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SOCIAL AND STRUCTURAL FACTORS ASSOCIATED WITH GREATER TIME WITH A PLASMA HIV-1 RNA VIRAL LOAD ABOVE LOG₁₀(1500) COPIES/ML AMONG ILLICIT DRUG USERS

Mary Clare Kennedy^{a,b,c}, Thomas H. Kerr^{a,b,d}, Evana Wood^{a,b,d}, Jeannie A. Shoveller^{b,c}, Julio S.G. Montaner^{b,d}, and M-J S. Milloy^{a,b,d}

^aBritish Columbia Centre on Substance Use

^bBritish Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital

^cSchool of Population and Public Health

^dDepartment of Medicine, University of British Columbia, Vancouver, British Columbia, Canada.

Abstract

Objectives: Although previous cross-sectional studies have identified correlates of detectable plasma HIV-1 RNA viral load (VL) among HIV-positive people who use drugs (PWUD), longitudinal factors associated with heightened HIV transmission potential have not been well described. Therefore, we longitudinally examined factors associated with amount of person-time spent above log₁₀(1500) copies/ml plasma among HIV-positive PWUD in Vancouver, Canada.

Design: Data were derived from a long-running prospective cohort of HIV-positive PWUD linked to comprehensive clinical records including systematic VL monitoring.

Methods: We used generalized estimating equations modeling to longitudinally examine factors associated with person-time (in days) with a VL more than log₁₀(1500) copies/ml plasma in the previous 180 days.

Results: Between December 2005 and May 2014, 845 PWUD were eligible and included in the study. Participants spent an average of 26.8% of observation time with a VL more than log₁₀(1500) copies/ml. In multivariable analyses, homelessness (Adjusted Rate Ratio [ARR] = 1.45) and lack of social support (ARR = 1.27) were positively associated with person-time with a VL more than log₁₀(1500) copies/ml. Older age (ARR = 0.97) and enrolment in addiction treatment (ARR = 0.75) were negatively associated with the outcome in multivariable analyses (all $P < 0.05$).

Conclusion: Social and structural factors, including periods of homelessness or lacking in social support, were independently associated with greater amount of time with heightened HIV

Correspondence: M-J S. Milloy, PhD, Assistant Professor, Research Scientist, B.C. Centre on Substance Use, B.C. Centre for Excellence in HIV/AIDS, St. Paul's Hospital, University of British Columbia, 608-1081 Burrard Street, Vancouver, BC, V6Z 1Y6, Canada. Tel: +1 604 558 6683; fax: +1 604 806 9044; bccsu-mjsm@cfenet.ubc.ca.

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transmission potential. These findings suggest the need for targeted efforts to address modifiable contextual factors that contribute to increased risk of onward HIV transmission among PWUD.

Keywords

HIV/AIDS; illicit drug use; prospective cohort; transmission; viral load

INTRODUCTION

Significant advances in the development of combination antiretroviral therapy (ART) have played a central role in reducing HIV-related morbidity and mortality among many HIV-seropositive populations worldwide [1]. Optimal and sustained adherence to ART has been shown to reliably suppress plasma HIV-1 RNA viral load (VL) to undetectable concentrations, impeding HIV disease progression and virtually eliminating risk of onward vertical, sexual or parenteral transmission [2,3]. In light of this evidence, numerous jurisdictions have adopted the United Nations-endorsed HIV Treatment-as-Prevention (TasP) approach, which aims to scale up access and adherence to ART among all people living with HIV to not only reduce HIV-related morbidity and mortality but to also curb the incidence of new infections [4].

Strong evidence demonstrates the effectiveness of ART among HIV-positive people who use illicit drugs (PWUD) at the individual and community level [1,5–7]. Unfortunately, many members of this key population continue to contend with barriers to accessing and adhering to ART and consequently experience high levels of suboptimal virologic outcomes and onward viral transmission [8–13]. As Rhodes' risk environment framework suggests, individual, social and structural forces interact to affect HIV-related outcomes [14,15]. In previous research, behavioral factors (e.g. ongoing illicit drug use) [16], and social and structural factors [17–23], including housing instability [19–22], incarceration [23], lack of employment [24] and limited social support [22], have been associated with greater likelihood of elevated VL among PWUD. However, to date, most research in this area has focused on temporary increases in VL, often to levels that may not increase risk of onward viral transmission [25,26]. We know of no existing studies that have longitudinally characterized extended periods of time with heightened HIV transmission potential among PWUD.

