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Social Determinants of Health and Substance Use among Women Living with HIV in Canada: Inequalities and Impacts

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Abstract

The objective of this doctoral research was two-fold: 1) to estimate inequalities with regard to a) social determinants of health (SDoH) and health-related quality of life, and b) substance use between women living with HIV and the general population of women in Canada; and 2) to assess the impact of the SDoH clusters/classes on a) illicit drug use and b) heavy alcohol drinking among women living with HIV. For the first objective, prevalences of social determinants, self-rated health status, and substance use were estimated from 1,422 women with HIV aged 16+ in the 2013-2015 Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS, time-point 1), and then compared with their counterparts estimated in 46,831 general population women in the 2013-2014 Canadian Community Health Survey (CCHS), standardized to the age/ethnoracial group distribution of women with HIV. For the second objective, we used longitudinal data from the 2013-2017 CHIWOS at time-point 1 (N=1,422) and time-point 2 (N=1,252). Findings showed that compared to general population women, a higher proportion of women with HIV reported a) adversities regarding the social determinants (e.g., poverty, food insecurity, poor social support), poor/fair self-rated health status [manuscript 1], and b) greater cigarette smoking and illicit drug use, but similar to lower likelihood of binge drinking [manuscript 2]. Latent class analysis was used to determine the clustering of SDoH. We identified four distinct classes: no/least SDoH adversities, discrimination/stigma, economic hardship, and most SDoH adversities. Inverse-probability weighted regression models showed a substantial difference in a) illicit drug use [manuscript 3], and b) heavy alcohol drinking [manuscript 4] between no/least SDoH class and other SDoH classes. These findings underscore the need for novel approaches to address socio-structural

adversities and substance use among women with HIV. We also discuss additional implications and future research directions.

Keywords: Social determinants of health; Substance use; Disparities; Women; HIV; Canada

Summary for lay audience

People with HIV now live longer. This is due to advances in HIV care and treatment services. But, these people continue to face challenges in their life. The two most important challenges are substance use and social adversities. In this study, we compared several social factors between women with and without HIV. We also compared the patterns of substance use between these two populations. We used two data sets: 1) 1,422 women with HIV and 2) 46,851 women without HIV. We showed that a higher proportion of women with HIV reported living with low income (70.3% versus 28.1%). Severe food insecurity was more common among women with HIV (54.1% versus 10.2%). Poor social support, gender discrimination, and race discrimination were also more common among women with HIV. Poor/fair health status was more frequent among women with HIV. Except for alcohol, the use of other substances was more prevalent among women with HIV. As shown, a higher proportion of women reported living with these challenges. In the next step, we examined whether social factors tend to co-occur among women with HIV. To do this, we used data of 12 social factors. Using statistical models, we identified four unique groups: a) no social adversities (group 1; 6.6%), b) mainly stigma and discrimination (group 2; 18.0%), c) mainly economic difficulties (group 3; 30.2%), and d) most social adversities (group 4; 45.2%). We finally examined the association of these groups with substance use. We found that illicit drug use was significantly lower among women in group 1 versus the other three groups. The same findings were observed for heavy alcohol use. Social vulnerabilities were shown to be significantly associated with a greater risk of substance use. To reduce harms due to substance use, social adversities are required to be addressed.

Co-Authorship Statement

All chapters of this doctoral research dissertation were written by Mostafa Shokoohi as part of the fulfilment of requirements for his Doctor of Philosophy from the Department of Epidemiology and Biostatistics. Chapters 2 and 3 were based on secondary data made available to Mr. Shokoohi from the 2013-2015 Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS; time-point 1) as well as the 2013-2014 Canadian Community Health Survey (CCHS), and chapters 3 and 4 were based on data from the 2013-2015 and 2015-2017 Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS; (time-point 1 and 2).

Mr. Shokoohi was responsible for conducting all statistical analyses in both CCHS and CHIWOS data sets, conducting literature review and the Introduction section of all papers and this thesis, writing Materials and Methods, Results, and Discussion sections of all papers. Mr. Shokoohi's supervisory committee (Dr. Greta Bauer, Dr. Mona Loutfy, and Dr. Igor Karp) provided guidance and feedback in the conceptualization of research questions and interpretation of findings. While Mr. Shokoohi drafted the full text of all manuscripts (percentage of contribution to all the four published papers were more than 90%), supervisory committee members and colleagues (Dr. Greta Bauer, Dr. Mona Loutfy, Dr. Angela Kaida, Dr. Ashley Lacombe-Duncan, Ms. Mina Kazemi, Ms. Brenda Gagnier, Dr. Alexandra de Pokomandy, Dr. Carmen H. Logie, Dr. M-J Milloy, Dr. Elisa Lloyd-Smith and Dr. Allison Carter) were listed as co-authors where they assisted in clarifying the concepts, interpreting the findings, and revising the manuscripts.

Dedications

This doctoral research is dedicated to:

i) People living with HIV

ii) Women living with HIV who took part in this community-based research (CHIWOS), and the Peer Research Associates (PRAs) who administered the survey and collected the data.

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List of Abbreviations

aHR	Adjusted hazard ratio
AIDS	Acquired immunodeficiency syndrome
aOR	Adjusted odds ratio
aRR	Adjusted risk ratio
cART	Combined Antiretroviral Therapy
CCHS	Canadian Community Health Survey
CHIWOS	Canadian HIV Women's Sexual and Reproductive Health Cohort Study
gbMSM	Gay, bisexual and other men who have sex with men
GIPA	Greater Involvement of People Living with HIV/AIDS
HIV	Human immunodeficiency viruses
HR	Hazard ratio
IDU	Injection drug use
IPW	Inverse-probability weight
LCA	Latent class analysis
MIWA	Meaningful Involvement of Women Living with HIV/AIDS
OR	Odds ratio
PLWH	People living with HIV
PRA	Peer Research Associates
RR	Risk ratio
RRR	Relative-risk ratio
SDH/ SDoH	Social determinants of health
SES	Socioeconomic status
SPD	Standardized prevalence difference
UNAIDS	The Joint United Nations Programme on HIV and AIDS
WHO	The World Health Organization
WLWH	Women living with HIV

1. Chapter 1: Objectives, introduction, and literature review

1.1. Thesis Objectives

The overall objective of this doctoral research work was to study the inequalities with regard to social determinants of health (SDoH) and the impact of the clusters of SDoH on substance use among women living with HIV in Canada. Specifically, this thesis had two main objectives:

Objective 1: To explore the inequalities associated with SDoH and substance use among women living with HIV comparing with women in the general population in Canada. To this end, we used data from the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS, at baseline 2013/15) and comparable information from the Canadian Community Health Survey (CCHS, 2013/14). This objective had 2 sub-objectives:

1a. To compare age- and ethnoracial-standardized prevalence of SDoH and self-rated quality of life between women living with HIV and the general population of women.

1b. To compare age- and ethnoracial-standardized prevalence of substance use between women living with HIV and the general population of women.

Objective 2: To investigate the clustered impact of SDoH on substance use among women living with HIV in Canada. To do this objective, we used data from CHIWOS for two time-points (Wave 1 in 2013/15 and Wave 2 in 2015/17) to explore the clustered impact of 12 SDoH on substance use. Specifically, this objective had two sub-objectives:

2a. To investigate the impact of the clusters of SDoH on drug use (opioid/stimulant use) among women living with HIV in Canada.

2b. To investigate the impact of the clusters of SDoH on heavy alcohol consumption among women living with HIV in Canada.

1.2. Thesis organization

Chapter 1: This chapter consists of a comprehensive review of the literature in line with the main objectives of this thesis.

Chapter 2: This chapter addresses Objective 1a: comparing SDoH between women living with HIV and the general population of women. A version of this chapter has been published in *PloS One* (Manuscript 1).

Chapter 3: This chapter addresses Objective 1b: comparing substance use between women living with HIV and the general population of women. A version of this chapter has been published in *Drug and Alcohol Dependence* (Manuscript 2).

Chapter 4: This chapter addresses Objective 2a: The clustered impact of SDoH on drug use among women living with HIV. A version of this chapter has been published in *Addiction* (Manuscript 3).

Chapter 5: This chapter addresses Objective 2b: The clustered impact of SDoH on heavy drinking among women living with HIV. A version of this chapter has been published in *AIDS and Behavior* (Manuscript 4).

Chapter 6: This chapter provides an integrated discussion, conclusions, and future directions.

Appendices: This section consists of questionnaires, and data sharing agreements.

1.3. Introduction

1.3.1 HIV profile, a global perspective

The human immunodeficiency virus (HIV) infection continues to be a major public health problem worldwide.[1] Since the beginning of the HIV epidemic, more than 77 million individuals have become infected with HIV and more than 35 million people have died from AIDS/HIV-related illnesses globally. Estimates from the Joint United Nations Programme on HIV/AIDS

(UNAIDS) in 2017 showed that approximately 36.9 million people were living with HIV globally, with 1.8 million people newly infected with HIV.[2] Women constitute approximately half of all people living with HIV globally; with 18.2 million women living with HIV in 2017. In 2017, approximately one million people died from AIDS-related illnesses, which was half of the estimate since the epidemic's peak in 2004 (i.e., 1.9 million).[3] The advent of combined antiretroviral treatment (cART) has been considered as the key reason for the significant reduction in HIV-related deaths worldwide.[4]

Since its introduction in 1996, treatment with cART has significantly improved such that cART regimens have become more effective, less toxic, and simpler with regard to pill burden and frequency; consequently, adherence to HIV treatment regimens has also been enhanced.[5-7] Both observational research[5] and randomized trials[6] have supported the improved treatment adherence due to advances in treatment regimens. The availability of cART has brought about sustained virologic (i.e., referring to viral load suppression) and immunological (i.e., mainly referring to CD4 cell count) responses.[4,8,9] Research shows that cART effectively reduces the plasma HIV-1 viral load to its undetectable level (i.e., HIV RNA < 50 copies/mL or less; a limit of detection of the most sensitive available clinical tests), leading to a significant immunological recovery through an increase in circulating CD4+ T-lymphocytes.[10,11] *Viral load* and *CD4 cell counts* are the two common clinical measures of HIV progression. Viral load refers the amount or concentration of HIV virus in the blood, with a level less than 50 copies/mL indicating undetectable/suppressed viral load (this limit may differ by clinical assays/tests, but 50 copies/mL is the most common limit used in the literature). CD4 cell count assesses the function of the immune system, with a CD4 count below 500 cells per mm^3 indicating increased vulnerabilities to immune suppression and associated opportunistic infections and diseases.

However, treatment *adherence* – typically defined as the extent to which individuals take their medication as prescribed[12,13] – is an important measure in determining undetectable HIV viral load,[14] with taking ≥ 95% of the medications defined as optimal adherence.[12]

Progress in viral load suppression and immunological function reconstitution have translated into significant improvements in life expectancy (as an important population health indicator) of people living with HIV,[4,7,15-18] particularly in high-income nations where individuals living with HIV have access to health care and cART.[4,19-23] For example, Teeraananchai et al. (2017) in a meta-analysis using data from eight cohort studies of individuals on cART aged ≥ 14 years found that the overall life expectancy in high-income countries was an additional 43.3 years and 32.2 years at ages 20 and 35 years, respectively, versus 28.3 and 25.6 additional years, respectively, in low/middle-income countries.[24] Research has also documented that life expectancy among individuals on cART is approaching that in the general population.[19,20] For example, a study in Switzerland showed that life expectancy at age 20 years increased from 11.8 years in the monotherapy era (1988–1991, where combination therapy was not yet introduced) to 54.9 years in the most recent cART era of the study (2006–2013), compared with 62.3 to 63.0 years, respectively, in the general population.[20]

While advances in HIV treatment have substantially improved the life expectancy, individuals with HIV are still experiencing lower quality of life. A study in the United Kingdom assessing health-related quality of life among individuals with HIV aged ≥ 18 years who were mostly virologically and immunologically stable found a lower level of quality of life for people with HIV compared with the general population; it has been hypothesized that a substantial part of this gap might be due to the higher levels of psychiatric symptoms such as anxiety and depression in people with HIV.[25]This hypothesis is consistent with evidence from studies

conducted in the United States (US) indicating that people living with HIV are approximately three times more likely to experience depression than do individuals without HIV.[26]

In general, existing evidence indicates that despite the notable improvements in their life expectancy, people living with HIV still experience greater morbidity and mortality in comparison to the general population.[27] In addition to the role of HIV itself and aging-associated conditions, behavioural or lifestyle factors such as substance use[27-29] and socio-structural conditions[27,30-36] (e.g., socioeconomic status, social support, employment status, and HIV stigma) have been introduced as the key contributing factors that negatively affect health-related quality of life of individuals with HIV, either independently or in combination.[27]

1.3.2 Global strategies to end the HIV/AIDS epidemic

To end the HIV/AIDS epidemic by 2030, UNAIDS and partners in 2014 launched three ambitious goals/targets that called on countries to reach by 2020:[37] i) to diagnose 90% of all HIV cases, ii) to provide cART for 90% of all persons diagnosed with HIV, and iii) to achieve viral suppression for 90% of people with HIV on cART. The UNAIDS *90-90-90 targets* are a commitment to increase access to cART treatment, prevent AIDS-related deaths, prevent HIV transmission, and meet the goals in line with human rights. The end target is to achieve an undetectable viral load in 73% of people with HIV.[37-39] While this strategy is a crucial step in eliminating the HIV epidemic, reports from the global HIV programmes indicate that greater efforts are required to help end the epidemic by 2030.[39] Actions should particularly focus on the challenges that individuals typically face along with all stages of the HIV treatment (i.e., the HIV care cascade). Recent updates show that out of an estimated 36.9 million living with HIV globally, only 75% were aware of their HIV status, 59% were on cART, and 47% were virally suppressed,[40] with the highest rates in resource-rich nations.[41] These estimates imply that while

enormous efforts have been made to control HIV/AIDS, national programs are still far from meeting the global targets.

To achieve the UNAIDS targets, evidence suggests that an effective HIV medical care program such as the "*HIV care cascade*" (or "HIV treatment continuum"), an internationally-recognized framework, is required. This framework forms the basis of the UNAIDS 90-90-90 targets. While various steps (stages) can be reported, this framework primarily focuses on the modeling of five main successive dynamic steps of HIV care, including HIV diagnosis, linkage to care, retention in care, adherence to cART, and viral load suppression.[42-45] Such a sequence of HIV medical care and delivery is commonly used to gauge the effectiveness of cART.[44] The success of this framework in preventing new HIV cases, HIV complications and HIV/AIDS-related morbidity and mortality rely on addressing each of these steps, from scaling up HIV testing to diagnose those not yet known to be infected with HIV, to linkage to care and treatment programmes to achieve viral suppression.[46,47] This framework aims to help depict estimates (i.e., proportions) for the successive steps from HIV diagnosis through viral suppression.[45] While addressing all steps along the HIV care continuum framework is highly important,[44] researchers have focused on those steps in the middle of this framework (i.e., linkage to and retention in care, and adherence to treatment), underscoring their significance in optimizing health and clinical outcomes among diagnosed individuals.[42,45,48,49]

With remarkable advances in the management of HIV and improved knowledge regarding the optimized practices for HIV care and treatment, reasons for people with HIV receiving poor linkage to and retention in care as well as suboptimal treatment adherence are not justifiable.[42] Despite the success attributable to the cART expansion and uptake, suboptimal HIV treatment remains a public health challenge worldwide. The findings of a meta-analysis of studies of

people with HIV in North America and Africa showed that only 55% and 77%, respectively, achieved over 80% adherence.[50] A global meta-analysis in 2011 among individuals on cART showed that, on average, 62% of individuals achieved optimal HIV treatment adherence.[51] The fact is that the complexity of the HIV care models as well as multiple social and structural factors may limit the ability of people with HIV to remain engaged in care, highlighting the need for a social determinants of health (SDoH) framework when addressing the challenges attributable to suboptimal treatment outcomes.[42,52] Such socio-structural-level barriers along with individual-level factors such as illicit drug use and heavy alcohol consumption have the potential to negatively impact coverage of each step along with the HIV care cascade.[46] These challenges and their associated consequences in the context of HIV are discussed in greater detail below.

1.4. Epidemiological profile of HIV in Canada

1.4.1 Prevalence and incidence

The national HIV statistics showed that there were an estimated 63,110 people living with HIV/AIDS in Canada at the end of 2016, an approximate 5% increase since 2014 (i.e., 2,945 new HIV infections since 2014).[53,54] This estimate corresponds to a prevalence of 173 per 100,000. Almost half (N = 32,762; 51.9%) of individuals living with HIV in Canada are gay, bisexual and other men who have sex with men (gbMSM), with a large number of cases (N = 30,980) attributed to having sex with men and a small number (N = 1,782) through either having sex with men and/or injection drug use (IDU) (these are based on the reporting categories). Other main modes of HIV transmission in Canada are: heterosexual sex (N = 20,543, 32.6%), and IDU (N = 10,986 (17.4%)), including 9,204 people whose HIV was attributed to IDU and 1,782 men whose HIV status could be attributed to either sex with men or IDU. The populations impacted by HIV infection vary from province to province. For example, based on the available estimates

in 2011,[55] the HIV epidemic is concentrated mainly in gbMSM in British Columbia (45.5% of people with HIV), and Ontario (56.0%), and Quebec (54.2%). Estimates also show that an estimated 14,520 females were living with HIV, representing approximately 23% (prevalent cases) of all individuals living with HIV in Canada.

