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Factors associated with initiation of antiretroviral therapy among hiv-positive people who use injection drugs in a Canadian setting

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Abstract

Objective—To identify behavioural, social and structural factors associated with time from HIV seroconversion to antiretroviral therapy (ART) initiation among people who use injection drugs (PWID).

Design—Two complementary prospective cohorts of PWID linked to comprehensive ART dispensation records in a setting of universal no-cost HIV/AIDS treatment and care.

Methods—Multivariable extended Cox models of time to ART initiation among baseline HIV-seronegative PWID who seroconverted after recruitment adjusted with a time-updated measure of clinical eligibility for ART.

Results—We included 133 individuals of whom 98 (74%) initiated ART during follow-up at a rate of 12.4 per 100 person-years. In a multivariable model adjusted for ART eligibility, methadone maintenance therapy (Adjusted Hazard Ratio [AHR] = 2.37, 95% Confidence Interval [95% CI]: 1.56 - 3.60) and a more recent calendar year of observation (AHR = 1.06, 95% CI: 1.00 - 1.12) were associated with more rapid ART initiation, whereas informal income generation (AHR = 0.51, 95% CI: 0.32 - 0.79) and incarceration (AHR = 0.52, 95% CI: 0.28 - 0.97) were negatively associated with ART initiation.

Conclusions—In this sample of community-recruited HIV-positive PWID with well-defined dates of HIV seroconversion, we found that two measures related to the criminalization of illicit drug use each independently delayed ART initiation regardless of clinical eligibility. Engagement

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BJ, EW and M-JSM conceived these analyses. SD and M-JSM performed all statistical analyses. BJ drafted the manuscript and incorporated all revisions. All the authors read the manuscript, made significant intellectual contributions and approved its submission.

in methadone promoted ART initiation. Programs to scale-up HIV treatment among PWID should consider decreased criminalization of PWID and increased access to opioid substitution therapy in order to optimize the impact of ART on HIV/AIDS-associated morbidity, mortality and HIV transmission.

Keywords

antiretroviral therapy; initiation; injection drug users; PWID; methadone

INTRODUCTION

Optimal and sustained engagement in antiretroviral therapy (ART) suppresses plasma HIV RNA viral load to below detectable concentrations, decreases HIV disease progression and nearly eliminates the risk of onward vertical, sexual or parenteral HIV transmission [1-9]. Thus, a large number of countries as well as the United Nations have endorsed Treatment-as-Prevention (TasP)-based strategies as a means to decrease HIV/AIDS-associated morbidity and mortality by ensuring the optimal health of people living with HIV disease and secondarily to decrease the incidence of new infections [10]. In order to reduce the time any individual living with HIV/AIDS has a detectable viral load and is at risk of transmitting the virus, TasP-based efforts rely on early detection and prompt engagement in treatment [11-13].

Despite the availability of effective antiretroviral therapy, HIV-infected people who use injection drugs (PWID) continue to experience relatively high levels of HIV/AIDS-related morbidity and mortality [14, 15]. Since PWID are at increased risk of HIV infection but are less likely to initiate treatment, efforts to rapidly engage PWID in evidence-based treatment for HIV infection are needed to control the pandemic.

Despite the urgent need to scale-up HIV treatment among PWID, there is a dearth of research on the factors that shape ART initiation. In particular, we are unaware of any longitudinal studies among PWID followed from HIV seroconversion to ART initiation in order to characterize the factors that predict ART initiation. Thus, using data from a long-running community-recruited cohort of HIV-negative and HIV-positive PWID, we sought to identify potentially modifiable behavioural, social and structural-level factors inhibiting or promoting ART initiation.