One measure that has recently been employed in the investigation of the potential for onward viral transmission is amount of person-time exceeding a VL of 1500 copies/ml plasma, a VL threshold recognized for increased risk for onward HIV transmission [25]. This longitudinal measure accounts for individual heterogeneity in VL dynamics over time, allowing for a more precise estimate of cumulative transmission potential than measures relying on data from a single point or short time period [25]. However, to our knowledge, this outcome has not yet been examined among PWUD. Guided by Rhodes' risk environment framework, we therefore undertook the present study to longitudinally investigate factors associated with amount of person-time with heightened HIV transmission potential among a community-recruited cohort of HIV-positive PWUD in Vancouver, Canada, a setting with universal healthcare access and no-cost HIV treatment.

METHODS

This study was conducted using data from the AIDS Care Cohort to Evaluate Access to Survival Services (ACCESS), an ongoing prospective cohort study of HIV-seropositive PWUD in Vancouver, Canada. The specific methods employed have been described in detail elsewhere [27]. Briefly, beginning in 1996, participants were recruited through self-referral and street-based outreach from Vancouver's Downtown Eastside neighborhood, a postindustrial area with an established drug market and high levels of poverty and homelessness. ACCESS eligibility criteria include: aged 18 years or older, HIV-infected, having used illicit drugs other than or in addition to cannabis in the previous month, and having provided written informed consent.

At baseline and semi-annually, participants complete an interviewer-administered questionnaire soliciting information on sociodemographics, drug use patterns, and other characteristics and exposures. At each of these visits, participants also undergo an examination by a study nurse and provide blood samples for serologic analyses. An honorarium of CAD\$ 30 is offered to participants at each study visit. Information collected at each study interview is augmented by comprehensive information on HIV care and treatment outcomes from a province-wide centralized HIV/AIDS registry. Specifically, through a confidential linkage, a complete retrospective and prospective clinical profile all CD4+ T-cell counts, VL observations, and exposure to specific antiretroviral agents for each participant are obtained. In British Columbia, all provision of ART is centralized through a province-wide ART dispensation program, where ART and related care are provided free of charge. The ACCESS study has been approved by the University of British Columbia/ Providence Healthcare Research Ethics Board.

We included all individuals who were enrolled between December 2005 and May 2014 and had at least two VL observations during the study period. The primary outcome of interest was amount of person-time (measured in days) exceeding a VL of $\log_{10}(1500)$ copies/ml (c/ml) plasma in the previous 180 days. Using a method employed by Marks et al.[25], this was measured by examining all consecutive pairs of VL observations and the time period between these observations. First, we extracted the full record of all HIV VL tests contained in the HIV clinical monitoring registry conducted either through the study or as a result of regular clinical care. VL observations (in copies/ml) were $\log_{10}$ -transformed. Using this transformed data and the date of each VL test, we imputed the VL value for each day between every VL pair from the earliest to the final VL test. Using this recreated history of VL values and the date of each study interview, we summed the number of days with a VL more than $\log_{10}(1500)$ c/ml during each 180 day observation period.

Selection of explanatory variables was informed by Rhodes' risk environment framework and previous literature on HIV-related vulnerabilities [14–23,28]. Variables considered included: age (per year older), gender (male versus non-male), ancestry (Caucasian versus non-Caucasian), education ($\geq$ high school diploma versus $<$ high school diploma), stable relationship (married or common law versus other), injection drug use (yes versus no), non-injection drug use (yes versus no), heavy alcohol use (yes versus no), binge drug use (yes versus no), incarceration (yes versus no), homelessness (yes versus no), social support (no

sources versus ≥ 1 source), enrolment in addiction treatment (any treatment modalities including methadone maintenance therapy (MMT), detoxification and residential treatment programs) (yes versus no), CD4+ cell count (per 100 cells/ μ l), engagement in ART (≥ 1 day versus 0 days) and number of VL measurements (per unit increase in measurements). Heavy alcohol use was defined according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA) criteria for 'heavy' or 'at-risk' drinking: average of more than three alcoholic drinks per occasion or more than seven drinks per week in the past 6 months for women, and an average of more than four alcoholic drinks per occasion or more than 14 drinks in total per week in the past 6 months for men [29]. As in previous analyses [7], we defined ART engagement using dispensation data from the HIV/AIDS treatment registry. Specifically, we defined an individual as being engaged in ART if (s)he was dispensed and picked up at least one day of ART in the previous 180 days. All time-varying variables are time-updated and refer to the 6-month period prior to the study interview unless otherwise indicated.

