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Does Initiation of HIV Antiretroviral Therapy Influence Patterns of Syringe Lending Among Injection Drug Users?

Laura Kuyper[a], **M-J Milloy**[b,c], **Brandon D.L. Marshall**[b,c], **Ruth Zhang**[c], **Thomas Kerr**[a,c], **Julio S.G. Montaner**[a,c], and **Evan Wood**[a,c,*]

[a] Department of Medicine, University of British Columbia, Gordon and Leslie Diamond Health Care Centre, Room 10203 – 2775 Laurel Street, Vancouver, BC, V5Z 1M9, Canada

[b] School of Population and Public Health, University of British Columbia, 2206 East Mall, Vancouver, BC, V6T 1Z3, Canada

[c] British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6 Canada

Abstract

The delivery of antiretroviral therapy (ART) to injection drug users (IDU) may be influenced by provider concerns regarding the potential for increased HIV-related risk behavior following the initiation of HIV treatment. We evaluated whether ART initiation was associated with changes in syringe lending patterns among a long-term prospective cohort of HIV-positive IDU in Vancouver, Canada. Among 380 ART-naïve individuals eligible for this analysis, the median age was 34.2 (interquartile range [IQR] 27.7 – 40.8), 171 (45.0%) were female, and the median follow-up duration was 60 months (IQR = 18 – 113). Between May 1996 and April 2008, 260 (68.4%) participants initiated ART. In a generalized linear mixed-effects model which compared each individual's likelihood of sharing syringes prior to and following the initiation of ART, syringe lending was not significantly associated with ART initiation in unadjusted (odds ratio = 0.72, 95% CI: 0.38 – 1.36) or adjusted (odds ratio = 0.78, 95% CI: 0.42 – 1.45) analyses. Concerns regarding increased injection risk behaviors following the initiation of ART were not observed in this setting.

Keywords

injection drug use; antiretroviral therapy; syringe lending; HIV

1. INTRODUCTION

The medical management of HIV infection has seen dramatic advances over the last 15 years. Highly active antiretroviral therapy (ART), which became available in the mid-1990s, has been shown to suppress plasma HIV-1 RNA viral load to undetectable levels, raise plasma $CD4^+$ cell counts, and substantially reduce HIV-related morbidity and mortality (Palella et al., 1998). Specifically, since the advent of ART, life expectancy from the time of HIV seroconversion has risen from 10 years in 1996 to over 22 years in 2005 (Harrison et al., 2010). However, there remain challenges related to delivery of ART to populations among whom HIV continues to spread rapidly. Outside of sub-Saharan Africa, an estimated

*Send correspondence to: Evan Wood, MD, PhD, Director, Urban Health Research Initiative, BC Centre for Excellence in HIV/AIDS, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC, V6Z 1Y6, Canada, Tel: 604-806-9692, Fax: 604-806-9044, uhri-ew@cfenet.ubc.ca.

one-third of new HIV infections have been attributed to injection drug use, and in some areas, such as Eastern Europe and Central Asia, more than 80% of HIV cases occur among people who use injection drugs (IDU) (Joint United Nations Programme on HIV/AIDS, 2008).

The medical treatment of HIV-positive IDU presents several challenges that are unique to this population. For instance, IDU experience addiction and drug dependence, are often homeless, and may have concomitant psychiatric illness, among other social and structural barriers to optimal HIV medical care (Wood et al., 2008b). Further complicating issues of ART access, prior studies have raised concerns regarding possible increases in HIV-related risk behaviors among IDU following the initiation of ART. Although results have been inconsistent (Bouhnik et al., 2002; Marshall et al., 2010; Vlahov et al., 2001), there may be evidence for increased sexual risk-taking behaviors following initiation of ART. These findings are generally attributed to improved health status following ART initiation, which may allow for resumption of higher risk sexual behaviors previously diminished as a result of HIV-related morbidity and/or patients' assumption of decreased potential to transmit HIV while viral loads are suppressed by ART (Crepaz et al., 2004; Tun et al., 2004). Since both of these mechanisms may be relevant to increases in unsafe injecting behaviors, the present study was conducted to determine whether the initiation of ART was associated with increases in syringe lending among HIV-positive IDU participating in a long-term cohort study.