METHODS

In this study, we used data from the Vancouver Injection Drug Users Study (VIDUS) and the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS). The VIDUS and ACCESS studies are ongoing prospective observational cohorts of illicit drug users centered in the Downtown Eastside (DTES) of Vancouver, British Columbia (BC). The DTES is an epicenter of HIV/AIDS in BC and an urban neighbourhood characterized by high levels of poverty, illicit drug use, sex work and hepatitis C seropositivity. Eligibility criteria and recruitment methods for VIDUS and ACCESS have been described previously [16, 17]. In brief, VIDUS includes HIV-seronegative individuals who report any injection drug use in the 30 days prior to recruitment. The ACCESS study includes HIV-seropositive individuals who

report any illicit drug use other than cannabis in the 30 days prior to recruitment. Individuals in VIDUS who seroconvert following recruitment are transferred to ACCESS for ongoing follow-up. The studies use harmonized data collection procedures at the baseline interview and all biannual follow-up interviews thereafter to allow for the comparison of HIV-negative and HIV-positive individuals. These procedures include an identical interviewer-administered questionnaire, examination by a study nurse, and a blood draw for serological analysis, including HIV antibody testing for all HIV-negative participants, and HIV clinical monitoring for all HIV-positive participants. At recruitment, participants provide their personal health number, a unique and persistent identifier issued for billing and tracking purposes to all residents of BC by the government-run universal no-cost medical system. The VIDUS and ACCESS studies have been approved by the University of British Columbia/Providence Health Care Research Ethics Board.

For ACCESS participants, information gathered through the interview and examination process is augmented with data on HIV treatment and clinical outcomes. This information is made available through a confidential linkage with the provincial Drug Treatment Program (DTP). As described in detail elsewhere [16], the universally-accessible and publicly-funded DTP administers the centralized distribution of ART to all people living with HIV/AIDS in BC and is administered by the British Columbia Centre for Excellence in HIV/AIDS (BC-CfE) according to the provincial Therapeutic Guidelines (Therapeutic Guidelines for Antiretroviral (ARV) Treatment of Adult HIV Infection, <http://www.cfenet.ubc.ca/therapeutic-guidelines/adult>). Data collected through the DTP provides a complete retrospective and prospective clinical profile for each participant including all CD4 cell counts and plasma HIV-1 RNA viral loads ascertained through the study or by participants' personal physicians, as well as all ART dispensations. Due to the no-cost provision of HIV/AIDS medications and care delivered through BC's province-wide and universal access healthcare system, we are able to evaluate the effects of various factors on treatment uptake unconstrained by the confounding influence of financial ability to pay for such care.

In the present analyses, we included all participants who were HIV-seronegative at the VIDUS baseline interview and were subsequently observed to have seroconverted to HIV-positive status at a follow-up interview. In addition, participants had to have completed at least one follow-up interview following seroconversion and completed 1 CD4 cell count and 1 plasma HIV-1 RNA viral load (VL) observation within 180 days of the follow-up interview at which the individual was first observed to be HIV-seropositive.

The primary outcome of interest in this study was time to ART initiation. As in previous analyses [18, 19], we estimated the time of seroconversion to be the mid-point between the last negative HIV antibody test and the date of the first HIV-positive antibody test. The time of ART initiation was defined as the date of the first dispensation of ART from the DTP between December 17, 1996 and December 16, 2012. Individuals with no record of ART dispensation by November 16, 2012, were right censored. We included all interviews conducted after the estimated date of seroconversion.

We considered a range of explanatory variables including: age (per year older); gender (non-male vs. male); self-reported Caucasian ancestry (yes vs. no); level of education attained (

high school diploma vs. < high school diploma); residence in the DTES (yes vs. no); homelessness (yes vs. no); non-injection crack use (daily vs. <daily); injection heroin use (daily vs. <daily); injection cocaine use (daily vs. <daily); self-reported binge drug use (binges in which the participant reported using more drugs than usual; yes vs. no); informal income generation (reporting income from sex work, drug dealing, theft, or other activities; yes vs. no); incarceration (reporting being held in custody in jail, prison or penitentiary at least overnight; yes vs. no); engagement in methadone maintenance therapy (MMT; yes vs. no); year of baseline HIV-positive interview (per year later); and clinical eligibility for ART (yes vs. no). All explanatory variables were time-updated and referred to the 6-month period prior to the follow-up interview except gender and Caucasian ancestry, which were time fixed. Homelessness, MMT status and clinical eligibility were time-updated and referred to current status.

