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Pilot Study to Enhance HIV Care Using Needle Exchange–Based Health Services for Out-of-Treatment Injecting Drug Users

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ABSTRACT *The introduction of highly active antiretroviral therapy (HAART) has resulted in marked reductions in mortality and acquired immunodeficiency syndrome (AIDS) incidence across all risk groups; however, the proportionate decrease among injecting drug users (IDUs) has been less impressive. Much of the disparity in benefit to IDUs has been a consequence of decreased access to and receipt of potent antiretroviral combinations. Strategies to increase access to and utilization of HAART have included entry into drug treatment and abstinence. Unfortunately, as few as 15%–20% of active drug users in the United States, and in many other countries, are in drug treatment at any one time. We report a pilot project among out-of-drug treatment IDUs infected with human immunodeficiency virus (HIV); HIV therapy was successfully provided to active heroin injectors using the Community Health Care Van (CHCV) at sites of needle exchange. Subjects were willing to initiate, but were not receiving, recommended HIV therapy and were not interested in formal drug treatment. Antiretroviral therapy regimens were selected and linked to heroin injection timing. Weekly visits were scheduled by CHCV staff to assess adverse side effects and encourage adherence. Of the 13 participants, the mean baseline HIV-1 RNA level and CD4 lymphocyte count were 162,369 (log 5.21) copies per milliliter and 265 cells per milliliter, respectively. By 6 months, the proportion whose HIV-1 RNA was below the limits of detection (<400 copies/mL) was 85% (N = 11); 77% (N = 10) had nondetectable levels by 9 months. By 12 months, 54% (N = 7) had a persistently nondetectable viral load, and the net increase in CD4 lymphocyte count was 150 cells per milliliter. As an additional and unintended benefit of this pilot project, 9 (69%) subjects chose to enter drug treatment after achieving a nondetectable viral load. Entry into drug treatment was associated with durability of viral suppression. This small pilot study suggests that health services based on needle exchange may enhance access to HAART among out-of-treatment HIV-infected IDUs. In addition, it demonstrates that this population can benefit from this therapy with the support of a nontraditional, community-based health intervention.*

KEYWORDS *Adherence, Antiretroviral therapy, Directly observed therapy, Health care, Injecting drug users, Intervention, HIV/AIDS, HIV therapeutics, Needle exchange, Substance abuse, Substance abuse treatment.*

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BACKGROUND AND SIGNIFICANCE

Morbidity and mortality from human immunodeficiency virus (HIV) disease have declined markedly as a result of advances of HIV therapy.[1] However, injection drug users (IDUs) have not shared equally in these benefits and advances. Initially, white men derived the greatest benefit from antiretroviral therapy (ART)[2]; only recently have IDUs begun to benefit similarly.[3] Much of the decreased benefit of HIV therapeutics among IDUs stems from both perceived and real inadequate access to and utilization of HIV care.[4] Injecting drug users often have multiple and often-unmet complex needs, including overlapping comorbid medical, psychiatric, and social problems. In addition, provision of clinical care for drug users with HIV disease is often difficult. Moreover, IDUs have increased difficulties with adherence to medications.[5–11]

Recent studies in the United States[12] and Canada[13] indicate that, among drug users who are clinically eligible for antiretroviral therapy, as few as 40% to 50% actually received it, and only 14% received potent combination therapy involving a protease inhibitor. In the US study, having a usual source of care, a consistent provider, and recent outpatient visits were associated with receiving combination therapies, including a protease inhibitor. In both studies, active drug use and not being in drug treatment were strongly correlated with not receiving antiretroviral therapy.

These studies clearly point out that barriers to proper HIV care remain for injection drug users, particularly for those actively using drugs, regardless of site and system. They also offer insight into some of the issues impeding availability and use of HIV therapies and their solution. The chaotic lifestyle of drug users often makes use of existing facilities difficult and erratic.[14] The rigid structure of HIV care facilities is often not conducive for participation by active drug users. Drug users often are mistrustful of the health care system and harbor expectations that they will be treated punitively. Thus, the development of strategies that seek to address active drug use, HIV care, and their comorbid conditions are urgently needed.

