

Understanding the correlates of attrition associated with antiretroviral use and viral suppression among women living with HIV in Canada

Running head: ARV USE AND VIRAL SUPPRESSION AMONG WLWH IN CANADA

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Manuscript keywords (search terms): HIV, women, CHIWOS, ARV use, viral suppression

ABSTRACT

Attrition along the cascade of HIV care compromises attainment of the UNAIDS 90-90-90 goals and achievement of desirable treatment outcomes for people living with HIV. Given known gender disparities in HIV care and outcomes, understanding the correlates of attrition at stages of the care cascade for women living with HIV (WLWH) is essential. Among the 1,425 WLWH enrolled in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS), we measured the proportion who reported not being currently on combination antiretroviral therapy (cART) and the proportion who reported a detectable viral load (≥ 40 copies/mL) despite cART use. Correlates of these cascade indicators were examined using univariate and multivariable logistic regression. Overall, 14.8% of women were not currently on cART. Of women who were on cART, 9.0% were not virally suppressed. In multivariable analyses, age between 26 and 34, unstable housing, food insecurity, current injection drug use, higher HIV-related stigma, and racial discrimination were associated with increased odds of not being on cART. Factors associated with increased odds of reporting a detectable VL among women on cART included age ≤ 34 years, less than a secondary education, unstable housing, and incarceration in the previous year. Programmatic efforts to support cART use and viral suppression for WLWH in Canada should focus on social determinants of health, including housing and food insecurity, social exclusion and education.

Introduction

For the benefits of combination antiretroviral therapy (cART) to be realized, people living with HIV (PLWH) must be fully engaged along the cascade of care – a continuum of care from the time of diagnosis to the provision of cART to ensure viral suppression^{1,2}. The use of cART, with sustained viral load (VL) suppression, is associated with [an exceedingly low risk of transmission](#)³; the concept of “Treatment as Prevention (TasP)” has been widely supported by several studies and mathematical modeling⁴⁻⁸ and is becoming more commonplace with the rise in pre- and post-exposure prophylaxis (PrEP and PEP).⁹ Incomplete engagement at any stage of the cascade will compromise the full benefits of cART at both the individual and societal level, and will result in increased risk of HIV-related morbidity, mortality and transmission.¹⁰ Thus disparities in cART prescription, uptake and adherence, and subsequent VL suppression are of paramount importance and have been prioritized by UNAIDS in their 90-90-90 objectives.¹¹

Women comprise 50% of all PLWH worldwide, and a growing body of evidence reveals marked gender disparities along the cascade of care.¹²⁻²⁰ Recent data from the United States (US) show that while a larger percentage of women living with HIV (WLWH) are retained in care compared to men, a smaller percentage are on cART and are virally suppressed.^{13,14} Similar findings have emerged from Canada that demonstrate women are less likely than men to be engaged along all aspects of the cascade of care.¹⁵⁻¹⁹ While it appears as though overall engagement in the cascade is improving with time for both men and women, attrition at each stage of the care cascade continues.^{21,22}

Few studies have focused on barriers to cART use among women specifically. There are ethno-racial disparities in cART use; in the US, women of Hispanic or Black ethnicities are significantly less likely to be using cART than white/Caucasian women.^{12,13,23-25} WLWH also

experience more psychosocial barriers to cART use including stigma, depression, substance and alcohol use.^{23,26,27} A large body of research has confirmed that the absence of health insurance compromises access to HIV care in the US including access to cART.²⁸⁻³⁰ Prior studies have shown similar barriers to VL suppression for WLWH.^{12,13} Barriers have been reported along social inequities,¹² among those of younger age,^{12,13} or with lower levels of education,²¹ and among those lacking financial resources.¹² Psychosocial barriers precluding VL suppression include depression, substance use and incarceration.¹²

In Canada, women's lack of access to cART has primarily been examined among women who experience marginalization, including women who inject drugs and women involved in sex work.^{15,31} There are limited studies looking at the broader socio-demographic profile and barriers of cART access and VL suppression among WLWH in a setting with universal access to health care. The purpose of this study was to determine the proportion of Canadian WLWH who are currently not on cART, and who report a detectable VL despite cART use among a large sample of women participating in a national study. Secondly, we aimed to identify factors associated with not currently being on cART and factors associated with having a detectable viral load among Canadian women who were taking cART.