To determine clinical eligibility for ART, we referred to the guidelines governing eligibility for ART in our setting from 1996 onwards, as in previous analyses [20]. Since 1996, the guidelines have remained consistent with those published by the International AIDS Society-USA [21]. To judge clinical eligibility at each follow-up interview, we referred to each individual's CD4 cell count, plasma VL and history of AIDS-defining illnesses, as applicable, from their HIV clinical profile data held by the BC-CfE. Eligibility criteria for ART during the study period were: CD4 count < 500 cells/ μ L, VL $\geq$ 30000 copies/ml, or ever experienced an AIDS-defining illness (1996); VL > 5000 copies/mL or AIDS-defining illness (1997 – 1999); CD4 count < 500 cells/ μ L, VL $\geq$ 30000 copies/mL, or AIDS-defining illness (2000 – 2001); CD4 count $\geq$ 200 cells/ μ L or AIDS-defining illness (2002 – 2007); CD4 count $\geq$ 350 cells/ μ L or AIDS-defining illness (2008 – 2009); and CD4 count $\geq$ 500 cells/ μ L or AIDS-defining illness (2010 – 2012). To determine clinical eligibility at the time of each study interview, we used the mean of all CD4 cell counts conducted in the previous six months or, if none, we used the most recent CD4 cell count observation. An analogous approach was used to determine VL.

As a first step in our analysis, we examined the baseline characteristics of all individuals stratified by whether or not they initiated treatment during the study period. To estimate the relationship between each explanatory variable of interest and time to ART initiation, we constructed univariable and multivariable extended Cox models. First, we estimated the univariable relationships between each explanatory variable and time to ART initiation. Next, we determined the covariates to be included in the final multivariable model using an *a priori*-defined model-building procedure, as in previous analyses [22]. The procedure started with all covariates with p-value < 0.2 in bivariable analyses, proceeding using a backwards selection process. The final multivariable with the lowest Akaike Information Criterion value was selected. All p-values were two-sided. Statistical analyses completed in R version 3.2.0 (R Software Foundation, Vienna, Austria.)

RESULTS

Between December, 1996 and December, 2012, 1943 HIV-negative PWID were recruited into the VIDUS study. Out of these individuals, 176 (9%) seroconverted to HIV during follow-up and were subsequently transitioned to the ACCESS study. Of these individuals,

133 (75%) met criteria for inclusion in this analysis. Those included did not differ from those excluded by age at seroconversion, gender or ancestry (all $p > 0.5$). These study participants contributed 788.3 person-years of observation. During the study period, 98 (74%) initiated ART, equal to a rate of 12.4 (95% Confidence Interval [95% CI]: 10.1 – 15.2) per 100 person-years. At ART initiation, the mean CD4 cell count was 250 (Inter-Quartile Range: 140 – 370) cells/ μL and mean VL was 4.6 (IQR: 3.4 – 5.0) copies/mL, log₁₀ transformed.

Select socio-demographic, behavioral, structural, and clinical characteristics of the study sample at their earliest study interview following seroconversion are presented in Table 1. Results are stratified by whether ART was initiated over the follow-up period (yes vs. no). Individuals who were clinically eligible at baseline were more likely to initiate ART over follow-up (Odds Ratio [OR] = 3.63, 95% CI: 1.57 - 8.37, $p = 0.003$). Individuals who reported homelessness at baseline were less likely to initiate ART over the follow-up period (OR = 0.36, 95% CI: 0.16 - 0.84, $p = 0.022$).