Successful models of HIV care for IDUs have been developed within drug treatment programs[15–17]and correctional settings.[18–20] The overwhelming majority of IDUs are active drug users who may cycle into and out of such structured settings. Therefore, settings for providing HIV-related health care to out-of-treatment drug users are critical so that they may derive the same benefit as drug users in structured settings.

One underutilized place to access many of these most medically marginalized and needy individuals is within the context of needle-exchange programs (NEPs), used on a continuing basis by active drug users. We developed the first street-based needle exchange–linked health care program in the United States. We describe the results of a pilot project designed to provide HIV therapy to active IDUs through this program.

METHODS

The Community Health Care Van (CHCV), a 36-foot mobile clinic with two examination and one counseling room, began services in 1993 and travels to five distinct neighborhoods within New Haven, Connecticut, in tandem with the New Haven Needle Exchange Program. The New Haven NEP provides clean syringes and para-

phernalia to approximately 250–300 unique clients monthly. The CHCV provides HIV counseling, case management, drug treatment coordination, health status assessment, and acute and episodic medical care. Linkage to medical care is also provided for clients.

All clinical and counseling services are provided at sites of needle exchange; however, services are not restricted to drug users. A clinician, a drug treatment coordinator, outreach workers, and an HIV counselor and various volunteers staff the CHCV.[21] The van is also used to mentor medical residents and nurse practitioner and physician assistant students during their urban health elective.[22] All CHCV services are provided free of charge, including provision of donated medication samples.

During this pilot project, HIV therapy was offered to CHCV clients who met the following criteria: (1) confirmed HIV status; (2) active use of heroin; (3) eligibility for antiretroviral therapy according to nationally recognized therapeutic guidelines (CD4 < 500 lymphocytes/mL or HIV-1 RNA > 20,000 copies/mL using the Roche Amplicor® assay)[23]; (4) willingness to initiate highly active antiretroviral therapy (HAART); and (5) have weekly visits made by CHCV staff.

Patients seen at the CHCV were informed about the program, but were not recruited to participate. Individuals who already had a site of clinical care but who were not receiving recommended therapy were required to sign a release of medical information. The CHCV clinician contacted community clinical providers and negotiated a comanagement arrangement for patients participating in the pilot program. All laboratory and clinical information was shared between the community and CHCV providers.

Each patient who participated underwent a routine and comprehensive clinical assessment of drug use patterns and past medical care. Health beliefs were explored as part of this process. In particular, the belief that coadministration of drugs of abuse and HIV medications results in adverse consequences was explored.[18] An antiretroviral regimen was decided based on three factors: (1) past experience with HIV medications, (2) expressed concerns over side effects and pill burden, and (3) number of heroin injections per day.

A unique regimen was tailored for each participant after completing the clinical assessment. The discussion and selection of a regimen occurred over a period of 2 to 4 weeks. Heroin injection was identified as the most consistent activity in their daily schedule, and the dosing of HIV medications was thus used as a reminder for taking HIV medications; most subjects identified injecting heroin two or three times per day. Thus, for those who injected three times per day, a thrice-daily antiretroviral combination was prescribed and linked to heroin use.

All patients considered for didanosine were provided a placebo "taste test" that involved either chewing or dissolving a placebo form of the medication to ensure palatability. All patients prescribed medications likely to cause gastrointestinal side effects were provided with antiemetics or antidiarrheals and were instructed in their use prior to starting their antiretroviral combination.

Patients were scheduled to be seen weekly by CHCV staff to address issues of side effects and adherence with medication. This visit was scheduled on the CHCV at a site proximate to patient residence. Most of the participants who opted to receive their HIV care on the CHCV lived in a single room occupancy (SRO) building close to an NEP stop. In some cases, an outreach CHCV clinical team would make a "home visit" to the SRO.