Methods

Study Population and Design

This study utilized baseline data collected between August 2013 and May 2015 from 1,425 WLWH participating in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS), a community-based, participatory, prospective cohort study of WLWH from Ontario, Quebec, and British Columbia (BC).^{32,33} The overall inclusion criteria were: 1) self-identifying as a woman (trans-inclusive), 2) living with HIV, 3) being 16 years of age or older

and 4) living in Ontario, BC or Quebec. For this analysis, we further restricted the inclusion criteria to women who answered the question on cART use (current or prior) (n=1,382).

Data Collection

WLWH, who were trained as peer research associates (PRAs), recruited self-identified WLWH aged 16 years or older from one of the three study provinces. Purposive, non-random, and venue-based sampling methods including word-of-mouth and online (e.g., Listservs for WLWH) methods were used to recruit participants. Participants were recruited from AIDS service organizations (ASOs), HIV clinics, community-based organizations (CBOs), and ethno-racial specific ASOs and CBOs. PRAs, then, administered a 90-minute structured, online questionnaire either in-person (e.g., home, HIV clinic), or by phone/Skype for rural or remotely located participants. A \$50 honorarium was given for participation.

Ethics approval was obtained from the respective Research Ethics Boards (REBs) of Women's College Hospital, Simon Fraser University and the University of British Columbia/Providence Health, and McGill University Health Centre. Study sites with independent REBs obtained their own approval prior to commencing enrolment. All participants gave informed consent prior to commencing the survey.

Outcome variables

Participants who reported ever accessing HIV medical care were asked about their history of cART use and categorized as never having used cART, used cART previously but not currently, and currently using cART. For the purpose of this analysis, those reporting previously but not currently using cART (n=67) and never using cART (n=137) were categorized as not currently

using cART (n=204) and compared to those who reported currently being on cART (n=1,178). Participants who reported ever accessing HIV medical care were asked about their most recent VL, categorized as undetectable (< 40 copies/mL), detectable (≥ 40 copies/mL), never received, don't know, or prefer not to answer (DK/PNTA). Those who reported undetectable or detectable VLs were included in the analysis and compared (n=1,130). All DK/PNTA or missing responses were excluded.

Correlates of cART use and viral suppression

Sociodemographic factors of interest included age, sexual orientation, immigration status, ethnicity, education, personal gross yearly income, main source of income (social assistance, jobs considered illegal (sex work, selling drugs, pan-handling), savings/loan/family, honoraria/other vs. paid job), and number of financial dependents. We assessed several other factors known to correlate with different points along the care cascade, including categorical variables such as: housing status (own, rent vs. unstable (self-contained room, housing facility, HIV care group home, transition/halfway/safe/outdoor housing or other), food security (insecure vs. secure), incarceration (current vs. previous and never), history of injection drug use (IDU) (currently vs. not currently but previously and never), method of HIV acquisition (non-consensual sex, sharing needles/contaminated needles, blood transfusion/other medical procedures, perinatal exposure, or other vs. consensual sex) and duration of time living with HIV (6 to 14 years or greater than 14 years vs. less than six years).

We also explored the association between each outcome and various continuous scaled measures such as depression, social support, HIV-related stigma, racial discrimination, and gender discrimination. We determined score ranges and Cronbach's alpha for the analytic sample

(n=1,382) who responded regarding cART use. Depression was measured using the 10-item CES-D (score range: 0-30; Cronbach's alpha=0.88).³⁴ Social support was measured using the 4-item version of the Medical Outcomes Survey Social Support Survey (MOS-SSS; score range: 4-20 with higher scores indicating higher social support; Cronbach's alpha=0.84).³⁵ HIV-related stigma was measured using the total score of the HIV Stigma Scale³⁶⁻³⁸ (score range: 0-100 with higher scores indicating higher IV stigma; Cronbach's alpha=0.84). Racial and gender discrimination were measured using two separate modified (8-item) versions of the 9-item Everyday Discrimination Scale (score range: 8-48 for both scales with higher scores indicating higher racial and gender discrimination; Cronbach's alpha= 0.96 for racism, 0.936 for sexism among cisgender women, 0.949 for gender discrimination among trans women and other gender identified participants).^{39,40}

Statistical Analyses

All outcomes and hypothesized factors associated with each outcome were described using medians and interquartile ranges (IQR) for continuous variables and frequencies and proportions for categorical variables. In bivariable analyses, categorical variables were compared using the Pearson's chi-squared or Fisher's exact test, and continuous variables were compared using the Wilcoxon rank-sum test. Logistic regression was used to study the univariate and multivariable associations between the explanatory variables and each outcome (never or not currently using cART vs. currently using cART; not being virally suppressed vs. viral suppression). Factors significant at $p < 0.05$, as well as correlates chosen a priori, were considered for the multivariable model. Model selections were conducted using a backward stepwise technique based on the Type III p-values and Akaike Information Criterion (AIC). The variable with the highest Type III p-value was dropped at each step of the selection process until the model reached the lowest AIC