The crude and adjusted longitudinal estimates of the hazard ratios of initiating ART are presented in Table 2. In a model adjusted for a time-updated measure of clinical ART eligibility, current residence in the DTES (Adjusted Hazard Ratio [AHR] = 1.65, 95% CI: 1.04 - 2.63, $p = 0.035$), engagement in MMT (AHR = 2.41, 95% CI: 1.59 - 3.66, $p < 0.001$) and later year of interview (AHR = 1.06, 95% CI: 1.00 - 1.12, $p = 0.047$) were positively associated with ART initiation. Engaging in informal income generation (AHR = 0.51, 95% CI: 0.33 - 0.80, $p = 0.004$) and being incarcerated (AHR = 0.52, 95% CI: 0.28 - 0.97, $p = 0.039$) were barriers to ART initiation, independent of clinical eligibility.

DISCUSSION

In this study, the first to our knowledge to longitudinally analyze ART initiation among injection drug-using individuals with incident HIV infections, we observed high rates of treatment initiation, with 70% of individuals initiating treatment during the study period at a rate of 12.4 per 100 person-years. In a multivariable model adjusted for a time-updated measure of clinical eligibility for ART, structural factors related to the criminalization and socio-economic marginalization of PWID, including incarceration and informal income generation, posed important barriers to ART initiation independent of clinical eligibility. As in previous analyses, engagement in MMT was strongly associated with ART initiation [23].

Although illicit drug use was not associated with ART initiation in our analysis, exposures to criminalization most likely related to injection drug use were identified as barriers to initiation independent of clinical status. We observed an association between incarceration and reduced rates of ART initiation. Exposure to correctional facilities has been associated with reduced ART adherence and viral suppression in previous studies of community-recruited HIV-positive PWID who had initiated treatment [22, 24]. The current study adds to this evidence by documenting how incarceration delays the timely initiation of HIV treatment, adding to the length of time an individual is viraemic. This has implications not only for disease progression but also viral transmission dynamics both within correctional facilities and among non-incarcerated populations following release from custody.

Incarcerated populations exhibit higher HIV prevalence than analogous non-incarcerated populations and incarceration has also been associated with syringe lending among PWID with detectable HIV-1 RNA viral loads [25, 26].

PWID are characterized as a group at high risk of incarceration and are likely to be involved with the criminal justice system [27]. Given these dynamics, correctional facilities have been suggested as a key venue to facilitate HIV testing and treatment initiation [28]. In our setting, HIV testing and antiretroviral treatment are available to incarcerated individuals in municipal, provincial and federal correctional facilities. However concern has been expressed about the delivery of care, for example, confidentiality within jail settings and linkages to non-correctional healthcare providers [29]. The current results suggest criminal justice exposure interferes with the delivery and uptake of evidence-based medical care for HIV-positive PWID even in a setting with an ongoing Treatment-as-Prevention-based HIV treatment scale-up initiative during much of the study period.

We also found that engaging in informal income generation, such as sex work, drug dealing and theft, was associated with a decreased rate of treatment uptake, independent of incarceration and clinical eligibility. Other studies show that informal income generating activities are common among PWID and associated with higher intensity drug use [30, 31]. Moreover, PWID involved in informal income generation activities, especially drug dealing and theft, may be evading prosecution, surveillance, or encounters with police or other institutions which monitor individual behavior or keep administrative records, and their willingness or ability to access healthcare may be limited as a result [32].

MMT is well established as an effective treatment for opioid addiction [33, 34]. In addition to reduced drug use, PWID engaged in MMT programs have more frequent contact with healthcare providers, more frequent HIV testing, are more likely to initiate treatment, exhibit better clinical outcomes of ART, and exhibit higher rates of adherence to ART [23, 35-37]. Our findings are consistent with a prior study showing a similar association between MMT and faster ART initiation among PWID [23] and we additionally demonstrate that this relationship persists independent of clinical eligibility. In addition to engagement in MMT, we observed that individuals with their first HIV-positive interview later in the study period had faster rates of ART initiation, regardless of clinical eligibility. This is consistent with the local community-wide TasP initiative beginning in the late-2000s.