As a first step, we used the explanatory variables described above to examine the baseline characteristics of our sample. For each strata, we calculated the percentage of participants with at least one day with a VL more than $\log_{10}(1500)$ c/ml and the mean percentage of time in the previous 180 days with a VL exceeding $\log_{10}(1500)$ c/ml plasma. Next, we fit generalized linear models with a Poisson link to model the number of days with a VL more than $\log_{10}(1500)$ c/ml, including an offset term for the total number of VL measurements in the 180 days prior to the baseline interview to generate rate ratios with 95% confidence intervals (CI). To incorporate all data observed during the study period, including multiple observations per participant, we used generalized estimating equations (GEE) modeling with a log-link function for a Poisson-distributed outcome and an offset for the number of days under observation in the previous 6 months to estimate the crude association between each explanatory variable and the outcome. Finally, we constructed a multivariable GEE Poisson model using an a priori-defined backwards selection procedure based on examination of quasiliikelihood under the independence model criterion statistic (QIC). In brief, we first fit a model that included all explanatory variables associated with the outcome at the level of $P < 0.10$ in bivariable analyses. After examining the QIC of the model, we sequentially removed the variable with the largest P-value and built a reduced model. We continued this iterative process and selected the multivariable model with the lowest QIC [30]. We did not include ART engagement in the process to build the final multivariable model, as we hypothesized that this lay on the causal pathway between the explanatory variables of interest and the outcome. All bivariable and multivariable GEE analyses were adjusted for number of VL measurements.

Finally, as a sensitivity analysis, we sought to determine whether restricting our sample to individuals who had a least one day with a VL more than $\log_{10}(1500)$ c/ml during the study period would alter our results. To do so, we applied the same a priori-defined multivariable model building procedure used with the full sample to this restricted sample. We conducted all statistical analyses with R version 3.2.0 (The R Foundation, Vienna, Austria). All P values are two-sided.

RESULTS

Between December 2005 and May 2014, 845 HIV-positive PWUD who had at least two VL observations were recruited and included in this study. Of these, 581 (69%) were male and 464 (55%) self-reported Caucasian ancestry. Over the study period, participants contributed 3366 person-years of follow-up, with a median follow-up duration of 47.1 (inter-quartile range [IQR]: 23.6–69.5) months. Time with a VL more than $\log_{10}(1500)$ c/ml was calculated using data from 17693 VL observations, or a median of 3 (IQR: 2–3) per 180-day observation period or 19 (IQR: 8–30) per participant.

At baseline, the mean percentage of time in the previous 180 days with a VL more than $\log_{10}(1500)$ c/ml was 43.0 (95% CI: 42.7–43.2). Table 1 presents the baseline characteristics of the sample with the percentage of participants with at least one day with a VL more than $\log_{10}(1500)$ c/ml and the mean percentage of time with a VL more than $\log_{10}(1500)$ c/ml for each strata. Over the study period, the mean percentage of time with a VL more than $\log_{10}(1500)$ c/ml was 26.8 (95% CI: 26.7–26.9), which declined from 56.4% (95% CI: 55.9–56.9) during the earliest interview period to 11.7% (95% CI: 11.5–11.9) during the final interview period. Of 845 participants, 575 (68.0%) had at least one day with a VL more than $\log_{10}(1500)$ c/ml during the study period.

Table 2 presents the results of the crude and adjusted estimates of the relationship between the explanatory variables and amount of person-time with a VL exceeding $\log_{10}(1500)$ c/ml plasma. In multivariable analyses, homelessness [adjusted rate ratio (ARR) = 1.45; 95% CI: 1.32–1.60, $P < 0.001$] and lack of social support (ARR = 1.27; 95% CI: 1.16–1.40, $P < 0.001$) were positively associated with amount of person-time spent exhibiting a VL more than $\log_{10}(1500)$ c/ml plasma. Older age (ARR = 0.97 per year; 95% CI: 0.96–0.98, $P < 0.001$) and enrolment in addiction treatment (ARR = 0.75; 95% CI: 0.67–0.85, $P < 0.001$) were negatively associated with amount of person-time spent with a VL more than $\log_{10}(1500)$ c/ml plasma in multivariable analyses.