HIV-1 RNA determinations were obtained at baseline and at months 1, 3, 6,

9, and 12. CD4 lymphocyte counts were obtained at baseline and at months 3, 6, 9 and 12. Other routine laboratory measurements were obtained as clinically indicated. Laboratory measurement was geared to predetermined time intervals within a given time period, but a 2-week interval before or after was considered acceptable (total 4-week latitude). In some cases, laboratory measurements were obtained from local HIV clinics or correctional facilities, depending on where the patient had been evaluated. The Yale University Institutional Review Board approved the project as part of continuing care on the CHCV.

RESULTS

We screened 15 HIV-infected IDUs for enrollment in the pilot project. Two were ineligible because they did not meet clinical criteria for initiating HAART. The 13 individuals who met eligibility criteria were enrolled and initiated antiretroviral therapy between August and October 1997. All subjects expressed an initial concern about "mixing" heroin and HIV medications because it either would make them "sicker" or would "eat up" their methadone.

Despite these baseline beliefs, all subjects completed a 12-month course of therapy and had clinical measurements available. The baseline characteristics are depicted in Table 1. Seven of the patients were women, three were Hispanic, five were black, and five were white. The mean baseline CD4 lymphocyte count was 265 lymphocytes per milliliter (range 20 to 450 lymphocytes/mL) and the mean HIV-1 RNA level was 162,369 copies per milliliter (log 5.21). Six patients were naive to antiretroviral therapy, while six had been on combination ART; one had only been on stavudine monotherapy.

Table 2 depicts the prior and newly prescribed antiretroviral regimens for each patient as well as their clinical response from baseline at months 3, 6, 9, and 12. Figures 1 and 2 demonstrate the mean increase in CD4 lymphocyte count and mean change in HIV-1 RNA levels over the course of clinical supervision. By 12 months, the mean CD4 lymphocyte count progressively increased to 416 cells per milliliter; this represents an increase of 150 cells per milliliter from baseline. At 6 months,

TABLE 1. Baseline characteristics of study participants

Characteristic	N = 13
Mean age, years	40.3 (34–48)
Gender	
Male	6
Feale	7
Race	
Black	5
Hispanic	3
White	5
Mean CD4 lymphocyte count	265
Mean HIV-1 RNA (copies/mL)	162,369
Mean HIV-1 RNA (log 10)	5.21
Antiretroviral experienced	7

HIV-1, human immunodeficiency virus type 1.

TABLE 2. CD4 lymphocyte and human immunodeficiency type 1 (HIV-1) RNA level changes from baseline over time

Subject	Prior ART experience	New ART regimen	Baseline CD4 count	Baseline Log HIV-1 RNA	3 Months CD4 count	3 Months Log HIV-1 RNA	6 Months CD4 count	6 Months Log HIV-1 RNA	9 Months CD4 count	9 Months Log HIV-1 RNA	12 Months CD4 count	12 Months Log HIV-1 RNA	Month entered drug treatment
1	D4T	CBV, NFV	445	4.36	485	<2.6	505	<2.6	498	<2.6	514	<2.6	6
2	ZDV, DDC	D4T, 3TC, NVP	450	4.43	520	<2.6	546	<2.6	514	<2.6	576	<2.6	5
3	ZDV, D4T	D4T, 3TC, NFV	360	4.65	418	<2.6	422	<2.6	436	<2.6	458	<2.6	4
4	ZDV, 3TC	D4T, 3TC, RTV, SQV	20	5.74	170	3.02	224	2.61	264	<2.6	288	<2.6	7
5	ZDV, 3TC	D4T, 3TC, NFV	310	4.79	362	<2.6	316	<2.6	383	<2.6	405	<2.6	No entry
6	ZDV, 3TC	D4T, 3TC, NFV	210	5.24	305	<2.6	320	<2.6	342	<2.6	338	3.65	No entry
7	D4T, 3TC	ZDV, DDC, IDV*	160	5.11	245	<2.6	270	<2.6	310	<2.6	346	3.32	5
8	Naive	CBV, RTV, SQV	90	5.50	225	2.99	266	<2.6	258	<2.6	272	4.74	No entry
9	Naive	DDI, D4T, NFV	280	4.76	412	<2.6	447	<2.6	470	3.17	482	4.39	7
10	Naive	DDI, D4T, NFV	420	5.09	510	<2.6	568	<2.6	543	3.36	538	5.05	No entry
11	Naive	DDI, D4T, NFV	160	5.40	310	2.67	430	<2.6	467	<2.6	410	4.26	7
12	Naive	DDI, D4T, NFV	355	4.59	398	<2.6	465	<2.6	428	<2.6	455	<2.6	4
13	Naive	D4T, 3TC, NFV	190	5.50	254	3.16	278	3.03	304	3.00	320	<2.6	8