This study has several limitations. First, our analytic sample cannot be seen as representative of all HIV-positive PWID due to non-random participant recruitment and the free availability of ART in our setting. Secondly, the possibility of unmeasured confounding variable influence cannot be excluded. To minimize the effects of confounding variables, we used multivariable modeling of data from a long-standing cohort of HIV-seropositive PWID and accounted for the changes in clinical eligibility for ART over the study period. Third, several explanatory variables such as drugs use, informal income generation and incarceration were derived from participant self-report, which might be susceptible to reporting or response bias. For example, a social desirability bias might engender the under-reporting of participant informal income generation, potentially resulting in the underestimation of its relationship to ART initiation rates. Despite these potential limitations, within the context of

BC's free healthcare and universal access to ART, confounding due to financial barriers to healthcare access has been reduced. Fourth, owing to limited statistical power, we were unable to assess whether rates of ART initiation might differ by length or location of incarceration events.

Within the context of an ongoing prospective cohort of HIV-seropositive PWID, we have identified several factors associated with time from HIV seroconversion to ART initiation. Engagement in MMT was independently associated with more rapid rates of ART initiation after accounting for clinical eligibility. Periods of informal income generation and incarceration were associated with decreased rates of ART initiation. The identification of these barriers in a setting with universal healthcare and an ongoing Treatment-as-Prevention initiative testifies not only to the pervasive impacts of the criminalization of illicit drug use, but also to the need to integrate social-structural interventions into efforts to scale-up treatment. Our findings support warnings [38] that laws, policies and programmes which treat illicit drug use as a matter of public security impair public health-based objectives to address the global HIV/AIDS pandemic. Given the increasing realization of the importance of earlier HIV treatment initiation to optimize the impact of antiretroviral therapy on HIV/AIDS-associated morbidity, mortality and HIV transmission, our findings stress the importance of engagement in evidence-based addictions treatment and addressing barriers related to criminalization of illicit drug use.

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REFERENCES

1. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012; 367:399–410. [PubMed: 22784037]
2. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011; 365:493–505. [PubMed: 21767103]
3. Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, Cohen CR, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet*. 2010; 375:2092–2098. [PubMed: 20537376]
4. He N, Duan S, Ding Y, Rou K, McGoogan JM, Jia M, et al. Antiretroviral therapy reduces HIV transmission in discordant couples in rural Yunnan, China. *PLoS One*. 2013; 8:e77981. [PubMed: 24236010]