In the multivariable model restricted to individuals who had at least one day with a VL more than $\log_{10}(1500)$ c/ml during the study period, periods of incarceration (ARR = 1.42; 95% CI: 1.03–1.96, $P = 0.035$) were positively associated with amount of person-time spent exhibiting a VL more than $\log_{10}(1500)$ c/ml plasma. Periods of lacking social support (ARR = 1.40; 95% CI: 0.98–2.00, $P = 0.063$) were marginally associated with greater time above this VL threshold in adjusted analyses among the restricted sample (data not shown).

DISCUSSION

In the present study, we observed that periods of heightened HIV transmission potential were common among a community-recruited prospective cohort of 845 HIV-positive PWUD in Vancouver, Canada, with two-thirds of study participants spending at least one day with a VL more than $\log_{10}(1500)$ c/ml over a median follow-up duration of 47 months. On average, participants spent 26.8% of observation time with a VL above this threshold. In multivariable analyses, periods of homelessness or lacking social support were independently associated with greater amount of person-time exhibiting a VL above

$\log_{10}(1500)$ c/ml. Enrolment in addiction treatment and older age were each independently associated with a shorter amount of person-time above this VL threshold. In a sensitivity analysis restricted to individuals who had at least one day with a VL more than $\log_{10}(1500)$ c/ml, incarceration was significantly and positively associated with observation time with a VL above this threshold and lack of social support was marginally and positively associated with the outcome in a multivariable model.

This study adds to a growing body of evidence pointing to the contribution of aspects of the broader risk environment of PWUD to HIV-related vulnerabilities [15,18–23,31]. The current study extends on insights gained from previous studies, which have primarily focused on risk factors for HIV acquisition, to demonstrate that social and structural factors, including homelessness and a lack of social support, were independently associated with prolonged periods of time with heightened risk of onward viral transmission among PWUD. As has been noted in previous studies [19,32], these associations likely operate through lower levels of optimal engagement in ART. Concurrently, illicit drug use behaviors were not significantly associated with transmission potential after adjusting for social, structural and other factors. Given that this study was conducted in a setting with no-cost HIV treatment and universal healthcare, we believe that these findings are independent of the potential confounding influence of financial barriers to HIV care.

Our finding of an association between homelessness and greater amount of time with heightened HIV transmission potential aligns with previous studies demonstrating the adverse impacts of housing instability on ART adherence and HIV treatment outcomes among PWUD [19–22,33–35]. For example, stable housing was associated with better ART adherence in a multisite prospective study of people who inject drugs in the United States [34]. Similar findings have been observed even in settings with universal access to no-cost HIV treatment and universal care [19–21,34]. For instance, in a previous study of PWUD in Vancouver, we found that homelessness was independently associated with a lower rate of VL suppression following ART initiation, an association mediated by lower levels of ART adherence [19]. A number of conditions associated with homelessness likely account for the observed relationship between periods of homelessness and greater amount of time with heightened VL. Specifically, homeless individuals may lack space in which to safely store medications, and may suffer from food insufficiency, which has previously been linked to suboptimal virologic outcomes [36]. Additionally, immediate concerns relating to securing basic needs, including temporary shelter, likely take precedence over the secondary demands of engaging in HIV care [37,38]. Moreover, homeless individuals may be more likely to engage in prohibited income generating activities such as sex work [39], to have higher intensity drug use patterns [40,41], to experience violence [42], and be the subject of criminalization [43], all of which may further complicate access to HIV care and ART adherence [16,23,32].

The present study also demonstrated an association between periods of lacking in social support and greater amount time with heightened HIV transmission potential. This finding builds on existing research suggesting a protective role of social support on HIV disease progression among PWUD [22,44–46]. For example, a multisite cross-sectional study of PWUD on ART in the United States found that those with high levels of social support had

more than four times the odds of achieving VL suppression (≤ 500 c/ml) compared to those with low levels of support [22]. The association we observed between lack of social support and heightened HIV transmission potential is likely explained by the mediating role of a number of factors related to deficiencies in social support. For instance, limited instrumental assistance (e.g. shared resources, assistance with obtaining medication refills), less consistent contact with healthcare providers, and higher levels of stress or depression, may hinder ART adherence [22,33,47–50]. However, further research is needed to better understand underlying explanations for this association.