(lower AIC indicates better model fit). All p-values were two-sided and considered statistically significant at $\alpha = 0.05$. Analyses were conducted using SAS version 9.4 (SAS, North Carolina, United States).⁴¹

Results

Participant sociodemographic and clinical characteristics

Overall, 85.2% (n=1,178/1,382) of women were on cART while 14.8% (n=204/1,382) of women were not currently receiving cART. Of those not receiving cART, 67.2% (n=137/204) had never received cART and 42.2% (n=86/204) reported a CD4 T+ cell count of greater than 500 cells/mm³. Table 1 summarizes the sociodemographic and clinical characteristics of women with complete data regarding cART use. The median age of women on cART was 44 (IQR 37-51) years vs. 36 (IQR 32-44) years for those not on cART (p<0.001). The majority (96.3%) of women on cART self-identified as cisgender vs. 93.1% for those not on cART (p=0.04). Similarly, 88.4% of women on cART self-identified as heterosexual vs. 80.9% for those not on cART (p=0.002). Women on cART were predominantly of white (40.7%) or African, Caribbean or Black (ACB) ethnicities (31.9%) vs. women not on cART were primarily of white (46.6%) or Indigenous (31.4%) ethnicities (p<0.001). Among women on cART, 91.0% women reported an undetectable viral load vs. 39.9% for those not on cART (p< 0.001).

Factors associated with not currently being on cART (n=204) compared to those currently on cART (n=1,178)

Table 2 shows the unadjusted and adjusted odds (aOR) of not currently being on cART compared to current cART. In unadjusted analyses, being less than or equal to 25 years of age or

26 to 34 years of age vs. greater than 35, of sexual minority status vs. heterosexual, selling drugs, pan-handling or sex work as the main source of income vs. a paid job, having less than two financial dependents vs. two to three, unstable housing vs. owning, food insecurity, current IDU, having greater social support and higher HIV-related stigma, racial and gender discrimination were all associated with increased odds of not being on cART. Persons of ACB ethnicity vs. white/Caucasian, having less than a secondary education vs. a post-secondary education, acquiring HIV through non-consensual sex, sharing needles, or through blood transfusion/other medical procedures vs. consensual sex, being diagnosed with HIV between 6 and 14 years ago or greater than 14 years ago vs. less than 6 years ago, and depression were associated with reduced odds of not being on cART. In multivariable logistic regression, age [being 26 to 34 years of age (aOR: 1.84, 95% CI: 1.15, 2.95) vs. greater than 35], unstable housing (aOR: 2.51, 95% CI: 1.08, 5.87) vs. owning, food insecurity (aOR: 1.69, 95% CI: 1.01, 2.83), current IDU (aOR: 2.56, 95% CI: 1.28, 5.15) and racial discrimination (aOR: 1.03, 95% CI: 1.01, 1.06) were associated with increased odds of not being on cART. ACB vs. white/Caucasian ethnicity (aOR: 0.32, 95% CI: 0.17, 0.59), having less than a secondary education vs. post-secondary (aOR: 0.35, 95% CI: 0.17, 0.75), having a personal income of less than \$20 000 (aOR: 0.30; 95% CI: 0.15, 0.59) or \$20 000 to \$40 000 per year (aOR: 0.31, 95% CI: 0.15, 0.67) vs. greater than \$40 000 per year, acquiring HIV through non-consensual sex (aOR: 0.40, 95% CI: 0.21, 0.75) or sharing needles (aOR: 0.52, 95% CI: 0.29, 0.93) vs. consensual sex, living with HIV for six to 14 years (aOR: 0.40, 95% CI: 0.26, 0.64) or greater than 14 years (aOR: 0.28, 95% CI: 0.16, 0.49) vs. less than six years, and depression (aOR: 0.97, 95% CI: 0.94, 0.99) were associated with decreased odds of not being on cART.

Factors associated with having a self-reported detectable viral load, among those on cART

Of the 1,178 women on cART, 91.0% had an undetectable VL and 9.0% had detectable VLs.