5. Ledergerber B, Egger M, Opravil M, Telenti A, Hirschel B, Battegay M, et al. Clinical progression and virological failure on highly active antiretroviral therapy in HIV-1 patients: a prospective cohort study. Swiss HIV Cohort Study. *Lancet*. 1999; 353:863–868. [PubMed: 10093977]
6. McGowan JP, Shah SS. Prevention of perinatal HIV transmission during pregnancy. *J Antimicrob Chemother*. 2000; 46:657–668. [PubMed: 11062184]
7. Montaner JS, Hogg R, Wood E, Kerr T, Tyndall M, Levy AR, et al. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet*. 2006; 368:531–536. [PubMed: 16890841]
8. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med*. 2000; 342:921–929. [PubMed: 10738050]
9. Montaner JS, Lima VD, Barrios R, Yip B, Wood E, Kerr T, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. *Lancet*. 2010; 376:532–539. [PubMed: 20638713]
10. UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. Joint United Nations Programme on HIV/AIDS (UNAIDS); Geneva, Switzerland: 2014. p. 37
11. Hall HI, Song R, Rhodes P, Prejean J, An Q, Lee LM, et al. Estimation of HIV incidence in the United States. *JAMA*. 2008; 300:520–529. [PubMed: 18677024]
12. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. *AIDS*. 2006; 20:1447–1450. [PubMed: 16791020]
13. Williams BG, Lima V, Gouws E. Modelling the impact of antiretroviral therapy on the epidemic of HIV. *Curr HIV Res*. 2011; 9:367–382. [PubMed: 21999772]
14. Obel N, Omland LH, Kronborg G, Larsen CS, Pedersen C, Pedersen G, et al. Impact of non-HIV and HIV risk factors on survival in HIV-infected patients on HAART: a population-based nationwide cohort study. *PLoS One*. 2011; 6:e22698. [PubMed: 21799935]
15. Spillane H, Nicholas S, Tang Z, Szumilin E, Balkan S, Pujades-Rodriguez M. Incidence, risk factors and causes of death in an HIV care programme with a large proportion of injecting drug users. *Trop Med Int Health*. 2012; 17:1255–1263. [PubMed: 22863110]
16. Strathdee SA, Palepu A, Cornelisse PG, Yip B, O'Shaughnessy MV, Montaner JS, et al. Barriers to use of free antiretroviral therapy in injection drug users. *JAMA*. 1998; 280:547–549. [PubMed: 9707146]
17. Strathdee SA, Patrick DM, Currie SL, Cornelisse PG, Rekart ML, Montaner JS, et al. Needle exchange is not enough: lessons from the Vancouver injecting drug use study. *AIDS*. 1997; 11:F59–65. [PubMed: 9223727]
18. Craib KJ, Spittal PM, Wood E, Laliberte N, Hogg RS, Li K, et al. Risk factors for elevated HIV incidence among Aboriginal injection drug users in Vancouver. *CMAJ*. 2003; 168:19–24. [PubMed: 12515780]
19. Kerr T, Small W, Buchner C, Zhang R, Li K, Montaner J, et al. Syringe sharing and HIV incidence among injection drug users and increased access to sterile syringes. *Am J Public Health*. 2010; 100:1449–1453. [PubMed: 20558797]
20. Nosyk B, Montaner JS, Colley G, Lima VD, Chan K, Heath K, et al. The cascade of HIV care in British Columbia, Canada, 1996–2011: a population-based retrospective cohort study. *Lancet Infect Dis*. 2014; 14:40–49. [PubMed: 24076277]
21. Gunthard HF, Aberg JA, Eron JJ, Hoy JF, Telenti A, Benson CA, et al. Antiretroviral treatment of adult HIV infection: 2014 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2014; 312:410–425. [PubMed: 25038359]
22. Milloy MJ, Kerr T, Buxton J, Rhodes T, Guillemi S, Hogg R, et al. Dose-response effect of incarceration events on nonadherence to HIV antiretroviral therapy among injection drug users. *J Infect Dis*. 2011; 203:1215–1221. [PubMed: 21459814]
23. Uhlmann S, Milloy MJ, Kerr T, Zhang R, Guillemi S, Marsh D, et al. Methadone maintenance therapy promotes initiation of antiretroviral therapy among injection drug users. *Addiction*. 2010; 105:907–913. [PubMed: 20331553]