ART, antiretroviral therapy; CBV = combivir (=zidovudine 300 mg + lamivudine 150 mg); DDC = zalcitabine; DDI = didanosine (dosed once daily); D4T = stavudine; IDV = indinavir; NVP = nevirapine; NFV = nelfinavir (dosed 1250 mg twice daily); RTV = ritonavir (dosed 400 mg twice daily); SQV = saquinavir (dosed 400 mg twice daily); 3TC = lamivudine; ZDV = zidovudine.

*Regimen dosed three times per day.

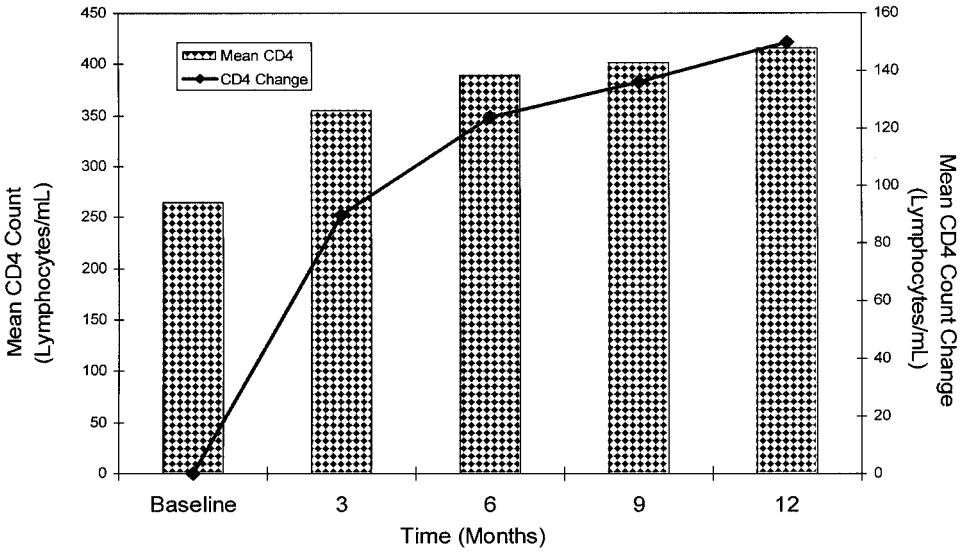

FIGURE 1. Mean CD4 increases from baseline.

the mean HIV-1 RNA level decreased from 5.21 log before initiating HAART to 2.38 log, and 11 (84%) fell beneath the limit of detection. At 9 months, 10 (77%) subjects had an HIV-1 RNA level below the limit of detection, and at month 12, there were 7 (54%) subjects who had a nondetectable HIV-1 RNA level. Among