2. METHODS

2.1 Sampling Procedures and Cohort Description

Data for these analyses were derived from the AIDS Care Cohort to Evaluate Exposure to Survival Services (ACCESS), a prospective observational cohort of HIV-positive IDU in Vancouver, Canada. This cohort has been described in detail previously (Wood et al., 2004), and was populated through snowball sampling and extensive street outreach. Individuals were eligible for ACCESS if they were 18 years of age or older, HIV-positive, had injected drugs during the previous month, and provided written informed consent. For this analysis, the study sample was restricted to individuals who were ART-naïve at baseline and had measurements of HIV-1 RNA levels and $CD4^+$ cell counts within 12 months of the baseline interview. At baseline and at each six-month follow-up visit, participants completed an interviewer-administered questionnaire that explored sociodemographic characteristics, drug use patterns, and other relevant exposures. They also underwent examination by a study nurse.

The local setting is rather unusual, given the presence of a province-wide centralized ART dispensation program and laboratory for HIV/AIDS clinical monitoring. Thus, a complete prospective profile of all patient $CD4^+$ cell count determinations and plasma HIV-1 RNA levels, as well as a complete prospective profile of antiretroviral therapy use, was available for all cohort participants. These data included the date of therapy initiation, the specific antiretroviral agents prescribed including dose, as well as a validated measure of patient adherence derived from prescription refill compliance (Wood et al., 2008a; Wood et al., 2003). Also, in this setting, all medical care, including ART dispensation and HIV/AIDS monitoring, was provided free of charge to all HIV-positive individuals. This enables the examination of HIV-related outcomes largely free of selection bias stemming from financial barriers to health care and HIV treatment. The study was approved by the Providence Health Care/University of British Columbia Research Ethics Board. Plasma HIV-1 RNA levels were measured using the Roche Amplicor Monitor assay (Roche Molecular Systems, Mississauga, Canada).

2.2 Study Hypothesis

For HIV-positive individuals, initiation of ART commonly leads to suppression of viral load, restoration of immune function, and relief from the symptoms associated with HIV disease. Concern has been expressed that these improvements in health and functioning could lead to a greater possibility of risk behaviors for HIV transmission (Miller et al., 2000; Tun et al., 2004). We therefore hypothesized that the initiation of ART would predict an increased likelihood of syringe lending, independent of other possible confounding factors.

2.3 Variables of Interest

We sought to investigate the association between ART initiation and syringe lending. The primary outcome was defined as lending a used syringe to someone else during the previous six months. Given that not all participants injected throughout the entire study period, visits during which injecting was not reported were included in the analysis as non-syringe lending observations. The exact date of ART initiation was derived through the confidential database linkage described above. Since ART initiation may have occurred at any time during follow-up, and since individuals typically experience symptomatic benefits of ART only after some months of therapy, we incorporated a lag period into the primary explanatory variable to ensure that we measured self-reported syringe lending during the questionnaire that most closely reflected the six-month period following ART initiation. Therefore, “ART initiation” was coded as a dummy variable corresponding to the first follow-up completed at least six months after the exact date of initiating therapy.

We also considered secondary explanatory variables that could possibly confound the relationship between the outcome and initiating ART. These included: age; gender; ethnicity (Aboriginal vs. non-Aboriginal); homelessness (yes vs. no); frequent heroin injection (≥ daily vs. < daily); frequent cocaine injection (≥ daily vs. < daily); methadone maintenance therapy (yes vs. no); $CD4^+$ count (per 100 cells/mL increase); and HIV-1 RNA plasma viral load (per $\log_{10}$ increase). All behavioral variables referred to the six-month period prior to each study visit, with the exception of methadone use and homelessness, which referred to current status at the time of the interview.

2.4 Statistical Analyses

As a first step, we examined selected characteristics of the cohort at the baseline interview, stratified by ART initiation over follow-up. Next, we estimated the bivariate relationships between the outcome and all explanatory variables over the follow-up period. To estimate the independent relationship between initiating ART and lending used syringes, we constructed a generalized linear mixed-effects multivariate model. This modeling strategy examines within-subject changes in behavior over time and allowed us to compare an individual’s likelihood of sharing syringes prior to and following the initiation of ART. The multivariate model was fitted using an *a priori* model-building protocol described previously (Maldonado & Greenland, 1993; Rothman et al., 2008), whereby we fitted a full model containing all explanatory variables. Then, using a manual backwards stepwise approach, we fitted a series of reduced models. For each reduced model, we noted the change in the regression coefficient for the primary explanatory variable relative to the value for the same coefficient in the full model. We removed the secondary explanatory variable causing the smallest relative change and repeated this process until the maximum change from the full model exceeded 5%. This procedure seeks to preserve secondary explanatory variables in the multivariate model that confound the relationship between ART initiation and syringe lending. This technique has been used successfully in previously published studies (Lima et al., 2007; Marshall et al., 2009).