24. Milloy MJ, Kerr T, Buxton J, Rhodes T, Krusi A, Guillemi S, et al. Social and environmental predictors of plasma HIV RNA rebound among injection drug users treated with antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2012; 59:393–399. [PubMed: 22134149]
25. Milloy MJ, Kerr T, Salters K, Samji H, Guillemi S, Montaner J, et al. Incarceration is associated with used syringe lending among active injection drug users with detectable plasma HIV-1 RNA: a longitudinal analysis. *BMC Infect Dis*. 2013; 13:565. [PubMed: 24289651]
26. Wood E, Li K, Small W, Montaner JS, Schechter MT, Kerr T. Recent incarceration independently associated with syringe sharing by injection drug users. *Public Health Rep*. 2005; 120:150–156. [PubMed: 15842116]
27. Jurgens R, Nowak M, Day M. HIV and incarceration: prisons and detention. *J Int AIDS Soc*. 2011; 14:26. [PubMed: 21595957]
28. Milloy MJ, Montaner JS, Wood E. Incarceration of people living with HIV/AIDS: implications for treatment-as-prevention. *Curr HIV/AIDS Rep*. 2014; 11:308–316. [PubMed: 24962285]
29. Small W, Wood E, Betteridge G, Montaner J, Kerr T. The impact of incarceration upon adherence to HIV treatment among HIV-positive injection drug users: a qualitative study. *AIDS Care*. 2009; 21:708–714. [PubMed: 19806487]
30. DeBeck K, Shannon K, Wood E, Li K, Montaner J, Kerr T. Income generating activities of people who inject drugs. *Drug Alcohol Depend*. 2007; 91:50–56. [PubMed: 17561355]
31. Sherman SG, Latkin CA. Drug users' involvement in the drug economy: implications for harm reduction and HIV prevention programs. *J Urban Health*. 2002; 79:266–277. [PubMed: 12023502]
32. Brayne S. Surveillance and System Avoidance: Criminal Justice Contact and Institutional Attachment. *American Sociological Review*. 2014; 79:367–391.
33. Donny EC, Brasser SM, Bigelow GE, Stitzer ML, Walsh SL. Methadone doses of 100 mg or greater are more effective than lower doses at suppressing heroin self-administration in opioid-dependent volunteers. *Addiction*. 2005; 100:1496–1509. [PubMed: 16185211]
34. Joseph H, Stancliff S, Langrod J. Methadone maintenance treatment (MMT): a review of historical and clinical issues. *Mt Sinai J Med*. 2000; 67:347–364. [PubMed: 11064485]
35. Palepu A, Tyndall MW, Joy R, Kerr T, Wood E, Press N, et al. Antiretroviral adherence and HIV treatment outcomes among HIV/HCV co-infected injection drug users: the role of methadone maintenance therapy. *Drug Alcohol Depend*. 2006; 84:188–194. [PubMed: 16542797]
36. Weber R, Huber M, Rickenbach M, Furrer H, Elzi L, Hirschel B, et al. Uptake of and virological response to antiretroviral therapy among HIV-infected former and current injecting drug users and persons in an opiate substitution treatment programme: the Swiss HIV Cohort Study. *HIV Med*. 2009; 10:407–416. [PubMed: 19490174]
37. Wood E, Montaner JS, Yip B, Tyndall MW, Schechter MT, O'Shaughnessy MV, et al. Adherence and plasma HIV RNA responses to highly active antiretroviral therapy among HIV-1 infected injection drug users. *CMAJ*. 2003; 169:656–661. [PubMed: 14517122]
38. Milloy M-J, Montaner JSG, Wood E. Incarceration of people living with HIV/AIDS: implications for treatment-as-prevention. *Curr HIV/AIDS Rep*. 2014; 11:308–316. [PubMed: 24962285]

Table 1
Baseline characteristics among 133 HIV-positive PWID in the six-month period prior to the first HIV-positive interview, stratified by incarceration during follow-up

Characteristic	No incarceration during follow-up n (%) n = 53 (39.8%)	Incarceration during follow-up n (%) n = 80 (60.6%)	OR ¹	95% CI ²	p - value
ART initiation					
No	14 (26.4)	21 (26.3)	1.00		
Yes	39 (73.6)	59 (73.7)	1.01	0.46–2.22	0.983
Age⁴					
Per year older (IQR ³)	36 (28–46)	34 (27–40)	0.97	0.93–1.01	0.089
Gender⁴					
Male	26 (49.1)	43 (53.8)	1.00		
Non-male	27 (50.9)	37 (46.2)	0.83	0.41–1.66	0.596
Caucasian⁴					
No	19 (35.8)	43 (53.8)	1.00		
Yes	34 (64.2)	37 (46.2)	0.48	0.24–0.98	0.043
Education⁵					
< HS diploma	41 (78.8)	65 (81.3)	1.00		
HS diploma	11 (21.2)	15 (18.7)	0.86	0.36–2.05	0.734
DTES residence⁶					
No	18 (34.0)	23 (28.8)	1.00		
Yes	35 (66.0)	57 (71.3)	1.27	0.60–2.69	0.523
Homelessness⁶					
No	43 (81.1)	57 (71.3)	1.00		
Yes	10 (18.9)	23 (28.7)	1.74	0.75–4.02	0.196
Non-injection crack use⁵					
< Daily	34 (64.2)	54 (67.5)	1.00		
Daily	19 (35.8)	26 (32.5)	0.86	0.41–1.79	0.689