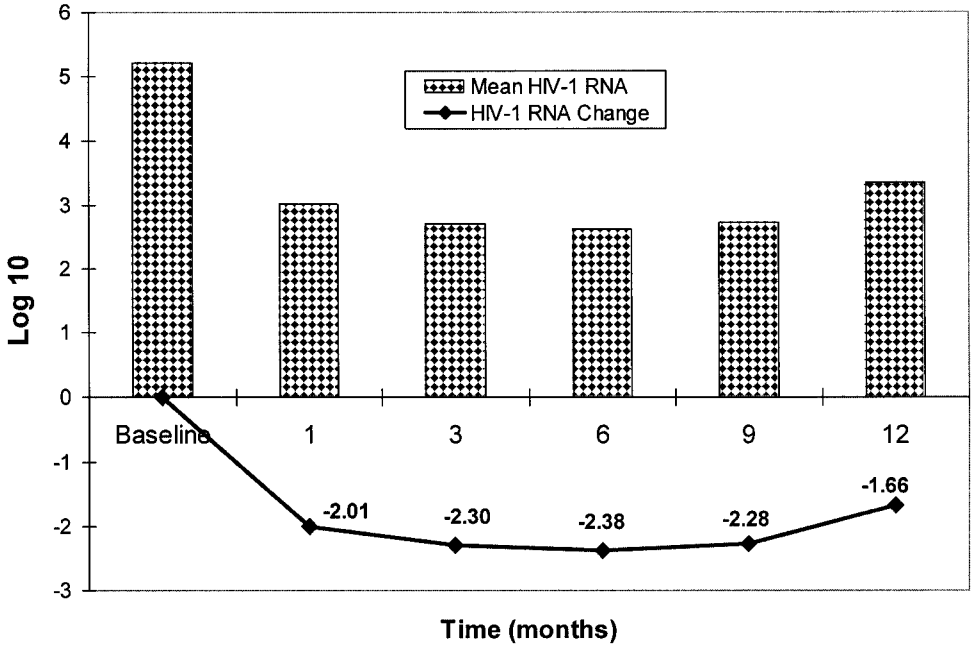

FIGURE 2. Mean human immunodeficiency virus type 1 (HIV-1) RNA changes from baseline.

the 7 antiretroviral-experienced patients, all achieved a nondetectable viral load by 9 months; 3 of 6 (50%) ART naive patients had successfully done so by 9 months ($P = .07$).

Of the 13 patients, 9 (69%) successfully entered drug treatment during the 12-month period of observation. Of the patients, 8 entered methadone maintenance, and 1 entered a long-term, residential, drug-free program. Entry into drug treatment was not immediate; it occurred at a mean of 5.9 months after initiating HAART. Each subject who entered drug treatment did so after achieving a nondetectable viral load. By month 12, 6 of 9 (67%) subjects who entered drug treatment had a nondetectable viral load compared to 1 of 4 (25%) individuals who did so among those who did not enter drug treatment ($P = .27$).

DISCUSSION

This small pilot study suggests that active drug users may benefit clinically from provision of potent combination therapy when such treatment is delivered in a nontraditional, community-based setting. While other studies have demonstrated the negative effect of alcohol[24] and illicit drugs on access to and adherence with ART,[25–33] this small pilot study suggests that gaining access to ART in a trusted setting may promote positive health behaviors (e.g., seeking and gaining access to drug treatment) and result in improved health outcomes among active drug users. In our study, the proportion of individuals who achieved an HIV-1 RNA level below the level of detection and an increase of the CD4 lymphocytes count is similar to results obtained in clinical trials in highly selected non-IDU patients.[34–36]

The results of our study are also similar to those obtained in correctional settings and noncorrectional settings with mandatory directly observed therapy (DOT) for HAART.[37–39] One recent study compared patients enrolled in clinical trials who received directly observed HIV therapy in a correctional setting to those in trials in community settings.[40] Results of this study showed that 80% of patients receiving DOT achieved a nondetectable viral load compared to 50% in the selected community-derived sample.[40] Rates of nondetectable viral load in patients receiving HAART in clinical care settings average[41–43] around 50%. While DOT has been demonstrated to provide a structural intervention for the treatment of tuberculosis,[1,44] limited feasibility has been demonstrated for the management of HIV outside highly structured correctional,[39,40] skilled nursing,[45] and methadone maintenance settings.[46]

Modified directly observed therapy (mDOT) has been suggested, but feasibility has yet to be demonstrated in community settings.[38,47] One such mDOT program in Providence, Rhode Island,[38] treated 37 patients with a twice-daily dosing regimen for a mean duration of 10 months. Of the 37 patients, 18 (49%) completed the program for a follow-up period of longer than 12 months. Furthermore, self-reported adherence of nonobserved administration doses reportedly improved, and they had a mean decrease in plasma viral load of 1.53 log 10 and a mean increase in CD4 cell count of 112 cells per milliliter.