Table 3 shows the unadjusted and adjusted odds of having a self-reported detectable VL compared to an undetectable VL among women on cART. In univariate logistic regression analyses, factors associated with higher odds of having a self-reported detectable VL among women on cART included: being 25 years of age or less vs. over 35, of sexual minority status vs. heterosexual, Indigenous vs. white/Caucasian, having less than a secondary or a secondary education vs. post-secondary, having any source of income (except savings/loan/family) vs. a paid job, earning between \$20 000 to \$40 000 per year vs. greater than \$40 000 per year, renting or unstable housing vs. owning, food insecurity, incarceration ever or last year vs. never, current IDU, and depression. Factors associated with lower odds of having a detectable VL among women on cART included: ACB vs. white/Caucasian ethnicity and having more than three financial dependents vs. two to three. In multivariable analysis, factors associated with significantly increased odds of having a self-reported detectable VL among women on cART included age [being under the age of 25 (aOR: 3.11, 95% CI: 1.26, 7.66) or between the ages of 26 and 34 (aOR: 1.93, 95% CI: 1.05, 3.54) vs. over 35], less than a secondary education (aOR: 2.50, 95% CI: 1.25, 4.79) vs. post-secondary, unstable housing (aOR: 5.21, 95% CI: 1.15, 23.60) vs. owning, and incarceration in the previous year (aOR: 2.89, 95% CI: 1.32, 6.34) vs. never.

Discussion

Our study utilized the cascade of HIV care framework to identify sociodemographic, psychosocial and clinical care factors associated with attrition at the points of cART use and VL suppression. In this study of 1,382 WLWH in Canada, 85.2% of women were taking cART, among whom 91.0% reported suppressed VLs. Among the remaining 14.8% of women who

were not taking cART, only 39.9% reported undetectable VLs. While these proportions are somewhat better than women in other industrialized countries such as the US,⁹ they are still less than the 90% cART use and viral suppression targets recommended by UNAIDS.¹⁰ These findings have important implications for both individual WLWH, as well as for health care policies and practices in Canada.

Despite the current international guidelines recommending early initiation of cART, approximately 15% of Canadian WLWH were not currently on cART.⁷ This may in part be explained by having used baseline data from WLWH as early as 2013, at which point cART was still being prescribed based on a CD4 count cut-off of less than 500 cells/ μ l.⁴² In fact, 42.4% of women who were not on cART reported a CD4 cell count of greater than 500 cells/ μ l, indicating that there was a sizeable proportion of women who were not on cART due to medical ineligibility at the time of interview. As such, our findings may be underestimating the true proportion of WLWH who were on cART. Another plausible explanation is that some of the women not on cART represented elite controllers or long-term non-progressors (approximately 40% of these women reported suppressed VLs). Since current guidelines fail to make strong recommendations for or against cART in this population, the majority of elite controllers remain off cART.⁷ However, more recently, experts have been recommending cART for elite controllers due to inflammatory cardiovascular benefits.^{43,44} Other WLWH may have chosen not to take cART for various reasons such as concomitant substance abuse, self-stigma, depression or previous negative experiences with drug toxicities.⁴⁵⁻⁴⁷ It may be worthwhile exploring women's and provider's knowledge and providers' prescribing practices following the revised guidelines as there may be a role for provider education regarding updated ART initiation guidelines.

Addressing some key sociodemographic and psychosocial correlates may help ensure that all WLWH are accessing and taking cART. Women who reported current IDU had the highest odds of not being on cART. While this may reflect less frequent contact with the health care system, evidence suggests WLWH with a known history of substance use are less likely to be prescribed cART by their providers due to provider-related stigma or fear of poor adherence and its consequences on resistance.¹² Furthermore, in our study, WLWH who endorsed racial discrimination had higher odds of not taking cART. These findings have broader implications for ongoing efforts in reducing harm associated with substance use and racial stigma and discrimination both at a structural and at a provider level. In addition, young WLWH (aged 26-34) had an almost two-fold greater risk of not being on cART. This finding raises important questions about young women's understanding of the importance of cART, as well as provider's understanding of the needs of younger women.¹⁸ Finally, food insecurity was found to be associated with higher odds of not being on cART, a finding that is likely associated with multiple factors. Food is often required for cART use and if not required, many women indicate that they get nauseated when taking cART without food.⁴⁷ Also food insecurity has been associated with poorer decision-making.⁴⁸ Finally, food insecurity is likely a surrogate marker for poverty. A better understanding of the way poverty and food insecurity affects cART use and access may be useful moving forward.

