 [32]. In this study, 152 IDUs were randomly selected from a methadone treatment program and 103 out-of-treatment IDUs were recruited by means of a chain referral technique. At entry into this study, 18% of the out-of-treatment subjects and 11% of the clients receiving methadone treatment tested positive for antibodies to HIV. After 18 months of study, 33% of the out-of-treatment cohort were infected, compared with 15% of the patients receiving methadone ($P < .01$). The incidence of new infection was strongly associated with lack of participation in a methadone treatment program. When incidence was examined in relation to whether the subjects remained in treatment, changed their treatment status, or remained out of treatment, dramatically different rates of incident HIV cases were observed. Those who remained out of treatment were nearly 6 times more likely to have become infected than were those who remained in treatment during the first 18 months of the study. Among those who remained in a methadone treatment program for the entire 18-month study period, 3.5% became infected. Among those who remained out of treatment, 22% became infected with HIV.

Friedman et al. [33] reported the results of analyses directed at examining the factors associated with seroconversion among 6882 IDUs who participated in the National AIDS Demonstration Research Projects and the AIDS Targeted Outreach Models projects. Subjects with at least 2 HIV tests were included in the analyses. The studies were conducted in 15 cities characterized as either high-prevalence (>20%) or low-prevalence (<8%) on the basis of baseline HIV infection rates. Having been in any drug treatment program during the follow-up interval was the only variable significantly "protective," and it was the only variable that reached significance in both high- and low-prevalence cities.

Data reported by Thiede et al. [34] provide additional evidence of the impact of treatment in reducing the frequency of injection and HIV transmission. Study participants ($n = 716$) were followed up for 12 months after entry into 4 methadone treatment programs in King County, Washington. Data comparing those who remained in a treatment program with those who left or interrupted their treatment program showed dramatic differences in the frequency of injection: of those who remained in a treatment program, injection frequency decreased by 80%; for those who left their treatment program, no differences were observed; and for those with interrupted treatment experiences, injection frequency decreased by 56%. Incidence of hepatitis B virus infection was 11% among those who left treatment compared with 4% for those with disrupted treatment and 3% for those who remained in treatment. Incidence of hepatitis C was 12% among those who left treatment, 10% among those with disrupted treatment, and 5% among those with continuous treatment.

**DISCUSSION**

As reviewed here, research studies conducted over the past 20 years have, with few exceptions, found associations between substance abuse treatments, reductions in HIV transmission risk behaviors, and increased protection from HIV infection. Collectively, these studies suggest that sustained treatment is associated with protection. Although it is important to remain cognizant of the diversity of substance abuse treatments and the various ways in which they are implemented and used by patients, the underlying mechanism of protection from HIV as supported by available data would appear to be rather simple. Persons who participate in effective treatment programs reduce their drug use. Lower rates of use lead to fewer instances of drug-related risk behavior. In turn, lower rates of drug-related risk behaviors result in fewer exposures to HIV and, consequently, fewer infections. Two comprehensive reviews of the literature on drug treatment as HIV prevention have arrived at essentially the same conclusions—that there is substantial and convincing evidence of the impact of drug treatment to alter patterns of use sufficiently to reduce risky behavior and infections with HIV [35, 36].

Although the mechanism through which effective treatments provide a protective effect is straightforward, there are many unanswered questions regarding the impact of such treatment. Clearly, further research is needed in all modalities to investigate the "active ingredients" of substance abuse treatment as well as the factors associated with treatment entry and retention. There is particular need to investigate treatments for noninjection cocaine use.

Perhaps the most available form of intervention for drug users globally is drug detoxification. On this point the literature is quite consistent: the impact of treatment on HIV infections has been observed only for those users who continue to receive treatment for significant amounts of time. Further, the literature suggests that the longer the duration of treatment, the greater the protective effects. Thus, brief detoxification at this point cannot be considered an effective strategy for HIV prevention unless it is followed by a longer course of treatment.

Although substance abuse treatment has been associated with
reductions in HIV transmission risk behaviors and infection, its public health impact has been limited by the fact that currently available drug treatments fail to meet the needs of many drug users, for a variety of reasons. Perhaps most important, access is severely limited. With a few notable exceptions, communities have not adequately funded treatment services. In some areas, in fact, funding for substance abuse treatment programs actually diminished during the course of the AIDS epidemic [9, 31]. In many areas of the world, waiting lists for eligible persons seeking treatment are a reality. In other areas, treatments are simply not available. The problems are particularly profound for those dependent on publicly funded services or those in areas where public policy restricts certain modalities of treatment, such as Russia, where agonist treatments (e.g., methadone and buprenorphine) for drug use are prohibited. It is likely no coincidence that these areas include drug users most at risk for HIV infection. Currently, drug treatment systems serve only a small proportion of the drug-using community. It is estimated that 5 of 6 drug users are not in treatment at any given point in time [9, 37]. Increasing the capacity and acceptability of drug treatment systems represents a critical public health challenge and an area of importance for future research.

References