HIV infection has slightly increased in Canada recently.[54-56] Estimates in 2016 showed that there were 2,165 new HIV infections (incident cases) in Canada, with a slight increase over the estimated 1,960 new cases in 2014. The national estimates in 2016 indicate that the number of new HIV cases slightly increased among females since 2014: from 436 new HIV infections (22.2% of all new cases in 2014) to 507 (23.4% of all new cases in 2016). The HIV incidence rate was 6.0 per 100,000 population in Canada in 2016, with 3.3 per 100,000 for females (based on available data in 2014).[54,56,57] According to the 2016 national estimates, heterosexual sex and injection drug use are the main drivers of HIV infection among females, with 78% and 22% of all new HIV cases among females attributed to heterosexual sex and injection drug use, respectively. According to the same data from the national estimates in 2016, females aged 20 to 49 (years) comprised almost three-quarters of all new HIV diagnoses among women. Black, Indigenous and white females (women and girls) constituted 37%, 36% and 21% of all new HIV diagnoses among women in 2016.

1.4.2 Treatment cascade and targets

In line with global commitments, Canada has made substantial progress in the control of HIV and AIDS. At the end of 2014, approximately 80% of all estimated 65,040 individuals with HIV knew their HIV status (i.e., an estimated 52,220 were diagnosed). Of individuals diagnosed with HIV, 76% were on HIV treatment (i.e., 39,790 individuals with HIV received cART). Of all individuals on treatment, 89% had achieved viral suppression (i.e., 35,350 individuals on

treatment were virally suppressed). Reports show that only 61% of all estimated individuals living with HIV in Canada received appropriate HIV treatment (the global expected percentage is 81%), and only 54% of all individuals living with HIV were virally suppressed[58] (the global target is 73%).[59]According to the Public Health Agency of Canada (PHAC),[58] achieving the first 90 target (i.e., 90% of all individuals with HIV know their HIV status) necessitates greater actions to enhance HIV test uptake and diagnosis through identifying and addressing the main barriers associated with HIV testing (e.g., increasing community knowledge, improving access to services). The low estimate for the second 90 target (i.e., 90% of all people with diagnosed HIV receive sustained cART) is assumed to be partly related to the "treat all" recommendation (i.e., treat all people with HIV at diagnosis[60]) being relatively new in 2016 when these targets were set. In other words, implementing this policy and adjusting to this recommendation may require more time for both clinicians and individuals with HIV.

1.4.3 Life expectancy

Reports indicate that mortality among Canadian people with HIV has declined considerably.[4,22] PHAC in 2016 reported that HIV-related deaths decreased by half between 1997 and 2011, and 5-year survival rates among individuals with AIDS increased from 7% in 1981–1986 to 65% in 1997–2012.[61] Notable improvements in life expectancy have also been reported among people with HIV in Canada. For example, Samji et al. (2013) using data from the United States and Canada suggested that life expectancy at age 20 increased from approximately 36 years in 2000-2002 to 51 years in 2006-2007, an estimate that is approaching that of a 20-year-old person in the general population.[22] Patterson et al. (2015), in a study in Canada in 2015, demonstrated a steady increase in life expectancy at age 20 from the calendar period 2000-2003 to 2008-2012 (31 vs. 54 years).[23] Using data from British Columbia, Eyawo et al. (2017)[62] found a remarkable

reduction in all-cause age-standardized mortality rates (ASMR) among individuals with HIV: approximately 127 per 1000 population in 1996 to 22 per 1000 population in 2011-2012 (83% decline), compared with 7.9 per 1000 population in 1996 to 6.8 per 1000 population among HIV-uninfected individuals (14% decline). These findings indicate that even though mortality rates have been significantly reduced over time among Canadians with HIV, mortality rates still remained in excess of that of HIV-uninfected individuals.

1.4.4 Women living with HIV

Globally, the intersection of various factors (e.g., biological, social, structural, and political factors) that contributes to women's increased vulnerability to HIV may also contribute to greater vulnerabilities to worse HIV- and treatment-related outcomes among women with HIV,[63-65] a phenomenon that is called the "*feminization of HIV*".[63,66,67] The unique challenges that women experience with regard to HIV may hamper or disrupt access to care, retention in care, and service utilization. Such challenges among women oftentimes result from their greater biological susceptibility to HIV acquisition, increased vulnerability to sexual and physical violence, and lower socioeconomic participations (e.g., lower educational achievement, lower participation in paid work, and lower income opportunities).[2,68,69] In Canada, the complex intersection of discrimination based on gender with other dimensions of identity (e.g., racism, and sexism) can also pose critical challenges to their engagement in HIV care.[63,70-72]

Consistent with international literature,[68,73-79] research in Canada, where individuals have universal access to health care, has also documented gender inequalities/differences, with women reporting a lower engagement along the HIV care cascade as well as subsequent poorer HIV outcomes over time than their male counterparts.[64,76,79-81] For example, Carter et al. (2014) documented gender inequalities in quality of HIV care during the first year after initiation of

treatment, and found that female gender predicted poorer quality of care (adjusted odds ratio (aOR)=1.22[†]). Among women, the likelihood of poorer quality of care was greater among those with injection drug use history.[79] Based on data from British Columbia, Lourenço et al. (2104) documented the high levels of heterogeneity in the HIV cascade of care across different population subgroups, with women having greater attrition at every step of the cascade than men.[80] They found that a lower proportion of women than men achieved virologic suppression (73% vs. 87%), transitioned from *linked to care* to *retained in care* (20% loss vs. 11% loss), transitioned from *retained in care* to *on cART treatment* (15% loss vs. 8% loss), and from *on cART* to *viral suppression* (27% loss vs.13% loss). Puskas et al. (2011) reviewed comparative data on treatment adherence stratified by gender in developed countries, with eight studies from Canada, and found that women were less likely to report optimal treatment adherence.[76] Using a population-based HAART Observational Medical Evaluation and Research (HOMER; N = 4,534) cohort in British Columbia,[64] Puskas et al. found that a lower proportion of women reported optimal treatment adherence than men (57.0% vs. 77.1%, respectively). Women were 45% less likely to be optimally adherent to cART treatment in the adjusted analyses (aOR = 0.55). Furthermore, a Canadian longitudinal study of injection drug users living with HIV (N = 545) identified female gender as an independent factor associated with a greater likelihood of suboptimal treatment adherence (aOR = 0.70).[82] Using data from the Canadian Observational Cohort (CANOC; N = 5442) collaboration, a multisite cohort study of individuals with HIV, Cescon et al. (2013)[81] also documented gender differences in poor clinical outcomes, with women at heightened vulnerabilities. Using Kaplan-Meier methods, the estimated probability of virologic suppression by 6 and 12 months post-ART initiation was respectively 38% and 52% for

[†] To report the measures of associations such as odds ratio and risk ratio, this rule was followed: *aa.a* for estimates greater than 10 (e.g., 12.3), *a.a* for estimates between 2 and 10 (e.g., 7.4), *a.aa* for estimates between 1 and 2 (e.g., 1.43), and *.aa* for estimates less than 1 (e.g., 0.89). For very small estimates, we followed this rule: *a.aaa* such as 1.003 and *.aaa* such as 0.006.

women, and respectively 47% and 65% for men. Adjusted analyses showed that women were 13% less likely to achieve virologic suppression than men (aHR = 0.87) and were 55% more likely to have virologic rebound (aHR = 1.55).

Traumatic and stressful events owing to socio-structural conditions have resulted in substantial inequalities in attrition across the cascade of care among women with HIV in Canada. For example, Kerkerian et al. using the baseline data of the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS; N = 1,424) found that 83% of women were on cART, of whom 68% were adherent and 72% were virally suppressed, with a considerable variability among those who experienced greater disadvantages concerning the social and structural determinants.[83] In fact, social determinants were found to be the main factors associated with attritions from one stage to another. For example, the greatest attrition between linkage to care and cART initiation occurred among women with unstable housing; and attrition between cART use and cART adherence happened mostly among women with illicit drug use and recent incarceration. Household annual income, racial discrimination, and incarceration history were among the significant contributing factors of attrition at viral suppression stage. According to the same data from Canadian women with HIV, Kronfli et al. (2017) documented that unstable housing, history of recreational drug use, and experiences of everyday racism were the main barriers to access to HIV care.[84]

Consistent with the evidence from developed countries,[4,20] life expectancy among Canadians living with HIV has also improved as mainly the result of the scale up of cART. While there are differences, available evidence in Canada indicates that life expectancy of individuals living with HIV on cART are approaching that of the general population,[22] with a considerable gap between men and women with HIV. Samji et al. in a study involving data from

the U.S. and Canada found that while life expectancy at age 20 years increased with calendar time in both men and women with HIV, it was lower among women. Life expectancy among men with HIV at age 20 years was estimated as 35.9 years in 2000/02 to 53.4 years in 2006/07 vs. women with HIV from 36.6 years in 2002/03 to 47.3 in 2006/07.[22] The 2009 estimate of life expectancy in the general population of Canada at age 20 years was 59.7 years for men and 63.9 years for women, indicating that life expectancy of men and women with HIV lags behind the life expectancy of men and women in the general population up to 6.3 and 16.6 years, respectively.[22] Other research in Canada using data from the Canadian Observational Cohort (CANOC) collaboration, including people with HIV aged ≥18 years receiving cART reported a lower life expectancy at age 20 among women with HIV versus men with HIV (32.4 vs. 39.2 years) and for participants with injection drug use history versus those without injection drug history (23.9 vs. 52.3 years).[23] A global systematic review of the literature in 2016, in which three studies from Canada were also included, showed that life expectancy among women with HIV was higher than that among men with HIV in all resource-rich settings, except for Canada.[85]

Research in Canada has found that women with HIV have a lower life expectancy compared to men,[23,86] a difference that may be due to variations in risk factors for HIV acquisition rooted in social and structural inequities, resulting in poor or suboptimal HIV-related health outcomes among women compared with men.[64,65] Analyses of data from British Columbia using a retrospective cohort study (2003-2011) of 3,653 people with HIV on treatment aged ≥ 20 years demonstrated that life expectancy of individuals living with HIV at age 20 years was 34.5 years, and it increased to 48.7 years (41% increase) when researchers considered only those who were alive after the first year follow-up.[86] The overall life expectancy at age 20 years among females was lower than males with HIV (27.2 vs. 37.5 years). Individuals with HIV were 3.2

times more likely to die than the general population (mortality rates: 28.8 vs. 8.9 deaths per 1000 person-years), with greater mortality among females with HIV (34.6 vs. 8.6 deaths per 1000 person-years) than males with HIV (27.6 vs. 9.3 deaths per 1,000 person-years). Another study based on data from British Columbia consisted of electronic health records from 9,310 individuals with HIV and 510,313 adults without HIV (1996-2012) found that health-adjusted life expectancy (HALE) at age 20 years was approximately 31 and 58 years among men with and without HIV, respectively.[87] Such estimates were approximately 27 and 63 years among women with and without HIV, respectively. The findings of these studies indicate much shorter overall life expectancies among women with HIV than among men with HIV, as well as their female counterparts in the general population.

1.4.5 Contributing factors in gender inequalities

These findings show that despite universal access and availability to cART in the Canadian context, the fact is that not all individuals with HIV have equally benefited from the available HIV treatment and care programs. Disparities in care engagement, HIV outcomes, and life expectancy across background (e.g., sex) and baseline characteristics (e.g., history of drug use) remain.[22] Multiple barriers may negatively impact the degree to which women with HIV remain engaged in HIV care and treatment services. Canadian research has consistently highlighted the contribution of social, economic and structural determinants – collectively known as the *social determinants of health (SDoH)* – to the poor HIV care and treatment outcomes among women. Suboptimal health-related outcomes are particularly overrepresented among those who face or continue to face socio-structural adversities and stressful events in their daily lives (e.g., poverty, discrimination, HIV-related stigma, violence). In addition to daily living conditions, other factors, more importantly, substance use (e.g., illicit drug use) and difficulties in accessing HIV

and support services are amongst significant barriers that may hinder access to HIV care, initiation or continuation of HIV care and treatment services, and retention in HIV care; consequently, they may negate the efforts in ending the HIV/AIDS epidemic. Of particular concern is that marginalized women in Canada are disproportionately infected with HIV, which underscores the necessity of understanding the social adversities as well as behavioural factors driving the disproportionate impact of HIV among women in Canada.[88]

Identification of these adversities that women with HIV may experience in excess of what their counterparts do in the general population (i.e., those who are or assumed to be without HIV) is an essential step in dealing with these barriers. PHAC's HIV strategy states that, "It is critical to continue to work towards creating supportive environments that address social determinants, decrease stigma and discrimination, and reduce barriers to prevention, treatment, care and support."[58] Therefore, it is essential to further investigate the individual/behavioural as well as socio-structural determinants that continue to negatively affect the health and well-being of Canadians with HIV, particularly women. The importance of these determinants and their role in poor HIV-related outcomes are further discussed below.

1.5. Social determinants of health

1.5.1 Definitions and importance

Over the recent decades, growing attention has been paid to understanding and addressing the social environment factors (e.g., income), physical environment factors (e.g., housing), structural factors (e.g., stigma), and access to health services, collectively known as the social determinants of health (SDoH).[89-91] These are the social and structural conditions that people typically experience in their *daily life* and impact their health and well-being.[91] Greater insights into SDoH have been gained as of 2005 when the Commission on Social Determinants of Health (CSDH)

was set up by the World Health Organization (WHO) to accumulate the evidence on health equity and how to promote it.[91] WHO provides a holistic SDoH conceptual framework[92] in which the principle of health inequality is explicitly articulated. Under this framework, WHO defines SDoH as, "The conditions in which an individual is born, grows, works, lives, ages, as well as the wider set of forces and systems shaping the conditions of daily life".[91] The unequal distributions of these determinants play a significant role in overall health and give rise to greater inequalities in the health of individuals. WHO underlines that understanding the social determinants helps identify the processes interacting to create avoidable inequities in health outcomes.[91] That being said, dealing with the social impacts on health is considered as a way to reduce health inequalities and improve the health and well-being of individuals and populations.[93]

The proposed WHO framework provides two levels of the SDoH, and the link between the determinants and health status. These two levels are: a) *structural mechanisms (determinants)*, which stem from the key institutions and processes of the socioeconomic and political context (e.g., macroeconomic policies, social policies, public policies, and culture and societal values). As this framework asserts, these structural mechanisms are responsible for stratification and social class divisions in the society and that define socioeconomic status of individuals within hierarchies of power, prestige and access to resources. Income, education, occupation, social class, gender, and ethnoracial identity are among the most important structural stratifiers. Together, context, structural mechanisms and the resultant socioeconomic status are "structural determinants", which are, in fact, referred to as the "social determinants of health inequities." These inequities operate through a set of intermediary determinants of health to cause health outcomes; and b) *intermediary determinants*: This level directly determines the vulnerability to

factors that affect health. These determinants include material circumstances (e.g., housing, food availability); psychosocial circumstances (e.g., lack of social support); behavioural factors (e.g., substance use), biological factors (e.g., genetic factors); and the health system (e.g., access to healthcare services).