We also observed that enrolment in addiction treatment, such as MMT, detoxification or residential treatment programs, was associated with shorter duration of time with heightened risk of onward viral transmission. This is consistent with previous work indicating that engagement in addiction treatment, particularly opioid agonist treatment such as MMT, contributes to improved HIV treatment outcomes among PWUD [51–56]. Specifically, studies have found that opioid-dependent PWUD engaged in opioid agonist treatment are more likely to initiate and optimally adhere to ART [51–53,55], as well as achieve viral suppression [54,56]. Engagement in such treatment likely decreases onward viral transmission potential through various mechanisms. For example, participation in addiction treatment may contribute to greater overall stability that allows for better ART adherence [52]. Further, addiction treatment engagement may enable more consistent contact with healthcare professionals to monitor HIV disease progression and administer and adjust ART treatment [54].

Our study also revealed that incarceration was associated with greater time with heightened HIV transmission potential among individuals who had at least one day with a VL above the $\log_{10}(1500)$ c/ml threshold during follow up. This finding extends on previous studies demonstrating links between exposure to correctional environments and suboptimal immunologic and virologic outcomes among PWUD in Vancouver and other settings [23,57,58]. This association is likely explained by factors that may complicate ART access and adherence in many correctional environments, including interruptions or delays in obtaining appropriate HIV medications, poor relationships with correctional healthcare professionals, and efforts to conceal HIV serostatus from other inmates due to fear of discrimination and violence [59].

Our findings underscore the need for policies and programs that target contextual drivers of suboptimal HIV treatment outcomes and risk of onward viral transmission among PWUD. For example, interventions that aim to improve housing stability among marginally housed PWUD may confer benefits not only on HIV-related morbidity and mortality but also on HIV transmission. Indeed, a recent local study estimated that eliminating homelessness could increase levels of viral suppression by 15% among the entire population of HIV-positive PWUD and by 82% among homeless HIV-positive PWUD specifically [60]. Several existing studies suggest that providing low-threshold or harm reduction-based housing (i.e. housing support that does not require abstinence from illicit drug use) or other forms of housing assistance may improve HIV treatment outcomes [61,62]. For instance, a randomized trial found that the provision of supportive housing combined with intensive case management to homeless HIV-positive individuals in Chicago resulted in lower median

VL at 12 months compared to the control arm of discharge planning and referral services [61]. Another study evaluated a Housing First initiative in New York City and found that VL suppression increased from 27 to 69% post intervention among homeless people living with HIV [62]. However, this study was limited by its small sample size, nonexperimental design, and lack of control group, and therefore further rigorous evaluation is needed to determine the effectiveness of specific housing interventions, including Housing First models, in improving HIV treatment outcomes. Nonetheless, these and our findings suggest that such interventions may help to prevent onward viral transmission among marginally housed PWUD.

Our findings also suggest the need for interventions designed to enhance social support among HIV-positive PWUD with limited support availability. As PWUD often contend with substantial contextual barriers to engagement in HIV treatment and care, including criminalization, stigma, discrimination, poverty and housing instability, support interventions that are responsive to these vulnerabilities may be more likely to promote the successful management of HIV and decrease risk of onward transmission [63,64]. For example, recent studies have found that complementing TasP initiatives with low-barrier programs that are tailored to the specific needs of PWUD and address multiple social and structural barriers to care simultaneously may help to promote ART adherence and VL suppression [63,64]. Thus, such programs should be scaled up as part of broader TasP-based efforts, and future research should continue to investigate how these may be optimized to better facilitate engagement and retention in HIV care among PWUD.

Policy and programmatic interventions that aim to improve access and adherence to addiction treatment as a means for preventing HIV transmission are also needed. In particular, evidence-based addiction treatment therapies, including MMT and other opioid agonist treatments, remain underutilized in many settings, despite being among the most cost-effective interventions for HIV prevention among PWUD [65]. Indeed, these treatments are illegal or not provided in many international settings, including those contending with uncontrolled outbreaks of HIV [66,67]. Further, in jurisdictions where such treatments are available, PWUD often face considerable systemic and programmatic barriers to access and adherence [68,69]. As such, there is a continued need to expand access to and improve engagement with MMT and other opioid agonist treatments in effort to reduce HIV disease progression and curb onward transmission. Additionally, studies investigating novel pharmacotherapies for the treatment of substance use disorder, including injectable opioid agonist treatments and potential substitution therapies for stimulant users, should be prioritized.