3. RESULTS

A total of 380 baseline ART-naïve IDU participated in this study, among whom 260 (68.4%) initiated ART between 1996 and 2008, for an incidence density of 26.8 (95% CI: 23.6 – 30.3) per 100 person-years. In the overall sample, 171 (45.0%) were female, the median age was 34.2 (interquartile range [IQR]: 27.7–40.8), 148 (38.9%) were of Aboriginal ethnicity, and the median follow-up duration was 60 months (IQR: 18–113). The sample contributed to 4090 cumulative study site visits and 2100 person-years of observation. A total of 94 (24.7%) participants reported syringe lending during the previous six months at the baseline interview. During follow-up, 216 (56.8%) individuals reported at least one six-month period of not injecting. Of the 4090 total study visits, these individuals contributed 1025 (25.1%) observations of no injecting.

The comparison of baseline and clinical characteristics of those who did and did not initiate ART during the study period is shown in Table 1. In comparison to those who did not initiate ART, those who initiated treatment were more likely to have lower baseline $CD4^+$ cell counts and higher baseline HIV-1 RNA viral loads.

In bivariate analysis (see Table 2), syringe lending was significantly associated with being homeless (odds ratio [OR] = 1.48, 95% CI: 1.02–2.15), frequent heroin injection (OR=2.84, 95% CI: 2.05–3.93), frequent cocaine injection (OR=3.17, 95% CI: 2.36–4.27), current enrollment in methadone maintenance therapy (OR=0.60, 95% CI: 0.42–0.85), and higher $CD4^+$ cell count (OR=1.16, 95% CI: 1.08–1.24) and viral load (OR=1.58, 95% CI: 1.37–1.82). Factors that remained in the multivariate model and thus confounded the relationship between ART initiation and syringe lending were frequent injection of cocaine (adjusted odds ratio [AOR] = 2.62, 95% CI: 1.98–3.47) and increased viral load (AOR = 1.45, 95% CI: 1.27–1.66). Syringe lending was not significantly associated with ART initiation in multivariate analysis (AOR=0.78, 95% CI 0.42–1.45).

4. DISCUSSION

In the present study, we found no evidence of increased syringe lending behavior following ART initiation among HIV-positive IDU. This pattern was consistent in both adjusted and unadjusted analyses that examined within-individual differences and changes in behavior over time using generalized linear mixed-effects models.

Many challenges that are unique to the HIV-positive IDU population create significant barriers to ART delivery. Among these is the common concern among physicians that among some IDU, HIV-related risk behavior may increase after the initiation of ART, thereby potentially increasing the risk of transmission of HIV and antiretroviral-resistant HIV in particular (Vlahov et al., 2001). Some studies describe changes in risk behaviors following ART initiation in terms of behavior relapse, which may be attributed to perceptions that one is less likely to transmit HIV with undetectable viral loads, thus leading to increased sexual or drug use activity (Vlahov & Celentano, 2006). Such relapses have been reported among gay men following initiation of HIV treatment (DiClemente et al., 2002; Miller et al., 2000) and may be particularly associated with risky sexual behaviors with partners who are reported to have undetectable viral loads (Van de Ven et al., 2005).

While IDU face major barriers as a result of physician reluctance to prescribe ART to this population (Clarke & Mulcahy, 2000; Loughlin et al., 2004), few studies have reported on HIV-related risk behaviors among IDU receiving ART. Earlier studies examined sexual risk behaviors among IDU and reported inconsistent results. One study from Baltimore reported slight increases in risky sexual behavior among IDU receiving ART (Vlahov et al., 2001). More recently, a French study reported decreased sexual risk-taking following ART

initiation (Bouhnik et al., 2002), and a study from Vancouver's IDU population showed no change in sexual behaviors following ART initiation (Marshall et al., 2010). As indicated earlier, the proposed mechanisms for increased sexual risk are relevant to injection-related risk behavior. For example, they involve behavior change attributable to decreased HIV-related morbidity, which could be relevant to increases in drug use behavior, as well as assumptions relating to decreased potential to transmit HIV as a result of decreased viral load, which could also contribute to injection-related risk. In this context, our results are reassuring that initiating ART was not associated with increased injection-related risk behavior, and are consistent with previous research suggesting that ART initiation is not associated with increases in other HIV-related risk behaviors.

Importantly, two recent studies examining ART receipt and risky injecting behaviors report a lower likelihood to engage in syringe lending (Metsch et al., 2007) and no association between ART receipt and sharing of injection equipment (Latkin et al., 2008). However, it is noteworthy that neither study evaluated ART receipt in multivariate analyses, nor did they examine behaviors related specifically to the period following ART initiation using prospective analyses, as was done in the present study. Earlier studies were also limited by self-reported ART receipt (Latkin et al., 2008; Metsch et al., 2007; Vlahov et al., 2001), which has been shown to have limitations (Wood et al., 2006), and short follow-up periods (Metsch et al., 2007). The present study addresses these limitations by using a centralized database to confirm the exact date of ART initiation, a relatively long follow-up duration, and an analytic technique allowing for within-individual changes in behavior prior to and following ART initiation.