Another pilot mDOT program was used to treat HIV-positive patients in Florida.[38] Of the 44 patients enrolled, 19 (43%) achieved a viral load less than 1000 copies per milliliter, and only 6 achieved a viral load less than 50 copies per milliliter. Most of the patients were antiretroviral experienced, and those with a lower mean CD4 count were likely to have a history of IDU.

There continues to be little information regarding DOT. However, DOT may

still provide the necessary structure needed by marginalized nonadherent populations, such as those who are actively using drugs.

In the present study, DOT was not provided, and adherence was not measured. However, the successful therapeutic results suggest adherence was high because the two are directly linked.[48–50] In fact, even more simplified structured settings than DOT have shown positive associations with improved adherence in such patients.[51,52] In a nonadherent group of 21 patients at the Miami Veterans Affairs Medical Center, of whom 50% had a history of IDU, simply providing structure by filling weekly pill organizers and focused medication adherence counseling was associated with increases in compliance with HIV medication refills and clinic appointments and with decreased hospitalizations.[51]

Recovering and active HIV-infected drug abusers rarely have such structured settings beyond case management services that attempt to link them to medical care and other necessary appointments. Combination antiretroviral therapy is difficult to adhere to due to the sometimes-high pill burden, side effects, and other comorbid infectious diseases, including tuberculosis and hepatitis C. Furthermore, adherence to HAART may be a low priority due to other factors, such as homelessness, unemployment, mental illness, and addiction.

Improving adherence to HAART for HIV-infected IDUs could be improved by using simpler regimens. Twice-daily therapies in incarcerated persons have even improved adherence and improved clinical outcomes, with improved HIV-1 viral load and CD4 lymphocyte counts.[37] True DOT will not likely be accomplished until once-daily regimens are truly available.[53] Approved once-a-day antiretrovirals now include didanosine, lamivudine, tenofovir, efavirenz, and the combination of amprenavir with low-dose ritonavir. Investigational drugs such as atazanavir and emtricitabine will add to this armamentarium.

Innovative and targeted solutions are needed to improve access to care, HIV therapies, and adherence to these therapies among out of treatment IDUs. These preliminary data suggest that health services based on needle exchange may be an important future mechanism to accomplish such goals. ART was linked to personal health beliefs, drug use, and an array of health and drug treatment services. Health beliefs regarding the mixing of ART and drugs of abuse have been associated with decreased perception of efficacy; however, these individuals were likely to overcome such perceptions through repeated encounters with a trusted group of professionals.[18]

It is not clear which components of the program have contributed most to its success. Use of CHCV services has demonstrated impressive use of prevention services[54] and a reduction in emergency room use by IDUs.[55] The repeated nonjudgmental contact with this group of marginalized and stigmatized active IDUs likely created mutual trust over time. Moreover, the individual was not required to maneuver through complex health care systems—the health care was conveniently available daily in the community. The CHCV expertise and comprehensive array of CHCV services, including expedited access to drug treatment, may have contributed to HIV treatment success as well.

Structural interventions, such as needle exchange, have been successful for HIV prevention efforts. Structural interventions for HIV care have been demonstrated for those engaged in drug treatment programs, particularly methadone maintenance programs. This pilot suggests that the consistency of needle exchange and interaction with clinical and outreach staff provided a combination of necessary components to maintain these individuals in care.

The proportion of patients with undetectable viral loads decreased between months 9 and 12. This is consistent with findings in clinical trials and clinical care; however, an important explanation in this particular series is likely. Successive police raids where many of the subjects lived disrupted fragile housing arrangements. This resulted in significant social destabilization for the inhabitants. As a consequence, many disappeared from the area and were temporarily lost from care on the CHCV. The secondary needs of positive health-related behaviors (i.e., taking medications) were subsumed by meeting primary needs such as food, shelter, and safety (from arrest).[56–58] Thus, this study must be seen as limited by and in the larger context of drug abuse social and personal needs and circumstance. Nevertheless, these results have important implications for the development of strategic community-based programs that address the complex medical needs of out-of-treatment IDUs with HIV disease. They also suggest that when services are organized in a way that is acceptable to drug users, they will utilize them and derive clinical benefit.

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