In the Canadian context, the concept of SDoH is seen as the social and economic circumstances that contribute to the health of individuals, communities, and jurisdictions as a whole. Dennis Raphael, the author of *Social Determinants of Health: Canadian Perspectives*,[94] provides two definitions for SDoH: i) A *narrow* definition as, "the primary determinants of whether individuals stay healthy or become ill", and ii) A *broad* definition as, "the extent to which a person possesses the physical, social, and personal resources to identify and achieve personal aspirations, satisfy needs, and cope with the environment." Raphael adds that SDoH "are about the quantity and quality of a variety of resources that a society makes available to its members."[94] While a wide range of SDoH have been developed over time, the most important ones in the Canadian setting, proposed by Dennis Raphael, include: Aboriginal status, gender, disability, housing, early life, education, income and income distribution, race, employment and working conditions, social exclusion, food insecurity, social safety net, health services, unemployment and job security.[94,95]

A social determinants of health (SDoH) approach is seen as an approach moving beyond a *medical model*, in which the body is seen as a mechanism that is either running well or in need of repair, and a *lifestyle approach*, in which the causes of diseases are to be found in individuals' *unhealthy choices*.[94] Said differently, the two approaches of biomedical and behavioural factors are relatively poor indicators of health status in comparison with a social-determinants approach. This does not mean that SDoH approach undermines the importance of the medical care models

that influence health, instead, the SDoH perspective emphasizes that medical care is not the only influence on health.[90,94,96] For example, in 2000, the number of deaths in the US attributable to three social factors of low education, racial segregation, and low social support was shown to be comparable with the number of deaths attributable to three medical conditions of myocardial infarction, cerebrovascular disease, and lung cancer, respectively.[97] Additionally, studies in the United States showed that medical care was responsible for only 10-15% of avoidable deaths.[98] Other studies have also consistently shown the leading role of daily living conditions (e.g., income, employment) on health-related outcomes.[99,100]

1.5.2 Social determinants and HIV

Despite substantial advances in HIV prevention and treatment strategies, people continue to be infected with HIV, and people with HIV continue to experience poor health-related outcomes, with considerable inequalities across population subgroups. While the reasons for such inequalities are complex, evidence has documented the interplaying role of the multifaceted factors impacting the effectiveness of HIV care and treatment programs. A set of social and structural determinants are among those contributing to health inequalities.[101-103]

In the context of HIV, the Centers for Disease Control and Prevention's (CDC's) National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP) defines SDoH as, "the complex, integrated, and overlapping social structures and economic systems that include the social environment, physical environment, health services and structural and societal factors."[104] In this definition, structural, cultural, and societal determinants are responsible for inequalities in health, which in turn influence individuals' ability to fight against HIV. Morin in 1988 described HIV as three separate but linked epidemics: HIV (viral) epidemic, AIDS (disease) epidemic as well as a set of epidemics defined as "the social, cultural, economic, and

political reactions to the HIV and AIDS".[105] The last one – that is termed as SDoH – has played a significant role in expanding the infection and changing the profile of the infection. Even after the acquisition of the infection, people with HIV are more likely to experience inequalities with regard to these determinants. As the effectiveness of HIV treatment is now heavily contingent on consistent linkage to and retention in care as well as sustained adherence,[44,106-108] recognizing these determinants and their overlapping nature is key to designing effective HIV care and treatment programs.[90,101,109]

The connection between SDoH and HIV is complex and multi-directional.[110] Despite the significant role the social determinants of health play in increasing vulnerabilities to HIV infection, living with HIV can itself elevate vulnerability to experiencing greater inequalities with regard to these daily life conditions. For example, living with HIV may reduce the income-generating opportunities or may exacerbate the extent of the socio-structural adversities through experiencing the unfair or unjust discriminatory behaviours due to their HIV status (i.e., HIV-related stigma).[110] In Canada, while the individuals most affected by HIV (e.g., men who have sex with men, heterosexual route, injection drug use) may have different life experiences, they may, however, share the experience of being socio-economically marginalized and victims of various forms of stigma and discrimination (e.g., homophobia, racism, and sexism, HIV-related stigma).[110] Inequalities with regard to social determinants not only add an additional burden of health problems, but they also impact the ability of individuals to seek care, treatment and support,[111] and then restrict individuals from access to resources that have potential to reduce their HIV-related complications. The negative impacts of socioeconomic and structural adversities on HIV outcomes are discussed in more detail below

1.5.3 Socioeconomic marginalization and HIV outcomes

Despite the substantial improvements in the survival and clinical outcomes of individuals living with HIV since the advent of cART, these individuals continue to experience difficulties in their livelihood. While consistent linkage in and retention to HIV care and optimal adherence to HIV treatment are necessary for individuals to gain the maximum benefits from the HIV programs/intervention, adversities with socioeconomic status are among the central challenges that individuals with HIV still face in the post-cART era.[112] Poverty, income insecurity, unemployment, and food insecurity are among the significant socioeconomic cofactors that not only affect the distribution of HIV infection,[103,113] but also increase the vulnerabilities to HIV-related clinical and health outcomes among individuals with HIV. Beyond their influence on a wide range of health problems, the health problems created by these determinants can result in conditions that, in turn, deteriorate social determinants as well as other health determinants.[94,114,115] For example, poverty has been linked with increased vulnerabilities to HIV infection which, in turn, reduces opportunities to engage in a secure employment condition, thereby exacerbating poverty itself as well as poverty-related outcomes.

The link between socioeconomic status (SES) and health inequalities in HIV infection does not seem to be similar to other chronic health conditions. While in many chronic conditions there is an SES-health disparities gradient, HIV infection has predominantly impacted individuals who face socioeconomic adversity or marginalization;[34] this is particularly pronounced for women with HIV. For example, the US Center for Disease Control reported that HIV infection occurs mostly among socioeconomically disadvantaged people (i.e., those at or below the poverty level).[116] In Canada, HIV infection occurs predominantly among marginalized subpopulations

with histories of drug use/injection, sex work involvement, incarceration, and other socioeconomic adversities.[61,63,85,86]

Adversity with respect to socioeconomic factors such as low education and unemployment has contributed to the HIV epidemic and HIV outcomes; for example, a high prevalence of HIV is seen among those with lower education and/or those without an occupation.[116,117] Research has demonstrated worse HIV related outcomes with lower socioeconomic positions.[118-120] Research examining HIV-related outcomes has found a set of socio-structural determinants that influence the risk of suboptimal HIV care and treatment outcomes, clinical outcomes, and morbidity and mortality. Extant research has shown that a large proportion of individuals living with HIV experience difficulties with achieving economic security or attaining employment as well as the subsequent suboptimal HIV care and treatment outcomes. In a review study in 2015 aiming at documenting factors associated with treatment initiation and adherence in Australia, Canada, and the United Kingdom, the economic factors were found to be the leading but under-reported barriers of HIV care.[121] A meta-analysis including 28 studies published between 1996 and 2014 from 14 countries (N = 8,743) showed a statistically significant association between being employed and cART adherence (overall pooled odds ratio = 1.27), and the association remained significant for studies from low-income and high-income countries (subgroup overall OR = 1.85 and 1.33, respectively).[122] Income, education, and employment were found to be independently associated with the level of HIV medication adherence in a systematic review.[123] Data from the Women's Interagency HIV Study (WIHS; N = 1,481), a multicenter cohort study in the United States, demonstrated that insured women with higher annual income (i.e., a yearly income of > $18,000) were 21% less likely to have a detectable viral load than those in the least annual income category (i.e., < $6000/yr).[124] Another study from the same cohort of women with HIV

(WIHS; N = 1,115) comparing socioeconomic data between women with and without HIV found that a higher proportion of women with HIV reported a low income level (69% vs. 64%) and not having an employment (77% vs. 57%).[125]

Evidence from Canada and internationally has consistently linked the socioeconomic indicators with HIV clinical indicators, including suboptimal cART treatment, elevated failure in immunological and virologic responses, and increased mortality rates.[118,126-131] For example, individuals with lower education in comparison with those with higher education reported experiencing delayed diagnosis (40.5% vs. 22.0%); reported lower immunological (68% vs. 84%) and virologic (76% vs. 86%) responses to HIV treatment; and higher risk of mortality (adjusted hazard ratio (aHR) = 2.3);[126] economically poor individuals had a significantly higher risk of mortality (aHR = 1.50), and that poverty (aHR = 1.60) and hunger (aHR = 1.70) continued to predict mortality after excluding the potential mediators;[127] individuals with no net wealth versus individuals with > $50,000 and individuals with an education less than high school versus those with college degree had greater hazard of mortality (aHR = 1.81, and 1.52, respectively);[128] in comparison with individuals who had tertiary education, the risk of mortality was significantly higher among those with secondary (aHR = 1.30), primary (aHR = 1.68), and incomplete primary education (aHR = 1.93), respectively,[130] and that the risk of HIV virologic success was lower among those with primary (aHR = 0.93) and incomplete primary (aHR = 0.80) education.[130]

Food insecurity is another key SDoH, and is defined as, "limited or uncertain availability of nutritionally adequate, safe foods or the inability to acquire personally acceptable foods in socially acceptable ways."[132,133] Food insecurity is prevalent among individuals with HIV,[132,134-137] and is considered as one of the main barriers to optimal care and treatment outcomes.[135]

Research has linked food insecurity with HIV outcomes among individuals with HIV. For example, in a study of 1,213 men and women with HIV in British Columbia, 48% were identified as food insecure (i.e., 27% as food insecure without hunger and 21% as food insecure with hunger), with greater prevalence among women than men.[132] Data from the Longitudinal Investigations into Supportive and Ancillary Health Services (LISA, N = 457) cohort in British Columbia documented food insecurity among 71% of individuals with HIV.[136] Weiser et al. presented a conceptual framework and theorized that adverse HIV outcomes may be linked with food insecurity through nutritional, mental health and behavioural pathways.[137] Studies among people with HIV receiving HIV treatment have found that food insecurity is associated with suboptimal adherence to HIV treatment, and incomplete HIV RNA suppression, and mortality.[134,135,138] Data from British Columbia found a high prevalence (48%) of food insecurity among 1,119 individuals living with HIV (1998-2007). Adjusted analyses showed that individuals who were food insecure and underweight were 94% more likely to die than those who were not food insecure or underweight (adjusted hazard ratio = 1.94).[135] Anema et al. in a study in British Columbia among 254 injection drug users living with HIV who initiated cART documented a high prevalence of food insecurity (71.3%), and found an independent association of food insecurity with mortality (aHR = 1.95).[134]

1.5.4 Stigma and discrimination

While evidence has consistently demonstrated that the advancements in HIV care and treatment have changed the profile of HIV from an acute to a chronic health condition, many other challenges such as HIV-related stigma and discrimination continue to exist and have potential to endanger attempts to manage HIV/AIDS in the post cART-era. Since the beginning of the HIV epidemic, HIV-related stigma has continued to occur globally, and has been considered as one of

the most serious and prevalent challenges for controlling the epidemic.[139-141] A systematic review in 2014 found that the prevalence of the experience of some types of stigma among individuals with HIV who were on HIV treatment varied from 42% in resource-rich nations to 82% in resource-limited nations.[142]

Erving Goffman, a Canadian sociologist, defines the term stigma as the "situation of the individual who is disqualified from full social acceptance."[143] Goffman further describes stigma as a term referring to an attribute or a characteristic (e.g., race/ethnicity, gender) that is deeply discrediting such that reduces a person in our minds "from a whole or usual person to a tainted, discounted one".[143] In the context of HIV, stigma is defined as discounting, discrediting and discriminating against individuals who are living with HIV and AIDS. The UNAIDS defines HIV-related stigma as "the negative beliefs, feelings and attitudes towards people living with HIV, groups associated with people living with HIV (e.g. the families of people living with HIV) and other key populations at higher risk of HIV infection, such as people who inject drugs, sex workers, men who have sex with men and transgender people."[140,144] Peter Piot, the former Executive Director of UNAIDS, in a viewpoint paper entitled *AIDS: from crisis management to sustained strategic response* published in The Lancet in 2006, introduced combating stigma and discrimination as one of five key imperatives for a sustained response to the HIV/AIDS epidemic.[145] Piot emphasized that wide access to antiretroviral therapy is helpful in combatting stigma and discrimination, but insufficient. Different types of HIV-related stigma have been introduced and been associated with worse HIV outcomes. Some of these types include: a) *perceived* stigma, which refers to the awareness of individuals with HIV from negative attitudes of other people in the society, and involves expectations of discrimination and prejudice from others owing to their HIV status; b) *internalized* stigma, which refers to negative beliefs, views

and feelings towards themselves and those with HIV/AIDS; c) *enacted* stigma, which refers to acts of discrimination (e.g., violence, exclusion) toward individuals with HIV because they are infected with HIV, and involves the experience of such discriminative behaviours.[141,146-151]

HIV-related stigma has been one of the most common barriers to HIV care and treatment programs. Various observational and review studies have shown the detrimental impact of HIV-related stigma and discrimination on multiple HIV and health-related outcomes.[33,141,142] While the reduction of HIV-related stigma is a crucial step toward reducing HIV inequalities and health inequities,[152] its complexity has been introduced as one of the main reasons for the insufficient response to this prevalent phenomenon.[141,146] Mahajan et al. believe that lack of a clear definition, difficulties in measuring the extent of HIV stigma, difficulties in assessing the impact of stigma on HIV outcomes and the effectiveness of HIV programs, and difficulties in developing interventions to reduce stigma are amongst those challenges that have hindered universal efforts to appropriately respond to HIV-related stigma.[141] The complexity in defining this phenomenon may partly originate from its interaction with a range of cross-cultural differences, socio-structural disparities, discriminative behaviours from health care providers, and social processes that are not usually measured in common practice.[146,153,154] HIV-related stigma can be particularly complex when compounded by marginalized behaviours (e.g., substance use, sex work) and demographic characteristics (e.g., gender and race/ethnicity).[141,146]

Women with HIV have frequently reported experiencing multiple forms of stigma beyond those related to their gender and HIV itself;[152] for example, stigma due to sexual minority orientation, transgender identity, substance use, history of sex work involvement, incarceration, and violence. Logie et al.[88] developed an "intersectional model of stigma and discrimination" in which intersectional stigma refers to mutually constitutive relationships between disadvantaged

societal attributes and inequities such as HIV-related stigma, discrimination due to gender (i.e., sexism), discrimination due to ethno-racial status (i.e., racism), and discrimination due to sexual orientation or gender minority status (i.e., homo/transphobia). These stigmas have been the key issues identified in previous research with populations at elevated risk for HIV infection in Canada.[88] While each type of stigma and discrimination can be studied independently,[152] they may also tend to co-occur and create clusters or combinations in which a group of individuals may follow certain patterns. The identification of the distinct pattern of these stigmas can help better understand the impact of these societal stigmas. This is a concept similar to what Logie et al. called "intersectional stigma and discrimination," referring to the overlapping, multilevel forms of stigma and discrimination that concomitantly pose barriers to health and wellbeing of women with HIV.[88]

Stigma can negatively impact the ability of individuals with HIV to manage their disease and multiple health and HIV outcomes,[33,155-158] ranging from its interfering impact on engagement in HIV care and treatment to inferior clinical indicators of HIV progression.[146,158-160] Previous studies have suggested that individuals who experience high levels of HIV-related stigma have lower access to, retention in and utilization of medical and HIV care as well as poorer treatment adherence and HIV clinical indicators. In a systematic review and series of meta-analyses (64 studies included), Rueda et al. found significant associations between HIV-related stigma and lower levels of medication adherence, and lower access to and usage of health and social services.[33]

The interlinked nature of HIV-related stigma with other social and mental health indictors in influencing the health and clinical outcomes among people with HIV have been well documented. For example, using data from a national cohort of women with HIV in Canada

(CHIWOS; N = 1,425), Logie et al. found a significant direct association between HIV-related stigma and gender discrimination on mental health-related quality of life (HR-QoL). In addition to their direct effects, these two indicators indirectly impacted HR-QoL through social support (acting as mediators) such that low social support accounted for 22.7% of the effect between HIV-related stigma and mental HR-QoL and 41.4% of the effect between gender discrimination and mental HR-QoL. For the impact of HIV-related stigma and racial discrimination on physical HR-QoL, economic insecurity accounted for 14.3% and 42.4% of the effect, respectively.[155] In another study, Logie et al. found that depressive symptoms mediated the association between personalized stigma and cART adherence as well as the association between negative self-image and both cART use and adherence.[161] Rao et al. in a cross-sectional study of individuals with HIV (N = 720) found that much of the effect of stigma on HIV treatment adherence was explained by depressive symptoms, suggesting the mediating role of depressive symptoms on the association between HIV-related stigma and HIV medication adherence.[156] Based on data from the Women's Interagency HIV Study (WIHS; N = 1168), Turan et al. found that depressive symptoms and low social support (or loneliness) each separately mediated the association between internalized stigma and suboptimal HIV treatment adherence;[162] meaning that a part of this association was explained by depressive symptoms and low social support. They also found that low social support operated through depressive symptoms to explain the indirect association between internalized HIV stigma and lower HIV adherence. Turan et al.[163] in another study in the same population (N = 1356) found that perceived discrimination in healthcare settings significantly reduced the likelihood of optimal cART adherence (aOR = 0.81). Through serial mediation analyses, they documented that internalized HIV-related stigma and depressive symptoms mediated the perceived discrimination-adherence association, suggesting the indirect

impact of perceived discrimination in healthcare settings on cART adherence, first through internalized HIV stigma, and then through depressive symptoms.

1.6. Substance use

Substance use (e.g., illicit drugs, alcohol use) is prevalent among individuals with HIV. Inequality in substance use between individuals with HIV and their counterparts in the general population has been documented, suggesting a higher prevalence among individuals with HIV. Previous research has also estimated the prevalence of use of various substances and examined their association with multiple HIV and health outcomes as well as mortality.[35] Substance use is not only a common driver of HIV infection, but also is directly and indirectly associated with suboptimal HIV care and treatment outcomes.