Nevertheless, the present study has limitations. Since syringe lending was self-reported, it is possible that this behavior was underreported, in particular given the possibility of socially desirable responses with regard to such a stigmatized behavior. Also, since IDU remain a largely marginalized population, and while we used extensive outreach methods and snowball sampling to derive the most representative sample possible, we cannot be certain that this cohort represents IDU in the community in general. However, prior reports have indicated that this cohort's demographics are similar when compared to other samples of Vancouver's IDU (Tyndall et al., 2001). Thirdly, we did not account for the possibility of cessation of injection drug use as a potential contributor to decreased syringe lending. However, it is noteworthy that our multivariate analyses adjusted for drug injecting patterns and our results remained unchanged. Reduced ART receipt among active injectors could also bias our results; however, our statistical adjustment for patterns of drug use should have served to limit this concern as well. Lastly, our findings may have been confounded by the possibility that IDU initiating ART are less likely to engage in risk behavior because of sterile syringes provided by primary care physicians. We do not think this explains our findings because of the widespread distribution of sterile syringes in our setting (Kerr et al., 2010).

In the present study, we found no evidence of increased syringe lending among HIV-positive IDU who initiated ART. These findings should be helpful in addressing the concern among ART prescribers that IDU may engage in more risky injecting behaviors after starting HIV treatment. In light of these findings, in addition to the known impact of ART on morbidity and mortality, ART delivery to IDU should be immediately scaled up to meet the needs of this marginalized and underserved population.

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Table 1

Baseline factors associated with treatment initiation among a cohort of antiretroviral-naïve HIV-positive injection drug users in Vancouver, 1996–2008 (*n* = 380).

Characteristic	Initiated ART* *Median (IQR) or n* (%) *n* = 260	Did Not Initiate ART* *Median (IQR) or n* (%) *n* = 120	Odds Ratio (95% CI)	*p* – value
Age	33.9 (27.7 – 40.3)	35.7 (27.6 – 41.7)	0.99 (0.96 – 1.01)	0.326
Sex				
Female	118 (45.4%)	53 (44.2%)	1.05 (0.68 – 1.62)	0.824
Male	142 (54.6%)	67 (55.8%)		
Aboriginal ethnicity				
Yes	105 (40.4%)	43 (35.8%)	1.21 (0.78 – 1.90)	0.398
No	155 (59.6%)	77 (64.2%)		
Baseline CD4 count	350 (250 – 530)	500 (310 – 640)	0.83 (0.76 – 0.91)	<0.001
Baseline viral load (per log10)	4.7 (4.2 – 5.1)	4.5 (3.9 – 4.9)	1.74 (1.29 – 2.35)	<0.001

Note:

*ART = antiretroviral therapy.

Table 2

Bivariate and multivariate longitudinal analyses of factors associated with lending used syringes among HIV-positive injection drug users (*n* = 380).

Characteristic	OR[a]	95% CI	*p* – value	AOR[b]	95% CI	*p* – value
ART initiation[*] (yes *vs.* no)	0.72	0.38 – 1.36	0.316	0.78	0.42 – 1.45	0.441
Age (per 10 years)	1.01	0.98 – 1.04	0.386			
Gender (female *vs.* male)	1.41	0.90 – 2.23	0.135			
Aboriginal ethnicity (yes *vs.* no)	0.68	0.43 – 1.09	0.108			
Homeless (yes *vs.* no)	1.48	1.02 – 2.15	0.041			
Frequent heroin injection (yes *vs.* no)[†]	2.84	2.05 – 3.93	<0.001			
Frequent cocaine injection (yes *vs.* no) [†]	3.17	2.36 – 4.27	<0.001	2.62	1.98 – 3.47	<0.001
MMT[c] (yes *vs.* no)	0.60	0.42 – 0.85	0.004			
CD4 cell count (per 100 units)	1.16	1.08 – 1.24	<0.001			
Plasma viral load (per log10)	1.58	1.37 – 1.82	<0.001	1.45	1.27 – 1.66	<0.001

Notes:

[*]ART initiation refers to the first follow-up completed at least 6 months following the date of therapy initiation; a Odds Ratio; b Adjusted Odds Ratio; c MMT = current enrollment in methadone maintenance therapy;

[†]Refers to injecting ≥ daily during the past 6-month period prior to the interview.

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