This study has several limitations. First, the ACCESS cohort is a nonrandom sample and therefore our findings may not be generalizable to HIV-positive drug-using populations in local or other settings. Second, this study included some data derived from self-report and therefore may be subject to reporting biases, including socially desirability bias. In addition, the methods employed herein may have overestimated or underestimated amount of person-time exceeding a VL of $\log_{10}(1500)$ c/ml, as these estimations were based on an assumption of a linear relationship between increments in time and increments in VL between consecutive VL observations [25].

In summary, we observed that periods of heightened HIV transmission potential were common among HIV-positive PWUD in a setting of no-cost HIV treatment and universal healthcare, with participants spending an average of 26.8% of observation time with a VL exceeding $\log_{10}(1500)$ c/m l plasma over a median of 47 months of observation. Periods of homelessness or lacking in social support were associated with a greater amount of person-time with a VL exceeding $\log_{10}(1500)$ c/m l plasma, while engagement with addiction treatment was associated with shorter amount of time exceeding this VL threshold. These findings highlight the need for targeted efforts to address modifiable social and structural factors that contribute to heightened risk of onward HIV transmission among PWUD.

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M-J.S.M. had full access to the data in the study and takes full responsibility for the integrity of the data and accuracy of the data analysis. M-J.S.M. conceived and conducted the statistical analyses. M.C.K. drafted the manuscript and incorporated suggestions from all co-authors. M-J.S.M., T.H.K., E.W., J.A.S. and J.S.G.M. revised the manuscript and contributed important intellectual content. All authors have read and approved the final version of the manuscript.

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Table 1.

Baseline characteristics and unadjusted rate ratios associated with person-time exceeding an HIV viral load of $\log_{10}(1500)$ copies/ml plasma among 845 HIV-positive people who use drugs in Vancouver, Canada (2005–2014).

Characteristic	Rate ratio	
	Unadjusted rate ratios (95% CI)	Adjusted rate ratios (95% CI)
Age ^a		
Per year older	0.96 (0.96–0.97)	0.97 (0.96–0.98)
Ancestry ^a		
Caucasian versus non-Caucasian	0.89 (0.77–1.04)	
Gender ^a		
Male versus Non-male	0.79 (0.68–0.91)	0.87 (0.75–1.01)
Education ^a		
High school diploma versus < High school diploma	1.10 (0.95–1.28)	
Social support ^{a,b}		
No sources versus 1 source	1.49 (1.34–1.65)	1.27 (1.16–1.40)
Stable relationship ^{a,b}		
Married/common-law versus other	1.01 (0.89–1.16)	
Injection drug use ^{a,b}		
Yes versus no	1.35 (1.18–1.55)	1.11 (0.97–1.26)
Non-injection drug use ^{a,b}		
Yes versus no	1.28 (1.08–1.51)	1.07 (0.91–1.26)
Heavy alcohol use ^{a,b}		
Yes versus no	1.26 (0.98–1.63)	1.13 (0.86–1.48)
Binge drug use ^{a,b}		
Yes versus no	1.17 (1.07–1.29)	1.07 (0.98–1.16)
Incarceration ^{a,b}		
Yes versus no	1.47 (1.30–1.66)	1.00 (0.89–1.13)
Homeless ^{a,b}		
Yes versus no	1.91 (1.73–2.11)	1.45 (1.32–1.60)
Enrolment in addiction treatment ^{a,b}		
Yes versus no	0.79 (0.70–0.90)	0.75 (0.67–0.85)
CD4 ⁺ cell count ^{a,b}		
Per 100 cells/ μ l	0.81 (0.78–0.84)	0.83 (0.80–0.86)
ART engagement ^{a,b}		
1 day versus 0 days dispensed	0.21 (0.19–0.24)	
Number of VL measurements ^b		

Characteristic	Rate ratio	
	Unadjusted rate ratios (95% CI)	Adjusted rate ratios (95% CI)
Per unit increase	0.94 (0.90–0.98)	0.97 (0.93–1.00)

ART, antiretroviral therapy; CI, confidence interval.

^aRate ratios were adjusted for number of viral load observations in each 180-day period.