There is limited research focusing on the patterns of substance use specifically in women with HIV, who appear to be of particular vulnerability to poorer HIV outcomes attributable to substance use[164-166] owing to elevated burdens of psychiatric comorbidity, underdiagnosed alcohol use disorder, and greater difficulties accessing substance use treatment due to greater socioeconomic, cultural and structural adversities.[166-168] Given such additional burdens of daily life adversities, women with concomitant HIV infection and substance use are indeed of particular vulnerability to poorer HIV outcomes.[168] In addition to inequalities with regard to income-producing opportunities, women with HIV experience a greater level of stress and stressful events such as posttraumatic stress disorder (PTSD) and intimate partner violence (IPV),[169] or are at greater risk for depression in their daily life.[169-172] Research suggests that substance use is one coping strategy through which individuals tend to escape or avoid their everyday stresses or stressful events.[173] Substance use, coupled with socioeconomic

marginalization and structural adversities, can bring about greater vulnerabilities toward suboptimal HIV outcomes among women with HIV.

Substance use is, in fact, one of the most frequently studied correlates of HIV treatment non-adherence.[174] Greater focus on substance use in the current era of cART is warranted for multiple reasons. One of the key reasons is due to the preponderant co-existence of HIV and substance use.[175] Vagenas et al.[175] reported that HIV and alcohol use, for example, "are intricately intertwined and mutually reinforcing epidemics" that have the potential for poor outcomes. Skalski et al.[176] also added other reasons such as: i) the direct and indirect contributions of substance use to the circulation of HIV infection, ii) their association with health-seeking behaviours and HIV care and treatment interventions such as non-adherence to cART treatment, and iii) their interference with virologic and immunologic responses to cART, and subsequently accelerating disease progression, and mortality. Identifying and remediating such common barriers to treatment adherence are major priorities of behavioural HIV research[177,178] and of particular importance for people with HIV themselves, as well as those bodies (e.g., care providers, policy-makers) that are committed to improve treatment outcomes and the health and well-being of these individuals.[175] Evidence suggests that optimal adherence can be improved via either the facilitation of interventions that improve adherence directly or through the mitigation of the key challenges at each step along the HIV treatment cascade.[179-183] Substance use is one of these challenges that has substantially contributed to suboptimal engagement of individuals with HIV at each step of the HIV cascade; consequently, it has negated the efforts in improving HIV treatment programs. Given the modifiable nature of this behavioural practice, interventions targeting substance use and its predictors can potentially

improve the management of HIV and then enhance treatment outcomes. Below, the importance of these behavioural practices is discussed in detail.

1.6.1 Alcohol consumption

Alcohol consumption, particularly heavy use (or hazardous use), is considered a major public health challenge among individuals with HIV due to its high prevalence as well as its contribution to worse HIV outcomes.[184-187] The World Health Organization (WHO) defines heavy/hazardous drinking as, "quantity or pattern of use that places patients at risk for adverse consequences," and heavy drinking is defined as, "quantity of pattern of use that exceeds a defined threshold."[184,188,189] The National Institute on Alcohol Abuse and Alcoholism (NIAAA) has also provided specific definitions for different measures of heavy/hazardous alcohol use, specifically, a) Hazardous (or, high-risk) drinking, defined as 7 drinks or more per week for women.[190] While hazardous drinking is not considered as alcohol use disorder (AUD), individuals who are involved in such hazardous practices are at elevated risk for the worse outcomes attributed to alcohol use;[191] and b) *Binge drinking*, defined as "a pattern of drinking that brings blood alcohol concentration levels to 0.08 g/dL," where typically happens after 4 drinks for women in about 2 hours.[192] A woman then can be considered as a binge drinker if she drinks 4 or more alcoholic drinks on the same occasion on at least 1 day within 30 days.[193] Heavy drinking can impact the HIV outcomes through a) behavioural mechanisms: by diminishing health-seeking behaviours of individuals with HIV and negate retention in care and treatment adherence (discussed below); and b) biochemical mechanisms: by its potential impact on the acceleration of disease progression.

Multiple studies have demonstrated the preponderance of heavy/hazardous alcohol consumption among individuals with HIV. For example, data from a nationally representative

sample of people with HIV in the United States in 2002 (N = 2,864) estimated that more than half (53%) of individuals with HIV who were in HIV care reported last-month alcohol consumption, with 8% of entire sample and 15% among those who reported alcohol drinking identified as heavy drinkers (defined as the weekly consumption of ≥ 5 drinks/day). No statistical difference was observed for heavy drinking between men vs. women with HIV (15.0% vs. 15.5%, respectively). Another study in the United States estimated a high prevalence of past-month alcohol use (60.6%), with binge drinking reported by 27.2% of the whole sample.[194] Studies of women with HIV have also suggested a high prevalence of alcohol consumption; for example, Cook et al. identified five distinct drinking trajectories among women with HIV: continued heavy drinking (3%), reduction from heavy to non-heavy drinking (4%), increase from non-heavy to heavy drinking (8%), continued non-heavy drinking (36%), and continued non-drinking (49%), indicating that almost 15% of the sample were involved in heavy drinking at some point during the follow-up.[195] Cook et al. in an 11 year follow-up study found that approximately half of women reported drinking alcohol and 14% to 24% reported past-year hazardous drinking, suggesting that approximately 1 in 5 met criteria for hazardous drinking.[185] Cook et al. in a qualitative research identified that women with HIV reported drinking alcohol to cope with multiple adversities, including biological (e.g., addiction, to manage pain), psychological (e.g., coping, to escape negative experiences, to feel in control), and social (e.g., peer/family pressure, to socialize).[196] Studies comparing the patterns of alcohol drinking between men and women have documented mixed findings. While some epidemiological research[197,198] found a higher prevalence among men vs. women, data from other studies[199] indicated that a higher proportion of women who classified as heavy drinkers than men (7% vs. 5%, respectively).

Both in vitro and epidemiological studies have shown the negative impact of heavy drinking on subsequent HIV outcomes. In vitro studies demonstrated that alcohol accelerate HIV disease progression through impacts on key inflammatory markers (e.g., elevation in plasma CD4, a marker of monocyte activation),[200] or alteration of the virus infectivity, the immune response of the host, and tissue injury.[201] Epidemiological studies have also introduced heavy drinking as an important barrier to every step of the HIV care cascade.[187,202] For example, a 2010-2015 systematic review[175] including 53 clinical studies examining the impact of alcohol use on each step of the HIV treatment cascade found that 77% of the included studies documented a negative association of alcohol consumption with at least one step of the treatment cascade. Other observational and review research have shown such negative impact of heavy alcohol consumption on the HIV care cascade outcomes; for example, retention in HIV care,[203] health care utilization,[204] and suboptimal adherence to treatment.[177,202,204,205] Aside from impacts on each step at the HIV care cascade, alcohol use has also been associated HIV progression indicators and mortality; for example, different patterns of heavy alcohol consumption have been associated with failing to achieve immunological response (i.e., CD4 cell count $\leq 200/mm^3$)[206,207] and virologic failure (i.e., detectable viral load)[208-210] as well as a higher risk of hospitalization[211] and mortality.[186]

1.6.2 Cigarette smoking

Cigarette smoking is also prevalent among people with HIV,[212,213] with its high prevalence contributes to a variety of poor outcomes.[194,213] For example, Mdodo et al. in a nationally representative cross-sectional study in the United States in 2009 demonstrated that individuals with HIV receiving medical care were approximately twice as likely to be current smokers compared with adults in the general population (37.6% vs. 20.6%), with a higher prevalence

among both men and women with HIV (40.9% and 34.6%, respectively) compared to their counterparts in the general population (23.3% and 18.0%, respectively).[213] Other epidemiological studies, mainly from the United States, have shown the high prevalence of current cigarette smoking among individuals with HIV.[194,214]

Cigarette smoking contributes to both HIV-related and non–HIV-related health outcomes among individuals with HIV.[213] Beyond its contribution to the elevated risk of non-communicable diseases such as chronic obstructive pulmonary disease (COPD),[215] cardiovascular disease,[215] and cancers,[216] cigarette smoking has been also shown to have a deleterious impact on HIV outcomes, such as health and treatment outcomes as well as mortality among individuals with HIV. Nicotine, the active ingredient in tobacco, and HIV have synergistic interaction to negatively regulate the synaptic plasticity gene expression and spine density which may contribute to the elevated risk of HIV-associated neurocognitive disorder (HAND),[217] as characterized by development of cognitive, behavioural and motor abnormalities, and reported among almost half of individuals with HIV.[218] Epidemiological research indicates that such lifestyle factors continue to negate advances in HIV outcomes.[219] For example, multiple studies have reported the negative impact of cigarette smoking on outcomes among individuals with HIV; e.g., suboptimal adherence.[220]

In addition to its impact on treatment interruption and non-adherence, smoking has also been associated with worse clinical indicators and increased risk of mortality. Such elevated vulnerability has been reported to be due mainly to a) biochemical mechanisms through which smoking can negatively influence immune and virological response, regardless of cART use,[221,222] and b) behavioural mechanisms in which smoking can potentially increase cART non-adherence.[223,224] Research shows that individuals with HIV who reported cigarette smoking are

at a greater vulnerability to poor immunological and virologic responses, as well as greater risk of developing AIDS and all-cause mortality.[214,225-227] Data from individuals with HIV enrolled in European and North American cohorts (N = 17,995) suggested a high prevalence of smoking (60%), and that smokers had a higher mortality rate than non-smokers (mortality rate ratio = 1.94; with 1.84 among men and 2.41 among women).[227] This study showed that mortality attributed to smoking is higher than mortality due to HIV itself. Furthermore, a lower level of quality of life has also been reported among individuals with HIV who were current smokers versus never smokers.[228]

1.6.3 Illicit drug use

Illicit drug use is also prevalent among individuals with HIV. Despite its substantial contribution to driving HIV acquisition and transmission, drug use – both injection and non-injection – has the potential to threaten the significant clinical benefits obtained in the control of HIV in the cART era.[229,230] Illicit drug use is of particular concern among people with HIV given its high prevalence and the negative effects on HIV treatment outcomes and morbidity and mortality.

Prior research from different contexts has suggested that a high proportion of individuals with HIV meet criteria for illicit drug use alone or in combination with other substances, alcohol use in particular. For example, Pence et al. reported a high prevalence of marijuana (12%) and crack (5%), with 11% reporting using a non-marijuana drug and 7% reporting polysubstance use (i.e., multiple substances at one time) at least weekly.[198] Gurung et al. reviewed electronic medical records of 4,965 individuals with HIV in New York City and reported that 12.7% had an alcohol use diagnosis and 26.4% had a recorded drug use diagnosis, with 8.7% having co-morbid alcohol and drug-use diagnoses.[231] Hartzler et al. using data from the Center for AIDS Research Network of Integrated Clinical Systems (CNICS; N = 10,652), a multi-regional U.S.-based data,

estimated the prevalence of any substance use disorders (SUDs) at 48% (50% for men vs. 36% for women), with 31% marijuana use, 19% alcohol use, 13% methamphetamine use, 11% cocaine use, and 4% opiate use, and 20% having polysubstance use disorder.[232] Of the limited research among women with HIV, Cook et al. found a high prevalence of illicit drug use among heavy drinkers: 30.2% cocaine use, 39.5% crack use, 42.1% marijuana use, and 21.5% heroin use.[185] Kuo et al. examined data from the HIV Prevention Trials Network (HPTN 064; analytic N = 1,882) Study, and found that 76.1% reported using one or more substances or binge drinking in the past six months (i.e., 37.5% as frequent users [i.e., daily or less than weekly] and 38.6% infrequent user), with 63.3% reported binge drinking (of them, 54.5% being as frequent users), followed by 25.0% cocaine use (of them, 29.5% as being frequent users) and 16.5% opioid use (of them, 54.5% being as frequent users).[233]

Illicit drug use can also negatively impact the pathobiology of HIV. Xu et al. investigated in vitro effects of cocaine and found that a direct effect of cocaine on four major immune competent cells (i.e., T cell function such as helper T cells [CD4], B cell function, natural killer [NK] cell function, and monocyte-macrophage function).[234] In vitro and animal models have documented that illicit drugs may impact the pathobiology of HIV through altering immune functions (e.g., NK cells, T cells, neutrophils and macrophages) and the ability of such immune cells to secrete immunoregulatory cytokines, and also enhancing the infectivity and/or replication of HIV virus.[235,236]

Apart from the biochemical mechanisms explaining such heightened risk of HIV outcomes, drug use negatively impacts on health seeking behaviours, treatment utilization and adherence, and subsequent outcomes among individuals with HIV.[237,238] Sohler et al. examined patterns of drug use (at baseline only, 6-month follow-up [i.e., starters], both periods [i.e.,

consistent user], and nonuse) and health care utilization, and found that any drug users were more likely to miss HIV medical appointments (aOR = 2.2 for starters [who newly started] vs. nonusers, aOR = 2.9 for consistent users vs. nonusers), more likely to use emergency services (aOR = 4.9 for starters vs. nonusers, aOR = 2.2 for consistent users vs. nonusers), less likely to use antiretroviral medication (aOR = 0.23 for starters vs. nonusers, aOR = 0.19 for consistent users vs. nonusers), and more likely to report unmet support services need (aOR = 1.8 for consistent users vs. nonusers).[239] Individuals who stopped using drugs within the follow-up did not significantly differ from nonusers with regard to these outcomes. Individuals reporting the use of hard drugs (i.e., cocaine, amphetamines, or heroin) were more likely to be cART non-adherent (aOR = 2.1), and had higher risk of AIDS progression or death with (aHR = 2.1) or without (aHR = 2.5) adjusting for non-adherence, suggesting a possible adherence-independent mechanism of harm associated with illicit drug use.[238] Research also showed that concurrent illicit drug use with other substance, e.g., alcohol use, exacerbated the negative impacts on HIV treatment outcomes. For example, concurrent hazardous drinking and active drug use was significantly negatively associated with the lowest odds of cART use (aOR = 0.40), cART adherence (aOR = 0.32), and viral suppression (aOR = 0.50).[240] Limited data on women with HIV also showed that substance users were 20% more likely to be suboptimal cART adherent (adjusted prevalence ratio (aPR) = 1.20).[241] They found that both marijuana use and non-marijuana illicit drug use predicted suboptimal adherence.

Epidemiological research showed that the association of illicit drug use with HIV treatment nonadherence has led to elevated likelihood of failure to achieve viral suppression and reduced CD4 cell recovery,[242] and consequently resulting in greater risk of HIV disease progression, opportunistic infections, and mortality.[243-246] In fact, illicit drug use facilitates HIV progression

through either curtailing treatment adherence among those receiving cART or independent of cART use. For example, compared to nonusers, abstinent heroin/cocaine intermittent users (aOR = 1.4); active intermittent users (aOR = 2.3); and persistent users (aOR = 2.1) were at greater risk of opportunistic infection. Persistent crack cocaine using women were at greater risk than non-users to die from AIDS-related causes (aHR = 3.6) and to develop newly acquired AIDS-defining illness (aHR = 1.65).[246] Both pattern and type of illicit drug use were associated with HIV progression and mortality. Kapadia et al. showed an elevated risk of progression to AIDS among consistent (aHR = 2.5), inconsistent (aHR = 1.63) and former (aHR = 1.56) illicit drug using women than never users, and an increased risk of progression for stimulant users (aHR = 2.0) and polydrug users (aHR = 1.65) compared with non-users. They also found that consistent drug users had greater risk of all-cause mortality (aHR = 1.43) and AIDS-related mortality (aHR = 1.42) than never users.[247]

1.7. Social determinants and substance use

As made clear above, evidence has well documented that individuals with HIV reported a higher prevalence of illicit drug use[248] than their counterparts in the general population, with mixed findings for heavy alcohol consumption.[249,250] Substance use as a public health problem is of particular concern among people with HIV due to its direct and indirect impacts.[251,252] Substance use impacts individuals' cognitive capacity and impairs their decision making and judgment, resulting in other risky practices.[253-255] The co-occurrence of substance use and care and treatment interruptions attenuates the public health benefits of HIV treatment.[256] As noted above, a large body of evidence has identified strong associations of substance use with HIV outcomes such as low retention in care, treatment non-adherence, poorer immunological and virologic responses, and elevated burdens on health systems.[28] For example, illicit stimulant drugs (e.g.,

crack-cocaine use) enhance viral replication, resulting in unsuppressed viral load, and blunt effector function of cytotoxic T lymphocytes.[257] In addition to such direct impacts, individuals with HIV who use substances have elevated prevalence and frequency of medical, psychiatric, and substance use disorders. The resulting complications contribute to multiple key challenges in the provision of HIV care. In addition, drug using individuals under care for HIV and taking cART have increased age-matched morbidity and mortality than do their counterparts who do not use substances.[258]

Few studies have explored the patterns of substance use among women with HIV and little research has compared such patterns with their counterparts in the general population to explore the inequalities associated with substance use. Given the fact that an increasing number of women become infected with HIV, the need to address modifiable barriers that directly or indirectly accelerate disease progression and negatively impact survival becomes more essential.[185] This is particularly important among women with HIV who are also at greater vulnerabilities for their daily living conditions. While there have been appreciable progresses in the understanding of the epidemiology of HIV and risk factors among women over the recent decade, epidemiological data remain limited with respect to the key modifiable risk factors that have potential to diminish the efforts made to control and manage the HIV epidemic. Substance use is one such modifiable risk factor; however, evidence indicates that less attention has been paid to substance use disorders given the fact that it is an important aspect of HIV care and treatment.[208] While the optimal benefits of HIV treatment are strongly tied to treatment adherence, substance use has the potential to interfere with treatment through non-adherence and then lead to poorer subsequent HIV treatment outcomes. In addition to inadequate evidence concerning substance use among women with HIV, the literature has also inadequately addressed

the modifiable risk factors associated with substance use, particularly through the SDoH perspective.