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Characteristic	No incarceration during follow-up n (%) n = 53 (39.8%)	Incarceration during follow-up n (%) n = 80 (60.6%)	OR ¹	95% CI ²	p - value
Injection heroin use⁵					
< Daily	37 (71.2)	43 (53.8)	1.00		
Daily	15 (28.8)	37 (46.2)	2.12	1.01–4.47	0.046
Injection cocaine use⁵					
< Daily	35 (67.3)	49 (62.0)	1.00		
Daily	17 (32.7)	30 (38.0)	1.26	0.60–2.63	0.537
Binge drug use⁵					
No	36 (69.2)	48 (60.0)	1.00		
Yes	16 (30.8)	32 (40.0)	1.50	0.72–3.14	0.281
Informal income generation⁵					
No	26 (49.1)	37 (46.3)	1.00		
Yes	27 (50.9)	43 (53.7)	1.12	0.56–2.24	0.751
Methadone maintenance therapy⁶					
No	37 (69.8)	64 (80.0)	1.00		
Yes	16 (30.2)	16 (50.0)	0.58	0.26–1.29	0.178
Year of baseline⁴					
Per year later	2002 (1999–2007)	1999 (1997–2002)	0.85	0.78–0.93	<0.001
ART eligibility⁶					
No	32 (60.4)	33 (41.3)	1.00		
Yes	21 (39.6)	47 (58.7)	2.17	1.07–4.41	0.035

¹Odds Ratio;

²95% Confidence Interval;

³Interquartile Range;

⁴Time invariant, measured at baseline;

⁵Time-updated, refers to six month period prior to the first HIV-positive interview;

ρ Current status.

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Bivariable and multivariable factors associated with time from HIV seroconversion to ART initiation among 133 PWID**Table 2**

Characteristic	HR ¹	95% CI ²	p - value	AHR ³	95% CI	p - value
Age⁵						
Per year older (IQR ⁴)	1.02	1.00 - 1.04	0.121			
Gender⁵						
Male vs. non-male	1.12	0.75 - 1.67	0.569			
Caucasian⁵						
Yes vs. no	0.96	0.64 - 1.42	0.827			
Education⁶						
Yes vs. no	1.30	0.82 - 2.06	0.256			
DTES residence⁷						
Yes vs. no	1.67	1.07 - 2.59	0.023	1.65	1.04 - 2.63	0.035
Homelessness⁷						
Yes vs. no	0.95	0.57 - 1.56	0.825			
Daily non-injection crack use⁶						
Yes vs. no	1.13	0.75 - 1.72	0.560			
Daily injection cocaine use⁶						
Yes vs. no	0.78	0.46 - 1.33	0.363			
Daily injection heroin use⁶						
Yes vs. no	0.87	0.55 - 1.39	0.571			
Binge drug use⁶						
Yes vs. no	0.98	0.61 - 1.57	0.930			
Informal income generation⁶						
Yes vs. no	0.65	0.42 - 0.99	0.046	0.51	0.33 - 0.80	0.004
Incarceration⁶						
Yes vs. no	0.51	0.28 - 0.94	0.030	0.52	0.28 - 0.97	0.039

Characteristic	HR ¹	95% CI ²	p - value	AHR ³	95% CI	p - value
Methadone maintenance therapy ⁷						
Yes vs. no	2.36	1.58 - 3.54	<0.001	2.41	1.59 - 3.66	<0.001
Year of observation						
Per year later	1.05	0.99 - 1.10	0.084	1.06	1.00 - 1.12	0.011
ART eligibility ⁷						
Yes vs. no	2.84	1.70 - 4.75	<0.001	3.51	2.06 - 5.97	<0.001

¹Hazard Ratio;
²95% Confidence Interval;
³Adjusted Hazard Ratio;
⁴Interquartile Range;
⁵Time invariant measured at baseline;
⁶Time-updated, refers to 6 month period prior to follow-up interview;
⁷Current status.