Our study findings outlining the correlates associated with viremia despite cART use parallel what has already been described in the literature.^{12,13} We found that young WLWH (≤ 25 years and between 26-34 years of age) were two to three times more likely to report detectable VLs on cART; decreasing age was directly proportional to increased risk of VL detectability. This presumably reflects issues with medication adherence (or due to lack of cART use in the

26-34 year old age category), likely due to competing factors such as substance use or depression, access, among many others. This finding reinforces the need for youth- and young adult-focused programs, as well as the prescription of single-tablet regimens containing third agents with high barriers to resistance in order to optimize adherence and minimize drug resistance.⁴⁹ We also found that WLWH who had less than a high school education had 2.5 fold higher odds reporting detectable VLs on cART. Exploring the role of education to assist with VL suppression for WLWH may be necessary as the downstream effects of low education such as poverty and non-adherence are palpable correlates associated with viral detectability. Furthermore, education captures the effect of childhood and young adulthood resource disparities, which may have long-term health consequences. The negative health effects of chronic stress brought on by poverty may be one area of inquiry. Finally, a history of incarceration in the previous year was associated with an almost three-fold increased risk of VL detectability. This is likely due to treatment interruption or difficulties maintaining adherence during the time of or just after incarceration, and is crucial to rectify through structural system changes.⁵⁰

A major social determinant of health affecting cART use and VL suppression that emerged from our study was housing insecurity. Women with unstable housing had 2.5 and over five fold higher odds not taking cART and reporting detectable VLs on cART, respectively, adding to current evidence that unstable housing is significantly associated with decreased care along the continuum of HIV care.^{51,52} Housing insecurity may itself reduce access to care, and, in addition, be a reflection of the interaction of complex social forces such as substance use, as well as poverty, lower education level, presence of mental health issues and adverse childhood experiences, among other possible contributing factors.^{26,53,54} Research and programming

focusing on women who are marginally-housed may consider developing partnerships with and providing referrals to organizations that address housing needs in addition to other intersecting factors such as substance use and food insecurity.³⁷ Recognizing the role that structural barriers have on the HIV care continuum has implications for addressing the social determinants of health when planning programmatic efforts to address attrition along the cascade of care for WLWH.

There are a few limitations to note related to this analysis and the overall study design. Importantly, a biological outcome such as VL would best be measured utilizing blood testing. However, we used self-reported VL at most recent visit, which is subject to recall and social desirability bias. To mitigate this concern, analyses were conducted to explore the validity of our self-reported VL measure, and we found a high degree of correlation between self-reported and laboratory VLs.⁵⁵ The use of venue-based sampling – whereby many participants were recruited from ASOs, CBOs, and HIV clinics – may have introduced a selection bias whereby we overestimated the proportion of women on cART.⁵⁶ However, several steps were taken to ensure adequate representation of women who experience multiple forms of social and structural marginalization (e.g., women who use substances, women who do sex work, young women) who may be outside of care.²⁷ Therefore, on the other hand, the word-of-mouth and purposive sampling may have overestimated those not on cART. The results in this analysis are not generalizable to all Canadian WLWH and must be taken in context of the non-random sampling. In addition, women not on cART were a combination of women who had not yet initiated cART and women who had used cART previously but not currently, leading to potential for misclassification. Ideally, a separate analysis would have been conducted for each group, but we combined these two categories due to small sample sizes. Lastly, the cross-sectional study design

does not allow for the establishment of causality, and reverse causality is an issue with regards to some factors (e.g., having a detectable VL could be a function of poor overall HIV-related health, which may influence poverty, rather than poverty influencing VL). Thus, some results should be interpreted with caution.

In conclusion, our study highlights several important sociodemographic, psychosocial and clinical care factors associated with a lack of cART use and VL detection despite cART use in a large cohort of Canadian WLWH. Programmatic efforts to improve cART access and use for WLWH in Canada should focus on young women (<35 years of age), women with low levels of education or food and housing insecurity, as well as those who use drugs and have a history of incarceration. If these important social determinants of health can be considered, addressed and modified, great strides will be made to ensure that Canadian WLWH reap the full benefits of cART.

Acknowledgements

The CHIWOS Research Team would like to thank women living with HIV for their contributions to this study. We also thank the national team of co-investigators, collaborators, and Peer Research Associates and acknowledge the national Steering Committee, our three provincial Community Advisory Boards, the National CHIWOS Aboriginal and African/Caribbean/Black Advisory Boards, the BC Centre for Excellence in HIV/AIDS for data support and analysis, and all our partnering organizations for supporting the study.

Funders: Canadian Institutes of Health Research (MOP-111041), the CIHR Canadian HIV Trials Network (CTN 262), the Ontario HIV Treatment Network (OHTN), and the Academic Health Science Centres (AHSC) Alternative Funding Plans (AFP) Innovation Fund.

Author Disclosure

The authors have not conflicts of interest to disclose.

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