The SDoH perspective highlights the leading role that the social and structural environments play in determining health outcomes and health status.[91,94,114,259] According to this framework, certain groups are at greater risk for poor health outcomes due mainly to inequitably experiencing adversities with respect to the social and structural determinants.[259] Even though the contribution of these determinants in the spread of the HIV epidemic has been well recognized, a relatively small number of studies have demonstrated the role of these determinants in the initiation or continuation of substance use among women with HIV. While evidence from different fields of research has suggested that the etiology of substance use is multifactorial, such that genetic, psychological, and social factors all contribute to substance use, Galea et al. believe that greater attention needs to be paid to the social aspects of substance use.[260] In addition to the fact that people are biologic and social organisms, these researchers believe that there are few biologic processes or behaviours that are not mediated through social context. In the case of substance use behaviour in particular, evidence indicates that the experiences have consistently been rooted in the social context.[260,261] In other words, social determinants have a direct impact on the patterns of substance use as well as the resultant levels of harms.[262] Marmot and Allen in support of the leading role of social determinants believe that investigators "need to understand and improve the social determinants of [unhealthy] behaviours to reduce health inequalities and improve health while simultaneously trying to facilitate and support better existing behaviours."[263] A better understanding of these key determinants of health and their association with substance use is imperative for identifying and developing effective interventions in the course of HIV management among women.[262]

Evidence, predominantly US-based research, has linked substance use with social determinants among individuals with HIV, with a substantial focus on social stratification characteristics such as gender, race/ethnicity, and socioeconomic status. For example, Chander et al.[191] investigated the contribution of gender, education, and race/ethnicity to both any alcohol use and hazardous drinking among a sample of individuals with HIV at 14 HIV primary care sites in the United States. They found the significant contribution of gender (aOR = 1.52 for male sex) and education (aOR = 1.87 for those with a college education vs. < high school) with any alcohol use, while no significant difference was observed across race/ethnicity groups. No significant association was observed between these three determinants and hazardous alcohol use. Crane et al.[264] using a sample of 8,567 people with HIV from seven U.S. sites from 2013–2015 found a significant contribution of gender (aOR = 0.77 for females vs. males) and race/ethnicity (e.g., aOR = 0.81 for Black vs. White) to binge drinking, and race/ethnicity to hazardous drinking (e.g., aOR = 0.74 for Black vs. White). Analyses stratified by sex showed that certain race/ethnic groups had different risk for heavy/hazardous alcohol consumption among males and females with HIV. Bilal et al. in a prospective sample of 7,906 people with HIV receiving care assessed clinical and sociodemographic predictors of alcohol misuse and alcohol use trajectory separately for men and women.[197] The only available SDoH indicator in their model was race/ethnicity, a non-modifiable SDoH measure. While certain race/ethnic groups had different risk for alcohol misuse among males, no difference was observed across race/ethnic groups in the sample of females. Alcohol consumption trajectories were also not different across race/ethnic groups for males and females. Kelso-Chichetto et al. using data from two cohorts of men and women with HIV in their model explored the role of only two SDoH indicators of annual income and race on heavy alcohol use separately for male and female

samples. Among women, those with lower annual income levels: < $10,000 (aOR = 0.76) and $10,000-$30,000 (aOR = 0.72) non-significantly had lower risk of heavy drinking vs. those in the higher income level (≥ $ 30,000), with significant differences observed across racial groups. Compared with individuals in higher income levels, those with < $10,000 annual income had a significantly increased risk of heavy drinking (aOR = 1.97).[199]

Research focusing on data from women living with HIV has also documented the contribution of a few social determinants to alcohol use. For example, Cook et al. found that women were significantly less likely to report hazardous drinking if they were employed (aOR = 0.80) and had higher education (aOR = 0.72 for those with more than high school education vs. those with high school or less), with no significant difference for race groups and marital status in the adjusted analysis.[185] Cook et al. in another study showed that among women without heavy drinking at baseline, those with more than high school education had a lower risk of heavy drinking trajectory than those with high school or lower education (aOR = 0.65), with no difference across racial groups, employment and marital status. Ghebremichael et al.[265] found a higher odds of alcohol use among women with a higher education (aOR = 1.53 for those with more than high school education vs. high school or less), with no significant difference for those with different income levels.

The same patterns of association between social determinants and illicit drug use have also been documented. For example, Pence et al.[198] found that women with HIV were less likely to report frequent non-marijuana drug use (aOR = 0.88) and polysubstance use (aOR = 0.46) than heterosexual males with HIV. No significant difference was observed for racial groups (minority vs. majority) and educational levels (beyond high school vs. high school or less). In addition to these determinants, these authors also assessed the association of other social determinants

including experienced trauma, stressful life, and social support on illicit drug use. Lifetime trauma increased the risk (per number of traumatic experiences) of frequent non-marijuana drug use by 13%, frequent crack use by 9%, and polysubstance use by 30%. In addition, stressful life events increased the risk of frequent non-marijuana drug use by 38% per event. Higher social support levels decreased the risk of frequent crack use by 18% and increased the risk of polysubstance use by 39%, even though these estimates were not statistically significant. Studies focusing specifically on data from women with HIV and assessing social determinants of illicit drug use is limited. Carter et al.[266] in a Canadian context found six distinct classes of substance use: abstainers (26.3%), tobacco users (8.8%), alcohol users (31.9%), 'socially acceptable' poly-substance users (13.9%), illicit polysubstance users (9.8%) and illicit poly-substance users of all types (9.3%). They also found a complex pattern for women with an annual household income < $20,000 vs. those with ≥ $20,000: women were significantly more likely to be illicit poly-substance users of all types (aOR = 2.8) while less likely to be alcohol users (aOR = 0.59). Violence as a key social determinant also significantly increased the odds of substance use. These studies have also found that recent experience of violence was independently associated with all classes of substance use, e.g., alcohol use (aOR = 2.6), illicit polysubstance use (aOR = 7.3), illicit poly-substance users of all types (aOR = 9.4). The contribution of social determinants to illicit drug use is even stronger among other subgroups living with HIV. For example, a cross-sectional sample of 2,216 youth (ages 12-26) living with HIV found that individuals with lifetime unstable housing reported a higher odds of non-marijuana illicit drug use (aOR = 2.2).[267]

As noted, research has generally focused on non-modifiable social stratification characteristics/positions such as ethnoracial identity in assessing the role of social and structural determinants and their inequalities on substance use. This might be since that disparity in the

United States is often referred to racial/ethnic differences in health, while this concept (commonly termed inequality) in the United Kingdom and European countries has referred to differences in health across individuals with different socioeconomic classes.[263] Undoubtedly, these groups of social determinants can highlight the significance of the social context of substance use; however, these do not provide enough help in recognizing the specific patterns of social determinants in relation to substance use. Therefore, to better address substance use and its associated harms, greater actions are required. Beyond the role of the social stratification characteristics, there is also a need for research on identifying the comprehensive social determinants that substantially influence and shape the behaviours of individuals with HIV. This is particularly important in the current context of HIV where effective care and treatment are available and accessible, and treatment has brought about significant advances in the life of individuals with HIV.[263] From the social determinants of health perspective, there is indeed a need to address larger environmental and social factors – also called the upstream level[268] – that influence individuals' behaviours.[268,269] The extent to which substance use is influenced by a comprehensive set of social and structural factors warrants additional study, particularly among women with HIV. Studying socio-structural factors and assessing their role in substance use have implications for HIV care and treatment.[270]

1.8. The current research

The current research was informed by the social determinants of health (SDoH) framework, a conceptual framework around the social and structural context of health. We aimed to document inequalities in daily life conditions and lifestyle factors among women with HIV in comparison to the general population. Informed by a social determinants of health framework, we first examined how social determinants of health may cluster together, and then how the identified

clusters of social determinants may have the differential influence on illicit drug use and heavy/hazardous drinking among women with HIV in Canada. In fact, this framework was used to help explain how substance use, that itself substantially contributes to poor HIV treatment outcomes, are patterned by social and structural environments. We hypothesized that the choices women with HIV make (here, substance use) are shaped by the choices they have (here, daily living conditions), which are themselves shaped by structural policies and processes. Growing interest in the socio-structural determinants of health has led to an increasing emphasis on understanding these fundamental causes (or *upstream* factors) and their contributions to health inequities.[271] Exploring a broad range of social, economic and structural determinants can help understand how these determinants play a fundamental role in lifestyle-related outcomes, substance use in particular in the present research, among women with HIV. There is a lack of research among women with HIV analyzing these determinants and exploring their contribution to substance use, as key lifestyle or individual-level factors that have the potential to negate the HIV treatment outcomes and mortality.

Studies of individuals with HIV have typically treated these social, economic and structural determinants as separate (or, independent) conditions or indicators when assessing their impacts on subsequent health outcomes, including substance use. For example, research has explored the independent impact of *food insecurity* on heavy alcohol use[272] and illicit drug use[273,274] as well as other HIV- and health-related outcomes such as treatment non-adherence,[275,276] and immunological and virologic responses to HIV treatment;[277-279] or the independent impact of *HIV-related stigma* on substance use,[280-282] late linkage to HIV care,[283] cART initiation and treatment uptake, and suboptimal ART adherence,[33,158,161,162] mental health conditions, access to and usage of health and social services;[33] or the independent impact of perceived *discrimination*

such as unfair treatment on cART adherence;[163,284] or the independent impact of *social support* on substance use,[285] risk behaviours;[286] or the independent impact of *under-housing* or *unstable housing***,** as a structural determinants of health, on substance use,[267] medical care, and health outcomes;[287] or the independent impact of *incarceration*, as a structural determinants of health, on substance use,[288,289] treatment adherence.[290,291]

Although assessing the independent impact of these indicators – i.e., using regression modeling with food insecurity, for example, as separate statistical predictors – may also have implications for HIV programs and interventions, methodologically, such an approach is not without limitation.[292] Social determinants have the potential to co-occur (i.e., co-present) and then may follow certain clusters/patterns (i.e., tend to be positively correlated). Therefore, such analytic approaches assessing the independent impacts may fail to account for the dependency and overlap of these social determinants.[292] While uncovering overlapping patterns of social determinants has been a challenge, other statistical approaches such as latent class analyses (LCA) enable researchers to account for the dependency across a set of overlapped indicators.[293,294] In the context of SDoH, this method offers an important methodological step forward for empirically considering the inter-relationships between social, economic and structural factors and their joint associations with substance use. We, therefore, used LCA to first identify the distinct groups of women with similar patterns of social determinants, and then assessed the impact of the clusters of these determinants on the study outcomes (a brief description of LCA can be found in **Appendix A**). This is in line with the available recommendations with respect to the use of dimensions to characterize SDoH, rather than separate assessment of such overlapping indicators.

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2. Chapter 2: Social Determinants of Health and Self-Rated Health Status: A Comparison between Women with HIV and Women without HIV from the General Population in Canada[1]

2.1. Introduction

Research has shown substantial improvements in health outcomes of people living with HIV (PLWH) since the introduction of combination antiretroviral therapy (cART); for example, life expectancy for those who receive cART has been approaching that of the general population.[1,2] Despite the remarkable successes achieved in HIV outcomes, they are still not ideal, particularly among women living with HIV. A recent Canadian study demonstrated that reductions in health-adjusted life expectancy among those living with HIV were larger for women than men.[2] In addition, Canadian studies have documented that a higher proportion of women experience poorer "quality of care" in Canada, indicating the existence of gender inequities in access and adherence to HIV treatment even in a universal healthcare system.[3,4]

Although HIV is now widely known as a chronic but manageable illness where appropriate care and treatment services are accessible,[5] multiple interpersonal and structural factors – situated within social determinants of health (SDoH), continue to limit HIV care and treatment efforts. The World Health Organization (WHO) defines the SDoH as "the conditions in which people are born, grow, live, work, and age."[6] Researchers have described the contribution of these socio-structural disadvantages in shaping the HIV epidemic among PLWH.[7-9]

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In turn, living with HIV can also cause greater vulnerability to socio-structural disadvantages; for example, PLWH experience food insecurity even after an HIV diagnosis, and employment loss, particularly among women.[10,11] Despite advances in HIV interventions, PLWH continue to experience challenges to maintaining their health due to the barriers linked with SDoH.[8,9,12] For example, socioeconomic inequities, housing instability, food insecurity, HIV-related stigma, and discrimination have been correlated with poorer HIV care, treatment responses, and clinical outcomes.[10,12-17] Women living with HIV are a population that face relatively lower socioeconomic status, and broader, systemic inequities that impact their health and wellbeing.[3,4]

In Canada, women now represent nearly one-quarter of the estimated 75,500 PLWH.[18] Women living with HIV in Canada are disproportionately from communities that experience marginalization. For example, according to 2014 national surveillance data, 35.6% and 30.6% of new HIV diagnoses in women were identified as Black and Indigenous (Aboriginal), respectively.[18] Canadian women living with HIV were shown having higher vulnerabilities to substance use, particularly cigarette smoking and illicit drug use, than Canadian women with a similar age/ethnoracial background.[19] Additional experiences of disadvantage, with regard to social determinants in particular, can result in poorer health outcomes, even in countries where cART is widely available.[9] However, the magnitude of inequalities in underlying socio-structural barriers among WLWH compared with the broader population have not yet been investigated as general population studies do not accurately identify HIV status, and HIV cohort studies often do not include enough women to ensure robust comparison to the broader population to assess differences. Understanding socio-structural barriers that WLWH face in excess of what would be

expected is essential to minimize vulnerability to HIV, eliminate inequities in the HIV care cascade, reduce vulnerabilities to poor outcomes, and improve health and well-being.

Therefore, this study took advantage of comparable measures in two large data sets— the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) for women living with HIV (WLWH) and the Canadian Community Health Survey (CCHS) for women of the general population—to investigate socio-structural determinants and self-rated health status among WLWH, and then compare them with the assumed HIV-negative general population of women, standardizing for age and ethnoracial variables.

2.2. Methods

2.2.1 Study cohorts

CHIWOS: We used data from the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) of WLWH enrolled at time-point 1 between 2013 and 2015. As a community-based research study, CHIWOS applied the Greater Involvement of People Living with HIV/AIDS (GIPA) and Meaningful Involvement of Women Living with HIV/AIDS (MIWA) principles such that WLWH were integral to all steps of the research process.[20,21] CHIWOS enrolled 1,422 WLWH aged ≥ 16, residing in British Columbia (BC), Ontario, and Quebec. Participants were recruited through peers, HIV clinics, AIDS Service Organizations, and online networks.[20] The survey was completed during an in-person interview at clinic or community sites or participants' homes, or via phone/Skype if this was not possible. Information was collected using structured questionnaires, administered by trained Peer Research Associates (PRA) in English or French. Participants provided written or oral informed consent at enrolment. CHIWOS was approved by the Research Ethics Boards of Simon Fraser University, University of British Columbia/Providence Health, Women's College Hospital and McGill University

Health Centre. CHIWOS was approved by the Research Ethics Boards of Simon Fraser University, University of British Columbia/Providence Health, Women's College Hospital and McGill University Health Centre.

CCHS: The Canadian Community Health Survey (CCHS) is a nation-wide population-based survey administered by Statistics Canada that collects self-reported data on various health-related information of approximately 65,000 Canadian residents annually.[22] Briefly, the CCHS uses a multistage, stratified cluster sampling design to target ~98% of Canadians aged ≥12 for inclusion in all provinces and territories. The CCHS excludes people living on reserves, full-time members of the Canadian Forces, the institutionalized residents, and residents of some remote areas. For the purpose of the present research, we used Statistics Canada's Public Use Microdata Files to create a combined CCHS dataset within two years of 2013/2014. For consistency with CHIWOS, we limited the CCHS's analytic sample to women aged ≥16 years old, residing in the three provinces (analytic sample = 46,851). To study day-to-day discrimination, we used the CCHS-Rapid Response on the Everyday Discrimination Scale (EDS) performed separately in 2013 (analytic sample = 6,936). CCHS collects data using both computer-assisted personal and telephone interviews. Statistics Canada's Research Data Centre at the University of Western Ontario provided researchers of the current study with access to the CCHS microdata.