^bRefers to 6 month period prior to study interview.

Table 2.

Generalized estimating equation analyses of factors associated with person-time exceeding an HIV viral load of $\log_{10}(1500)$ copies/ml plasma among 845 HIV-positive people who use drugs in Vancouver, Canada (2005–2014).

Characteristic	<i>n</i> (%)	<i>n</i> (%) with 1 day VL > $\log_{10}(1500)$ c/ml ^{<i>b</i>}	Mean % person-time VL > $\log_{10}(1500)$ c/ml ^{<i>b</i>}	Rate ratio (95% CI)
Age ^{<i>a</i>}				
>42.7 years ^{<i>c</i>}	425 (50.3)	205 (41.2)	37.4	0.65 (0.58–0.74)
42.7 years	420 (49.7)	292 (58.8)	55.7	
Ancestry ^{<i>a</i>}				
Caucasian	483 (57.2)	278 (55.9)	45.3	0.95 (0.84–1.08)
Non-Caucasian	362 (42.8)	219 (44.1)	48.1	
Gender ^{<i>a</i>}				
Male	559 (66.2)	322 (64.8)	44.6	0.87 (0.76–0.99)
Non-male	286 (33.8)	175 (35.2)	50.4	
Education ^{<i>a</i>}				
High school diploma	386 (45.7)	220 (44.3)	44.9	0.94 (0.83–1.06)
<High school diploma	459 (54.3)	277 (55.7)	47.9	
Social support ^{<i>a,b</i>}				
1 source	584 (69.1)	344 (69.2)	47.4	1.05 (0.92–1.20)
No sources	261 (30.9)	153 (30.8)	44.6	
Stable relationship ^{<i>a,b</i>}				
Married or common-law	231 (27.3)	141 (28.4)	49.7	1.11 (0.97–1.27)
Other	614 (72.7)	356 (71.6)	45.3	
Injection drug use ^{<i>a,b</i>}				
Yes	670 (79.3)	417 (83.9)	49.3	1.46 (1.24–1.73)
No	175 (20.7)	80 (16.1)	36.0	
Non-injection drug use ^{<i>a,b</i>}				
Yes	777 (92.0)	458 (92.2)	46.2	0.86 (0.69–1.08)
No	68 (8.0)	39 (7.8)	50.4	
Heavy alcohol use ^{<i>a,b</i>}				
Yes	32 (3.8)	18 (3.6)	43.0	1.04 (0.73–1.44)
No	813 (96.2)	479 (96.4)	46.7	
Binge drug use ^{<i>a,b</i>}				
Yes	370 (43.8)	219 (44.1)	45.6	0.98 (0.87–1.11)
No	475 (56.2)	278 (55.9)	47.2	
Incarceration ^{<i>a,b</i>}				
Yes	116 (13.7)	81 (16.3)	55.0	1.24 (1.04–1.46)

Characteristic	<i>n</i> (%)	<i>n</i> (%) with 1 day VL >log ₁₀ (1500)c/ml ^{<i>b</i>}	Mean % person-time VL >log ₁₀ (1500) c/ml ^{<i>b</i>}	Rate ratio (95% CI)
No	729 (86.3)	416 (83.7)	45.2	
Homelessness ^{<i>a,b</i>}				
Yes	266 (31.5)	202 (40.6)	59.7	1.55 (1.37–1.76)
No	579 (68.5)	295 (59.4)	40.4	
Enrolment in addiction treatment ^{<i>a,b</i>}				
Yes	406 (48.0)	226 (45.5)	43.6	0.85 (0.75–0.96)
No	439 (52.0)	271 (54.5)	49.2	
CD4 ⁺ cell count ^{<i>a,b</i>}				
>360 cells/μl	420 (49.7)	212 (42.7)	38.2	0.78 (0.69–0.88)
360 cells/μl	425 (50.3)	285 (57.3)	54.8	
ART engagement ^{<i>a,b</i>}				
1 day dispensed	510 (60.4)	207 (41.6)	28.7	0.32 (0.29–0.37)
0 days dispensed	335 (39.6)	290 (58.4)	73.7	

ART, antiretroviral therapy; CI, confidence interval.

^{*a*}Rate ratios were adjusted for number of viral load observations in the previous 180 days.

^{*b*}Refers to 6-month period prior to study interview

^{*c*}Median age = 42.7 years.