2.2.2 Measures

The most widely used Canadian SDoH framework recognizes that the following socio-structural determinants can help elucidate existing health differences: Aboriginal status, disability, early life events, education, employment and working conditions, food insecurity, health services, gender, housing, income and income distribution, race, social exclusion, social safety net, and unemployment and job security.[23] We chose only those measures whose content and/or wording

were similar in the question stems allowing the measures to be comparable between the two surveys.

The following measures were compared: *relationship status* (single, living common-law or married, and separated/widowed/divorced), *education level* (below high school, completed high school, above high school to non-university degree, and obtained university degree), *yearly personal income* (<$20,000, $20,000 to $39,999, ≥ $40,000, and Not Stated), *yearly household income* (<$20,000, $20,000 to $39,999, and ≥ $40,000), and the *main source of income* (wages/salaries [paid jobs], employment insurance/compensation/welfare, others [e.g., Dividends and interest, Benefits from Pension Plan, no income, etc.], and don't know/not stated).

CHIWOS examined *food sufficiency* and *food security* using Statistics Canada's 4-item adult measure from the Household Food Security Survey Module.[24] The matched items were also found in CCHS. *Food sufficiency* was measured with a question about past-year household food sufficiency, with responses recoded into three categories: always had enough of the kinds of food they wanted to eat, had enough but not always the kinds of food they wanted to eat, and sometimes/often did not have enough to eat. Household *food security* over the last 12 months was measured by three items, "worried that food would run out," "The food did not last, and there was no money to get more," and "could not afford to eat balanced meals." Binary response options for each item were created as 1 for "Sometimes/Often true" and 0 for "Never true." We summed these three items to form a four-category ordinal measure: 0: food secure, 1: mildly food insecure, 2: moderately food insecure, and 3: severely food insecure. CCHS did not measure food security in BC; for comparability, we provided estimates for only Ontario and Quebec in CHIWOS.

Perceived social support was measured using a 4-item abbreviated version of the Medical Outcome Study Social Support Survey (MOS-SSS),[25] measuring four domains of emotional/informational, tangible, affectionate, and positive social interaction. Possible responses included strongly disagree (score 0), disagree, agree, and strongly agree (score 3) in CCHS and a five-point Likert scale, with responses recoded into four categories as none of the time (score 0), a little of the time, some or most of the time, and all of the time (score 3). Items were summed (range 0–12 points), with higher scores implying greater perceived social support. For the purpose of comparison, we created a binary measure with ≤6 indicating poorer social support. The analysis was limited to data from Quebec as CCHS did not measure social support in BC and Ontario.

Racial discrimination and *gender discrimination* measures were quantified using a modified version of the Everyday Discrimination Scale,[26] with 5-item version in CCHS and 6-item version in CHIWOS. CCHS respondents were asked to specify how often they had experienced various forms of day-to-day mistreatments "because of your race" or "because of your gender." Items included "You are treated with less courtesy or respect than other people," "You receive poorer service than other people at restaurants or stores," "People act as if they think you are not smart," "People act as if they are afraid of you," and "You are threatened or harassed." CHIWOS asked the first question in two separate items, "You are treated with less courtesy," and "You are treated with less respect." The CCHS's items were on a five-point scale (at least once a week, a few times a month, a few times a year, less than once a year, never), while they were on a six-point scale in CHIWOS (never, almost never, not that often, sometimes, frequently, almost every day). Two three-category measures were created for racial and gender discrimination, representing: never or almost never experienced any of the mistreatments,

infrequent experience indicating less than once a year or not that often for any of the mistreatments, and frequent experience indicating more than once, or sometimes, or more in a year for any of the mistreatments.

Self-rated health status was measured in both surveys using a single question, "In general, would you say that your health is…?" We included an ordinal variable with five possible responses (excellent, very good, good, fair, and poor), and a binary recoded variable (poor/fair vs. good/very good/excellent).

2.2.3 Statistical analyses

Proportions and associated 95% confidence intervals (CIs) for each measure were first estimated in CHIWOS (i.e., *observed* estimates). Then, the proportion of the same measure was estimated in the CCHS. Survey weights were incorporated into the analyses to account for the survey complexity and provide population-level estimates. The 95% CIs were constructed through the bootstrap variance estimation technique using a set of 500 replicates to account for the complex survey design effects.[27] Standardization method was used to account for the differences in population structure by age and ethnoracial group (**S Table 2.1)**. These two variables are considered as important confounders representing non-modifiable characteristics that differ between the study samples but are not a result of HIV status. To do this, we first produced a 16-category variable representing CHIWOS's age and ethnoracial group structure (i.e., age with four categories: 16-35, 36-45, 46-55, or >55; and ethnoracial statues with four categories: white, African, Caribbean, Black (ACB), Indigenous, or other/multi-ethnicities. We applied CHIWOS's combined age and ethnoracial distribution to the CCHS sample to make the two study populations of CHIWOS and CCHS identical with regard to the distribution of these two variables. After controlling the confounding impact of these two variables, we then provided the

age-/ethnoracial-standardized estimates (i.e., *expected* estimates) of the SDoH measures and self-rated health. Standardization combines stratum-specific prevalence into a single summary estimate through taking a weighted average.[28]

We reported the standardized prevalence differences (SPDs) to quantify the differences between the two study samples for each SDoH measure as well as self-rated health. The SPDs were calculated as the proportion of the observed estimates in CHIWOS minus the expected estimates from the CCHS adjusted for age/ethnoracial group identity; with the SPDs > 0 indicating a greater proportion of the given determinant among WLWH and can be interpreted as the proportion of WLWH experiencing an excess above what would be expected based on the general population women. The 95% CIs were calculated using the methods of variance estimates recovery (MOVER).[29] CIs excluding 0 are indicative of statistical significance at $p<0.05$. All analyses were performed using Stata version 15.

2.3. Results

2.3.1 Demographics

Women in the general population (CCHS data) were older than those in the CHIWOS sample: 34.4% of the general population women versus only 12.0% of WLWH were >55 years old. Around three-quarter of general population women were White (75.2%) and the rest were either Black (3.2%), Indigenous (2.4%) or other/multi ethnicities (19.2%). However, the ethnoracial identities of CHIWOS sample were White (41.1%), African/Caribbean/Black (29.4%), Indigenous (22.3%), and other ethnicities (7.2%). The distribution of age and ethnoracial groups for both CHIWOS and CCHS is presented in (**S Table 2.1)**.

The mean age of all WLWH at time-point 1 was 42.8 (standard deviation [SD]: 10.6). The majority identified as cisgender/non-transgender women (sex-labeled-at-birth and gender identity congruent) (96%) while the rest identified as transgender women. Almost one-quarter (25.1%) were living with HIV for 5 years or less, 40.2% were living with HIV for 6-14 years, and less than one-third were living with HIV for more than 14 years. Overall, 61.0% were optimally on HIV treatment (i.e., treatment adherence ≥ 95%), 22.0% were sub-optimally on HIV treatment (treatment adherence < 95%), while the rest at time-point 1 of the survey were not engaged in HIV treatment. Among those who were on treatment (either optimally or sub-optimally), 87.0% reported an undetectable viral load (i.e., <50 copies/mL). The history of lifetime injection drug use, sex work involvement, and incarceration was reported by 30.9%, 16.6%, and 36.9% of WLWH, respectively (**S Table 2.2)**.

2.3.2 Relationship, education, income and source of income

Proportions of indicators of relationship status, education, poverty, and main source of income differed significantly between WLWH and estimates expected based on the age-/ethnoracial-standardized general population. The proportion who were single was higher among WLWH compared with the general population (48.7% vs. 26.6%; SPD 22.1% [95% CI: 18.8, 25.4]), while a lower proportion of WLWH reported being married or in a common-law relationship status than their general population counterparts (32.1% vs. 55.3%; SPD -23.2% [95% CI: -26.7, -19.6]). A lower proportion of WLWH had a university education than the general population (14.1% vs. 27.9%; SDP -13.7% [95% CI: -16.8, -10.6]), whereas a higher proportion had an education level of less than high school (16.1% vs. 12.3%; SPD 3.8% [95% CI: 1.5, 6.1]). More than two-thirds (70.3%) of WLWH versus less than one-third (28.1%) of women of the general population reported a personal income <$20,000 annually, yielding an SPD 42.2% (95% CI:

39.1, 45.2). A higher proportion of WLWH also reported a household income <$20,000 than the estimate expected in the general population sample (65.3% vs. 10.9%; SPD 54.4% [51.5, 57.3]). Finally, 22.1% of WLWH compared with 69.9% of their counterparts in the general population reported having wages/salaries (i.e., paid jobs) as their main source of income (SPD -47.8% [-50.9, -44.6]), while a high proportion of WLWH (62.2%) reported having an employment insurance/compensation/welfare as their main source of income versus only 9.5% of the general population women (SPD 52.7% [95% CI: 49.5, 55.8]) (**Table 2.1**).

Table 2.1: Comparing Sociodemographic Variables of Women Living with HIV (CHIWOS; 2013-2015) and the General Population of Women in Canada (CCHS; 2013-2014)

	CHIWOS*	CCHS estimates*		SPD¥
		CCHS£	AER Std.†	
	(1)		**(2)**	**(1) – (2)**
Relationship status				
Single	48.7 (46.1, 51.3)‡	24.3 (23.7, 24.8)	26.6 (24.6, 28.7)	22.1 (18.8, 25.4)
Married or common-law	32.1 (29.7, 34.6)	58.0 (57.3, 58.7)	55.3 (52.7, 57.9)	-23.2 (-26.7, -19.6)
Separated/divorced/widowed	19.2 (17.2, 21.3)	17.7 (17.2, 18.3)	18.1 (15.8, 20.4)	1.1 (-1.9, 4.2)
Education				
Less than high school	16.1 (14.2, 18.1)	15.4 (14.9, 16.0)	12.3 (11.0, 13.6)	3.8 (1.5, 6.1)
High school completed	37.6 (35.1, 40.2)	24.7 (24.0, 25.4)	23.9 (21.9, 25.9)	13.7 (10.5, 16.9)
Diploma/trade/college	32.2 (29.8, 34.7)	30.6 (29.8, 31.3)	35.9 (33.4, 38.4)	-3.7 (-7.1, -0.11)

University degree (≥Bachelor's degree)	14.1 (12.4, 16.1)	29.3 (28.6, 30.1)	27.9 (25.4, 30.4)	-13.8 (-16.8, -10.6)
Yearly personal income [a]				
<20,000 CAD [b]	70.3 (67.8, 72.6)	29.1 (28.4, 29.9)	28.1 (26.1, 30.0)	42.2 (39.1, 45.2)
20,000 to <40,000 CAD	17.2 (15.3, 19.3)	24.8 (24.1, 25.5)	24.5 (22.4, 26.7)	-7.3 (-10.1, -4.1)
≥ 40,000 CAD	10.1 (8.7, 11.8)	30.0 (29.2, 30.8)	33.1 (30.4, 35.8)	-23.0 (-26.1, -19.5)
Not stated	2.4 (1.7, 3.3)	16.1 (15.5, 16.8)	14.3 (12.3, 16.3)	-11.9 (-14.0, -9.7)
Yearly household income				
<20,000 CAD	65.3 (62.8, 67.8)	9.3 (8.9, 9.8)	10.9 (9.5, 12.3)	54.4 (51.5, 57.3)
20,000 to <40,000 CAD	20.6 (18.5, 22.8)	20.4 (19.7, 21.0)	18.9 (16.8, 21.1)	1.7 (-1.29, 4.74)
≥ 40,000 CAD	14.1 (12.3, 16.0)	70.3 (69.6, 71.1)	70.2 (67.8, 72.6)	-56.1 (-59.1, -53.0)
Main source of income				
Wages/salaries (paid jobs)	22.1 (20.0, 24.3)	59.2 (58.4, 60.1)	69.9 (67.6, 72.2)	-47.8 (-50.9, -44.6)
Employment insurance/ compensation / welfare	62.2 (59.6, 64.7)	4.8 (4.40, 5.1)	9.5 (7.6, 11.4)	52.7 (49.5, 55.8)
Others (ex. dividends and interest, pension, no income, etc.))	15.0 (13.3, 17.0)	29.4 (28.7, 30.0)	17.0 (15.7, 18.3)	-2.0 (-4.1, 0.4)
Don't know or not stated	0.70 (0.38, 1.30)	6.6 (6.2, 7.1)	3.6 (2.6, 4.6)	-2.9 (-3.9, -1.7)

[*] The Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS; N=1,422) and the Canadian Community Health Survey (CCHS; analytic N=46,851); [‡] Data are % (95% Confidence Intervals (CIs)); [£] Unstandardized weighted estimates are reported from CCHS; [†] AER Std.: Age- and ethnoracial-standardized expected estimates from CCHS; [¥] SPD: standardized prevalence difference (% (95% CIs)), with positive (negative)

values indicating higher (lower) prevalence in WLWH in excess of (less than) what would be expected of Canadian women of similar ages/ethnoracial backgrounds; [a] aged > 17 years old; [b] Canadian dollar (CAD)

2.3.3 Food security

Proportions of food insufficiency and food insecurity were substantially higher in WLWH compared with expected estimates from the general population women. A higher proportion of WLWH reported *sometimes* or *often* their household did not have enough to eat over the last 12 months (15.7% vs. 2.6%; SPD 13.1% [95% CI: 10.9, 15.7]), and had enough but not always the kinds of food (53.7% vs. 15.3%; SPD 38.4% [95% CI: 34.4, 42.4]). The analysis of the individual items of food security scale showed that a higher proportion of WLWH reported their household sometimes/often "worried that food would run out before you got money to buy more" (65.7% vs. 17.9%), "the food bought didn't last and there wasn't any money to get more" (62.9% vs. 14.3%), and "couldn't afford to eat balanced meals" (62.7% vs. 14.0%). Overall, a higher proportion of WLWH reported experiencing severe (54.1% vs. 10.2%; SPD 43.9% [95% CI: 40.2, 47.5]), moderate (10.3% vs. 5.3%; SPD 5.0% [95% CI: 2.6, 7.6]), and mild (8.2% vs. 5.2%; SPD 3.0% [95% CI: 1.1, 5.1]) food insecurity than the expected values in the general population (**Table 2.2**).

Table 2.2: Comparing Food Sufficiency and Food Security between Women Living with HIV (CHIWOS; 2013-2015) and the General Population of Women in Canada (CCHS; 2013-14)

	CHIWOS*	CCHS estimates*		SPD¥
		CCHS£	AER Std.†	
	(1)		**(2)**	**(1) – (2)**
Food sufficiency				
Always had enough of	30.5	89.6	82.0	-51.5

the kinds of food	(27.8, 33.4)‡	(88.9, 90.2)	(79.2, 84.8)	(-55.4, -47.5)
Had enough, but not always the kinds of food	53.7 (50.7, 56.7)	9.1 (8.5, 9.7)	15.3 (12.7, 18.0)	38.4 (34.4, 42.4)
Sometimes or often did not have enough to eat	15.7 (13.7, 18.1)	1.3 (1.1, 1.6)	2.6 (1.7, 3.6)	13.1 (10.9, 15.7)
Food security items				
Item 1) Food run out				
Never	34.3 (31.5, 37.2)	90.8 (90.2, 91.4)	82.1 (79.5, 84.7)	-47.8 (-51.5, -43.8)
Sometimes/often	65.7 (62.7, 68.5)	9.2 (8.6, 9.8)	17.9 (15.3, 20.5)	47.8 (43.8, 51.5)
Item II) Food did not last				
Never	37.1 (34.3, 40.1)	93.3 (92.7, 93.9)	85.7 (83.3, 88.0)	-48.5 (-52.2, -44.7)
Sometimes/often	62.9 (59.9, 65.7)	6.7 (6.1, 7.2)	14.3 (12.0, 16.7)	48.5 (44.7, 52.2)
Item III) Could not afford for balanced meal				
Never	37.3 (34.4, 40.3)	92.8 (92.2, 93.3)	86.0 (83.5, 88.4)	-48.6 (-52.4, -44.8)
Sometimes/often	62.7 (59.7, 65.5)	7.2 (6.6, 7.7)	14.0 (11.6, 16.5)	48.6 (44.8, 52.4)
Overall Food security [a]				
Food secure	27.4 (24.8, 30.2)	88.6 (88.0, 89.3)	79.3 (76.7, 82.0)	-51.9 (-55.6, -48.0)
Mildly food insecure	8.2 (6.7, 10.0)	4.1 (3.7, 4.5)	5.2 (4.1, 6.4)	3.0 (1.1, 5.1)
Moderately food insecure	10.3 (8.6, 12.3)	2.7 (2.4, 3.0)	5.3 (3.6, 6.9)	5.0 (2.6, 7.6)
Severely food insecure	54.1	4.5	10.2	43.9

	(51.0, 57.0)	(4.0, 5.0)	(8.1, 12.2)	(40.2, 47.5)

[*] CHIWOS-Ontario/Quebec (N=1,066) and CCHS-Ontario/Quebec (N=33,704); [‡] Data are % (95% Confidence Intervals (CIs)); [£] Unstandardized weighted estimates are reported from the Canadian Community Health Survey (CCHS); [†] AER Std.: Age- and ethnoracial-standardized expected estimates from CCHS; [¥] SPD: standardized prevalence difference (% (95% CIs)), with positive (negative) values indicating higher (lower) prevalence in WLWH in excess of (less than) what would be expected of Canadian women of similar ages/ethnoracial backgrounds; [a] The summation of three binary items (0, indicating Never true and 1, indicating sometimes/often true) of the scale produced an index ranging from 0 to 3; 0: food secure, 1: mild food insecurity, 2: moderate food insecurity, and 3: severe food insecurity.

2.3.4 Social support and discriminations

Analyzing the overall binary measure of perceived social support showed that a higher proportion of WLWH reported poorer social support compared with the general population women adjusted for age and ethnoracial group status (30.3% vs. 2.9%; SPD 27.4% [95% CI: 22.2, 33.0]). WLWH reported experiencing frequent racial discrimination (46.4% vs. 9.6%; SPD 36.8% [95% CI: 31.9, 41.8]) and frequent gender discrimination (54.4% vs. 8.4%; SPD 46.0% [95% CI: 42.6, 51.6]) than the expected values of the general population women (**Table 2.3**).

Table 2.3: Comparing Social Support, and Racial and Gender Discrimination between Women Living with HIV (CHIWOS; 2013-2015) and the General Population of Women in Canada (CCHS; 2013-2014)

	CHIWOS	CCHS estimates		SPD[¥]
		CCHS[£]	AER Std.[†]	
	(1)		**(2)**	**(1) – (2)**
Perceived social support[*,a]				
Poor	30.3 (25.6, 35.5)[‡]	1.9 (1.5, 2.3)	2.9 (0.7, 5.1)	27.4 (22.2, 33.0)
Good	69.7 (64.5, 74.4)	98.1 (97.7, 98.5)	97.1 (94.9, 99.3)	-27.4 (-33.0, -22.2)
Race discrimination[**]				
Never	45.6	93.5	87.1	-41.5

	(43.0, 48.2)	(92.2, 94.8)	(82.2, 92.1)	(-47.1, -36.0)
Infrequent	8.0 (6.7, 9.6)	1.1 (0.65, 1.48)	3.3 (0.5, 6.1)	4.7 (1.7, 7.9)
Frequent	46.4 (43.8, 49.0)	5.4 (4.1, 6.6)	9.6 (5.3, 13.8)	36.8 (31.9, 41.8)
Gender discrimination[**]				
Never	37.5 (35.0, 40.0)	89.3 (88.2, 90.5)	89.4 (87.0, 91.7)	-51.9 (-55.3, -48.4)
Infrequent	8.2 (6.9, 9.7)	2.6 (2.1, 3.1)	2.2 (1.2, 3.2)	6.0 (4.3, 7.8)
Frequent	54.4 (51.8, 56.9)	8.1 (7.0, 9.0)	8.4 (6.2, 10.6)	46.0 (42.6, 51.6)

[*] CHIWOS-Quebec (N=355) and CCHS-Quebec (N=11,780); [**] CHIWOS-all N=1,422 and CCHS rapid survey (N=6,936); [‡] Data are % (95% Confidence Intervals (CIs)); [£] Unstandardized weighted estimates are reported from the Canadian Community Health Survey (CCHS); [†] AER Std.: Age- and ethnoracial-standardized expected estimates from CCHS; [¥] SPD: standardized prevalence difference (% (95% CIs)), with positive (negative) values indicating higher (lower) prevalence in WLWH in excess of (less than) what would be expected of Canadian women of similar ages/ethnoracial backgrounds; [a] The summation of four items, each having four options (0 to 3), produced an index ranging from 0 to 12; with a lower score indicating lower level of social support. A binary measure was created based on the mid-point threshold score: score mid-point or below (i.e., ≤ 6) indicated poor/low perceived social support, and scores above mid-point (i.e., > 6) indicated better/good perceived social support.

2.3.5 Overall health status

A higher proportion of WLWH reported poor and fair overall health status than the estimates expected based on the age-/ethnoracial-standardized assumed HIV-negative women. The aggregated proportion of these two options (i.e., fair/poor health condition), indicating a lower level of overall health status, was higher among WLWH than the general population women (24.8% vs. 12.6%; SPD: 12.2% [95% CI: 9.4, 15.0]) (**Table 2.4**).

Table 2.4: Comparing Self-rated Overall Health Status between Women Living with HIV (CHIWOS; 2013-2015) and the General Population of Women in Canada (CCHS; 2013-2014)

Self-rated health	CHIWOS (1)	CCHS estimates		SPD[¥] (1) – (2)
		CCHS[£]	AER Std.[†] (2)	
A five-category measure				
Excellent	8.3 (6.9, 9.8)[‡]	20.7 (20.0, 21.4)	21.9 (19.5, 24.2)	-13.6 (-16.3, -10.8)
Very good	26.9 (24.6, 29.3)	37.5 (36.7, 38.3)	35.8 (33.6, 37.9)	-8.9 (-12.0, -5.7)
Good	40.1 (37.5, 42.6)	30.0 (29.1, 30.8)	29.7 (27.3, 32.1)	10.3 (6.8, 13.8)
Fair	19.0 (17.1, 21.2)	8.8 (8.3, 9.2)	8.9 (7.5, 10.2)	10.2 (7.8, 12.7)
Poor	5.7 (4.6, 7.1)	3.0 (2.8, 3.3)	3.7 (2.8, 4.7)	2.0 (0.51, 3.6)
A binary measure				
Excellent/v. good/good	75.2 (72.9, 77.4)	88.2 (87.6, 88.7)	87.4 (85.8, 89.0)	-12.2 (-15.0, -9.4)
Fair/poor	24.8 (22.6, 27.1)	11.8 (11.3, 12.3)	12.6 (11.0, 14.2)	12.2 (9.4, 15.0)

[*] The Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS; N=1,422) and the Canadian Community Health Survey (CCHS; analytic N=46,851); [‡] Data are % (95% Confidence Intervals (CIs)); [£] Unstandardized weighted estimates are reported from CCHS; [†] AER Std.: Age- and ethnoracial-standardized expected estimates from CCHS; [¥] SPD: standardized prevalence difference (% (95% CIs)), with positive (negative) values indicating higher (lower) prevalence in women living with HIV (WLWH) in excess of (less than) what would be expected of Canadian women of similar ages/ethnoracial backgrounds.

2.4. Discussion

Drawing on data from the largest cohort study of WLWH in Canada, we found that 42.2% and 43.9% of WLWH respectively reported an annual personal income <$20,000—a low income cut-off indicating poverty—and severe food insecurity, in excess of what would be expected of Canadian women of similar ages/ethnoracial backgrounds. Additionally, a higher proportion of

WLWH reported experiencing the proxy indicators for social exclusion including poor perceived social support, and racial and gender discriminations compared with what would be expected. The self-rated health, as a proxy but holistic measure of health, was also lower in WLWH. While previous research highlighted the greater socio-structural disadvantages and economic hardships among WLWH, we are not aware of previous comparisons between these two populations.

Although this analysis did not permit assessment of whether living with HIV exacerbated inequities in SDoH or whether such inequities increase risk of acquiring HIV or (likely) a mixture of both, a large proportion of WLWH in Canada are living with multiple and overlapping disadvantages with regard to social and economic participation is unjust and of huge concern. The concentration of financial hardship, food insecurity, and social exclusion – with having the potential for exposure to increased magnitude of chronic and acute stressors, poses a wide range of barriers that negate the ability of individuals to consistently engage in the HIV care/treatment cascade, e.g., retention in care[30] and cART initiation and continuation,[12] and further undermine attempts to optimize treatment outcomes. Recent studies have documented the role of food insecurity, for example, on cART non-adherence and incomplete HIV viral suppression.[10,15] Such level of risk has also been realized for social exclusion determinants[14] as found notably prevalent in WLWH in the present study. These findings highlight the need for multi-component interventions targeted at SDoH inequity reduction, particularly in those women with an increased risk for treatment interruptions, discontinuation, and non-adherence due to limited socio-structural resources.

The substantial differences in the study determinants and self-assessed health identified between the two samples would provide evidence on the socio-structural determinants of WLWH to aid with policy development and resource allocation. Given the concern surrounding

the growing proportion of WLWH in Canada,[18] our findings have implications for evoking calls for gender-specific tailored service, a complex and multidimensional model of care and service delivery, as the current care approaches appear to be inadequate to address women's comprehensive needs. The women-centered model of HIV care that has already been envisioned by target population is recommended to be a useful model of care for guiding policy and practice to improve care and health outcomes.[31] Such models of care require targeting the persistent health inequalities in women with HIV, relative to either men with HIV[3,4] or women of the general population, through a social-determinants framework, an approach in which a wide range of disciplines contribute to addressing the underlying barriers and reducing health inequities.[32] The socio-structural approach of addressing the fundamental causes of health inequities are imperative to achieve the UNAIDS "90-90-90 targets"—the universal commitments of HIV epidemic elimination by 2030.[33]

This analysis has also significant implications for designing strategies that support WLWH through social service programs, and reinforcing social support and resilience with the objective of facilitating women's access to care, promoting health and wellbeing, health equity, and social justice. Programs supporting social service delivery have important implications, especially now that HIV care has shifted toward chronicity. The provision of transportation supports, financially accessible complementary services, and providing flexible program schedules can facilitate access to care among women with socio-economical disadvantages.[34] The integration of social programs into health service delivery can help address socio-structural adversities and facilitate women's participation in HIV care.

2.4.1 Strengths and Limitations

To our knowledge, this is the first research investigating the inequities with socio-structural determinants of health and the self-rated health between WLWH and assumed HIV-negative women of the general population. However, this study is not without limitations. First, we compared the health determinants among WLWH with the *assumed* HIV-negative women of the general population. However, due to small population estimates of WLWH in Canada—97 per 100,000 females[18]—we believe the inclusion of WLWH in the comparison group would not substantially impact on our findings. Furthermore, the substantial differences identified between the two surveys may be partly due to differences in population structure other than age/ethnoracial group, factors which were not accounted for in standardization. Moreover, self-report data may be prone to social desirability bias, particularly in CCHS data. CHIWOS attempted to mitigate the impact of this bias using trained peer research associates (PRAs), who shared an experience of living with HIV, to administer the surveys. Also, CHIWOS's non-random sampling design may undermine the generalizability of these findings.

2.4.2 Conclusion

These findings provide information on the upstream determinants of health inequalities in WLWH indicating that a high proportion of WLWH in Canada experienced much worse economic hardships, food insecurity, social exclusions as well as poor/fair self-reported health, in excess of what would be expected. These findings support the need for the integration of socio-structural approaches and health equity into practice to address women's unique needs. These findings also advocate for social service delivery and programming as well as further resource allocation to reduce socially constructed, unjust, and avoidable inequalities in health in this population. Addressing these needs when providing individual-tailored HIV care and

treatment services will promote the clinical care of a sizable proportion of women with HIV living in poverty. Future research needs to focus on targeted exclusion-reduction interventions, e.g., poverty- and discrimination-reduction strategies, in this population. Future research could also assess the independent and/or clustered impact of these social determinants of health (e.g., race discrimination, gender discrimination) plus other relevant social determinants in the field of HIV such as HIV-related stigma on health outcomes of WLWH. Applying advanced statistical techniques such as decomposition analysis[35] – a technique to assess health inequalities through decomposing the overall inequality in the study outcomes into the inequality in each contributing determinants, and latent class analysis (LCA)[36] – a method to identify the latent class/clusters of individuals who experience the unique adversities with respect to the social determinants, can help researchers better explore the association of these determinants with HIV outcomes. This data on SDoH inequalities can help investigators develop interventions to address disparities experienced by WLWH to improve their health outcomes, and identify mechanisms through which these determinants may reinforce or directly contribute to inequitable vulnerabilities among WLWH.

2.5. Supplementary Tables

S Table 2.1: Age-Ethnoracial Distributions of both the CHIWOS (2013-2015) Cohort of Women Living with HIV and the CCHS (2013-2014) Data of the Corresponding General Population Women in Canada.

		CHIWOS estimates (N=1,422)	CCHS estimates (N=46,851)[a]	
		%	Unstandardized %	Standardized %
Ethnoracial and age groups				
White	16-35 (years)	10.2[b]	21.1[c]	10.2[d]
	36-45	11.4	11.2	11.4
	46-55	12.5	13.9	12.5
	> 55	7.0	29.0	7.0
Black	16-35	7.5	1.1	7.5
	36-45	11.5	0.7	11.5
	46-55	7.8	0.8	7.8
	> 55	2.6	0.7	2.6
Indigenous	16-35	7.0	1.0	7.0
	36-55	8.4	0.4	8.4
	36-45	5.2	0.4	5.2
	46-55	1.7	0.6	1.7
Others	16-35	1.4	7.9	1.4
	36-45	2.4	4.4	2.4
	46-55	2.6	3.1	2.6
	> 55	0.8	3.7	0.8

[a] Out of 128,310 respondents, 46,851 (36.5%) were the corresponding general population women for the current study: women aged 16+ residing in three provinces of BC, ON, QC; [b] Data are presented as percentages; [d] Chi Square test showed a significant difference between the two samples of CHIWOS and unstandardized CCHS (P-value < 0.001); [c] Standardization made the two study populations of CHIWOS and CCHS identical with regard to the distribution of age and ethnoracial group.

S Table 2.2: Characteristics of Women Living with HIV (WLWH) – the Baseline Survey of the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS), 2013-2015

Variables	n (%) or mean [SD]
Age, year (mean [SD])	42.8 [10.6]
Age groups (years) (N = 1,422)	
16-35	372 (26.2)
36-45	479 (33.7)
46-55	400 (28.1)
> 55	171 (12.0)
Ethno-racial group (N = 1,422)	
White	584 (41.1)
African/Caribbean/Black	418 (29.4)
Indigenous	318 (22.3)
Other	102 (7.2)
Study province (N = 1,422)	
Ontario	717 (50.4)
British Columbia	356 (25.0)
Quebec	349 (24.6)
Years living with HIV (N = 1,374)	
< 6 years	345 (25.1)
6-14 years	552 (40.2)
> 14 years	477 (34.7)
Taking treatment (N = 1,415)	
Yes, optimal (≥ 95%)	863 (61.0)
Yes, suboptimal (< 95%)	312 (22.0)
Not engaged in treatment	240 (17.0)
Undetectable (50 copies/mL) viral load among WLWH on	1018 (87.0)

treatment (N=1,170)	
History of injection drug use (N = 1,421)	439 (30.9%)
History of sex work involvement (N=1,321)	219 (16.6)
History of incarceration (N=1,420)	5246.9)

2.6. References

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3. Chapter 3: Substance use patterns among women living with HIV compared with the general female population of Canada[1]

3.1. Introduction

Substance use is a common health risk behaviour among people living with HIV (PLWH), who have a demonstrated greater prevalence than their general population counterparts.[1-3] Substance use is considered a major barrier to successful HIV care and treatment[4-9] despite the substantial advances obtained from combination antiretroviral therapy (cART), e.g., improved life expectancy in PLWH.[10] Substance use independently or by interaction with other factors such as psychiatric disorders and socioeconomic marginalization has the potential to limit the remarkable benefits of cART and pose additional barriers to HIV prevention efforts and medical care.[6-9,11-14]

Previous studies have reported the negative impacts of tobacco smoking,[12] problematic alcohol consumption,[13] and illicit drug use (e.g., heroin)[4,8] on HIV care cascade outcomes. The optimal levels of these outcomes such as retention in care and adherence to HIV treatment are critical in promoting the health of PLWH and maintaining treatment as prevention (TasP) targets.[15] Beyond its interruption of care and treatment, substance use can also interfere with cART metabolism and virological response,[16,17] and contribute to excess mortality.[12,18] For example, in a study of 17,995 PLWH on treatment, smoking increased the rate of death by 1.94 times, with 1.84 and 2.41 times in men and women with HIV, respectively.[18]

[1] A version of this chapter has been published: Shokoohi M, Bauer GR, Kaida A, et al. Substance use patterns among women living with HIV compared with the general female population of Canada. *Drug Alcohol Depend*. 2018 Oct 1;191:70-77. doi: 10.1016/j.drugalcdep.2018.06.026.

Substance use vulnerability appears to have greater impacts on HIV and clinical outcomes among women than men with HIV. For example, women with injection drug use (IDU) history and Indigenous ancestry had lower optimal adherence to treatment (47.8%) relative to their male HIV-positive counterparts with (57.7%) and without (83.8%) such vulnerabilities.[19] Women with IDU history were also found to be 18% less likely to achieve HIV RNA viral suppression than their male counterparts.[20] Other than the unique experiences of HIV infection among women (e.g., pregnancy), drug use along with greater experiences of other psychosocial, economic and structural challenges may account for gender-related differences in HIV outcomes.[20-22]

However, substance use prevalence among women living with HIV (WLWH) has not been well-characterized, particularly in Canada. Population-based research has either overlooked collecting data on WLWH, or has not had adequate sample size to provide estimates for WLWH and comparisons to the broader population.[23,24] Women now constitute more than half of all individuals living with HIV worldwide[25] and represent nearly one-fourth of the estimated 75,500 PLWH in Canada; almost doubled from the 1990s.[26] Understanding the prevalence of substance use in a geographically diverse sample of WLWH relative to general population women is important because of the profound implications for HIV management and to assess the need for harm reduction and socio-structural supports for women who use substances.

Therefore, the objective of this research was to characterize the prevalence of cigarette smoking, alcohol consumption, non-prescribed cannabis use, and illicit drug use from the Canadian HIV Women's Sexual and Reproductive Cohort Study (CHIWOS), a large community-based study of WLWH in Canada. We estimated the prevalence for substance use in CHIWOS, and compared them with data from HIV-negative women of the general population, standardized to the age/ethnoracial distribution of WLWH. Our aim was to document substance

use disparities among WLWH, to explore differences based on HIV status and to identify needs with regard to resource allocation, particularly given the implications of substance use in the context of HIV-related medical care.

3.2. Methods

3.2.1 Participants

CHIWOS sample: We used data from the baseline survey of the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) conducted between 2013 and 2015. CHIWOS is a large community-based study of WLWH (≥16 years; 3.8% trans women), residing in British Columbia (BC), Ontario, and Quebec. Study design and sampling procedure were published elsewhere.[27] Briefly, we applied the Meaningful Involvement of Women Living with HIV/AIDS principle, reflecting the recognition of the rights and responsibilities of individuals living with HIV as equal partners to actively engage throughout the design and delivery of HIV/AIDS services to strengthen the responses to HIV/AIDS epidemics.[28] A sample of 1,422 WLWH were recruited from HIV clinics, AIDS Service Organizations, peers, and online networks.[24] The survey was administered by Peer Research Associates (PRAs), many of whom also shared the experience of living with HIV, who were hired and trained in community-based research conduction.[27] The average 120-minute-long surveys were administered either through in-person interviews at clinic, community sites, or participants' homes, or via phone/Skype. CHIWOS was approved by the Research Ethics Boards of Simon Fraser University, University of British Columbia/Providence Health, Women's College Hospital and McGill University Health Center.

CCHS sample: We used data from the 2013-2014 cycle of the Canadian Community Health Survey (CCHS), a nation-wide cross-sectional survey administered by Statistics Canada.

Detailed documentation is available elsewhere.[29] Briefly, CCHS is designed to provide nationally representative estimates on health status, health care utilization, and health determinants of Canadians aged 12 years or older residing in private dwellings of all provinces and territories (~98% coverage), excluding populations living on reserves/Indigenous settlements, institutions, Canadian Force Bases, and some remote regions. Data are collected using computer assisted personal and telephone interview software. Consistent with CHIWOS, CCHS analyses were restricted to women aged ≥16 years old, residing in the three provinces (analytic sample = 46,851). Measures of cigarette smoking, alcohol consumption, non-prescribed cannabis use and illicit drug use with similar content and wording were compared between the two surveys.

3.2.2 Measures

Although cigarette smoking and alcohol consumption were collected from all CCHS respondents, measures of drug use were not collected in Ontario and Quebec; for comparability, we provided estimates of drug use for only BC participants in CHIWOS.

Cigarette smoking: In CHIWOS, cigarette smoking history was measured as, "What is your cigarette (tobacco) smoking history?" with four response options (regular, occasional, former, and never). In CCHS, the same question was asked with three response options (daily, occasionally, not at all). To be consistent with the CCHS definition, we categorized WLWH who reported at least one cigarette/day (equivalently, at least 30 cigarettes/month) as "daily" smokers irrespective of how they were self-identified. As such, 67 self-identified occasional smokers were recoded as daily smokers and two cases who reported cigarette smoking regularly were recoded as occasional smokers. Two measures were created to compare the two surveys: a) nonsmokers at the time of interview (i.e., former or none) versus current smokers (i.e., daily or

occasional), and b) a three-category measure: nonsmokers, occasional smokers, and daily smokers. We also reported cigarette smoking intensity/quantity among current smokers. A five-category measure was created to compare the two surveys: nonsmokers (former or never), <1 cigarette/day or <30 cigarettes/month, 1-10 cigarettes/day, 11-19 cigarettes/day, and ≥20 cigarettes/day.

Alcohol consumption: Last-year alcohol consumption pattern was examined in both CHIWOS and CCHS. A four-category comparable measure was created in each survey: none (did not drink in the past 12 months), ≤1 time/week, 2-3 times/week, and ≥4 times/week. CCHS measured the monthly pattern of binge drinking as, "How often in the past 12 months have you had 4 or more drinks on one occasion?" with six response categories: never, less than once a month, once a month, 2 to 3 times a month, once a week, and more than once a week. The same question but in the last month was measured in CHIWOS, with an open-ended response option indicating the number of times. Binge drinking was compared between the two surveys under the assumption that past-year binge drinking patterns were consistent with past month. We created a measure with similar response categories: no alcohol consumed, alcohol consumed but no binge drinking, binge drinking less than once a week (i.e., equivalently, less than 3 times a month), and binge drinking at least once a week (i.e., equivalently, four times or more a month). In CHIWOS, 33 women reported last-month binge drinking without specifying the number of times over the last month; therefore, instead of treating them as missing values, we categorized them into "less than once a week."

Drug use: We compared the use of the following drugs available in the two surveys in BC: cannabis, cocaine or crack, speed (amphetamine), and heroin. CCHS asked respondents, "Have you used [any of these drugs] in the past 12 months?", affirmative responses were further

followed, “How often [did you use any of these drugs in the past 12 months]?” with the following response options: less than once/ month, 1 to 3 times/month, once/week, more than once/week, and every day. CHIWOS measured cannabis use as, “What is your cannabis use history?” with the following response categories: a) regularly in the last 30 days, b) occasionally in the last 30 days, c) used in the past year but not in the past 30 days, d) used in the past but not in the past year, e) never used or only ever used it once or twice. To be consistent with CCHS, CHIWOS’s response options ‘b’ and ‘c’ were considered as occasional cannabis use. CHIWOS participants with a positive history of cannabis use were also followed, “Have you used cannabis mainly for medicinal reasons or recreational reasons, or both?” We recoded medicinal (prescribed) use of cannabis use as non-recreational use, while any other recreational reasons (alone or in combination with medicinal use) were considered as non-prescribed cannabis use. This distinction was made as CCHS aimed to measure the use of illicit drugs, but not prescription drugs.

CHIWOS assessed the use of crack or cocaine, speed, and heroin over the last 3 months. Positive responses were additionally followed to measure the frequency of use as, daily, at least once/week, and less than once/week. The same information was assessed in CCHS, but over the past year. Crack and cocaine use were measured in one single question in CCHS, while CHIWOS measured them separately. Therefore, daily use of any of these two drugs was considered as daily crack or cocaine use.

For the purpose of comparison, we created a three-category measure for cannabis use and crack or cocaine use as: none (i.e., former or never), occasional (< once/week), and regular use (≥ once/week). As the absolute “n” for speed (amphetamine) and heroin use did not meet the

minimum CCHS vetting guideline, we combined regular and occasional use and then created a binary variable for each of these two drugs: none vs. occasional/regular use.

3.2.3 Data analysis

We reported the prevalence and the 95% confidence intervals (CI) of each substance from the CHIWOS sample. We then obtained the prevalence of the same substances from the CCHS sample, using sampling weights that Statistics Canada assigned each respondent to correspond to the number of Canadian residents they represent. The bootstrap variance estimation technique using a set of 500 replicates was used to obtain the 95% CI of the CCHS estimates.[30] To address the imbalanced distribution of age and ethnoracial groups, we used a standardization method which combines stratum-specific prevalences into a single summary estimate through taking a weighted average.[31] Standardization obtains these weights in averaging from a *standard* population. In the present study, these weights were obtained from the CHIWOS data set and applied to CCHS data. To do this, we created a 16-category variable representing CHIWOS's age and ethnoracial group distribution (i.e., four age categories: 16-35, 36-45, 46-55, or >55; four ethnoracial categories: white, African, Caribbean, Black (ACB), Indigenous, or other/multi-ethnicities). We then applied CHIWOS's age and ethnoracial group distribution to CCHS to produce a second set of estimates in which CCHS and CHIWOS samples had a similar distribution with respect to these two variables.

The standardized prevalence differences (SPD) were reported to quantify the differences between the two surveys for each substance use. The SPD is a commonly used measure for the purpose of population health assessment and provides information on the public health impact. The SPD was computed by subtracting the CCHS *expected* estimates standardized to age and ethnoracial groups from the CHIWOS *observed* estimates; with an SPD greater than zero (i.e.,

the null) denoting a greater prevalence of the given substance in WLWH. The SPD's 95% CI was provided using the methods of variance estimates recovery (MOVER),[32] with 95% CI excluding 0 indicating statistical significance at $p<0.05$. The analyses were performed using Stata version 15.

3.3. Results

3.3.1 Demographics

WLWH differed from the unstandardized general population data by age and ethnoracial groups as well as relationship status, education and yearly personal income levels (**Table 3.1**). Greater proportions of women in the unstandardized general population were older and belonged to white ethnoracial group than WLWH. Other characteristics of these two samples are presented in **Table 3.1**, along with the prevalences in the standardized CCHS data. After standardization, the CCHS estimates had identical age and ethnoracial group structure. All subsequent comparisons of substance use were conducted using standardized data.

Overall 83% and 87% of WLWH reported taking HIV medication and having a suppressed viral load (i.e., <50 c/mL), respectively. The median time living with HIV since diagnosis was 11 years (IQR: 7, 17) (data not shown).

Table 3.1: The Distribution of Age, Ethnoracial Groups, Relationship Status, Education Status, and Yearly Personal Income in the Cohort of Women with HIV Compared with the Assumed HIV-Negative Women of the General Population in Canada.

		CHIWOS estimates (N=1,422)		CCHS estimates (N=46,851)*		
		N	% (95% CI)	N	Unstandardized % (95% CI)	Standardized % (95% CI)[c]
Ethnoracial and age groups						
White	16-35 (years)	145	10.2 (8.7, 11.9)	8,749	21.1 (20.6, 21.7)	10.2[d]
	36-45	162	11.4 (9.8, 13.2)	4,582	11.2 (10.6, 11.5)	11.4
	46-55	178	12.5 (10.9, 14.3)	5,775	13.9 (13.4, 14.5)	12.5
	> 55	99	7.0 (5.7, 8.4)	12,020	29.0 (28.5, 29.6)	7.0
Black	16-35	107	7.5 (6.3, 9.0)	457	1.1 (0.9, 1.3)	7.5
	36-45	163	11.5 (9.9, 13.2)	280	0.7 (0.5, 0.9)	11.5
	46-55	111	7.8 (6.5, 9.3)	333	0.8 (0.6, 1.1)	7.8
	> 55	37	2.6 (1.9, 3.6)	268	0.7 (0.5, 0.8)	2.6
Indigenous	16-35	100	7.0 (5.8, 8.5)	424	1.0 (0.9, 1.2)	7.0
	36-55	120	8.4 (7.1, 10.0)	161	0.4 (0.3, 0.5)	8.4
	36-45	74	5.2 (4.2, 6.5)	176	0.4 (0.3, 0.5)	5.2
	46-55	24	1.7 (1.1, 2.5)	255	0.6 (0.5, 0.7)	1.7
Others	16-35	20	1.4 (0.9, 2.2)	3,286	7.9 (7.4, 8.4)	1.4
	36-45	34	2.4 (1.7, 3.3)	1,837	4.4 (4.0, 4.9)	2.4

46-55	37	2.6 (1.9, 3.6)	1,271	3.1 (2.7, 3.5)	2.6
> 55	11	0.8 (0.4, 1.4)	1,539	3.7 (3.4, 4.1)	0.8
Relationship status					
Single	689	48.7 (46.1, 51.3)	10,438	24.3 (23.7, 24.8)	26.6 (24.6, 28.7)
Married, common-law	545	32.1 (29.7, 34.6)	24,971	58.0 (57.3, 58.7)	55.3 (52.7, 57.9)
Separated/divorced/widowed	271	19.2 (17.2, 21.3)	7,636	17.7 (17.2, 18.3)	18.1 (15.8, 20.4)
Education status					
Less than high school	227	16.1 (14.2, 18.1)	6,568	15.4 (14.9, 16.0)	12.3 (11.0, 13.6)
High school completed	532	37.6 (35.1, 40.2)	10,514	24.7 (24.0, 25.4)	23.9 (21.9, 25.9)
Diploma/trade/college	456	32.2 (29.8, 34.7)	12,998	30.6 (29.8, 31.3)	35.9 (33.4, 38.4)
University degree (≥Bachelor's degree)	200	14.1 (12.4, 16.1)	12,474	29.3 (28.6, 30.1)	27.9 (25.4, 30.4)
Yearly personal income [a]					
<20,000 CAD[b]	997	70.3 (67.8, 72.6)	12,263	29.1 (28.4, 29.9)	28.1 (26.1, 30.0)
20,000 to <40,000 CAD	244	17.2 (15.3, 19.3)	10,425	24.8 (24.1, 25.5)	24.5 (22.4, 26.7)
≥ 40,000 CAD	144	10.1 (8.7, 11.8)	12,620	30.0 (29.2, 30.8)	33.1 (30.4, 35.8)
Not stated	34	2.4 (1.7, 3.3)	6,795	16.1 (15.5, 16.8)	14.3 (12.3, 16.3)
Trans women	54	3.8 (2.9, 4.9)	--- [e]	--- [e]	--- [e]

* Out of 128,310 respondents, 46,851 (36.5%) were eligible for the current study: women aged 16+ residing in three provinces of BC, ON, QC; [a] aged > 17 years old; [b] Canadian dollar (CAD); [c] 95% CIs were not estimated for standardization variables; [d] Standardization made the two study populations identical with regard to age and ethnoracial group structure; [e] Not available as CCHS does not contain data identifying trans status.

3.3.2 Cigarette smoking

A higher prevalence of cigarette smoking frequency and intensity was reported among WLWH compared with estimates expected based on the age-/ethnoracial-standardized women of the general population. Current cigarette smoking (i.e., daily/occasional) was reported by 43.7% of WLWH relative to 17.8% of the expected estimates of general population (SPD 25.9%), indicating that 25.9% (i.e., 259 per 1000) of WLWH reported current cigarette smoking, in excess of what would be expected of Canadian women of similar ages/ethnoracial backgrounds. Daily cigarette smoking was reported by 40.7% of WLWH versus 13.9% of expected estimates from general population women (SPD 26.8%). WLWH tended to smoke cigarette more intensely than the expected estimates of the general population (**Table 3.2**).

Table 3.2: Comparison of Cigarette Smoking between Women with HIV (N=1,422) and Assumed HIV-Negative Women of the General Population (N=46,851).

Cigarette smoking measures	CHIWOS	CCHS estimates		SPD[¥]
		CCHS[£]	AER Std.[†]	
	(1)		**(2)**	**(1) – (2)**
Overall cigarette smoking				
Nonsmoker (i.e., former/never)	56.3 (53.7, 58.9)[‡]	84.3 (83.7, 84.9)	82.2 (80.8, 83.7)	-25.9 (-28.9, -22.9)
Current smokers (i.e., daily/occasional)	43.7 (41.1, 46.3)	15.7 (15.1, 16.3)	17.8 (16.3, 19.2)	25.9 (22.9, 28.9)
Current cigarette smoking status				
Nonsmoker (i.e., former/never)	57.0 (54.4, 59.6)	84.3 (83.7, 84.9)	82.2 (80.8, 83.7)	-25.2 (-28.2, -22.2)
Occasional smokers [a]	2.3 (1.6, 3.2)	3.8 (3.5, 4.2)	3.9 (3.2, 4.6)	-1.6 (-2.6, -0.5)
Daily smokers [b]	40.7	11.9	13.9	26.8

	(38.1, 43.3)	(11.3, 12.4)	(12.5, 15.2)	(23.9, 29.7)
Intensity of cigarette smoking				
Nonsmoker (i.e., former/never)[c]	57.0 (54.4, 59.6)	84.4 (83.8, 85.0)	82.4 (80.9, 83.9)	-25.4 (-28.4, -22.4)
<1 cig/day or <30 cig/month	2.3 (1.6, 3.2)	2.5 (2.3, 2.8)	2.5 (2.1, 2.9)	-0.2 (-1.0, 0.8)
1 to 10 cig/day	20.4 (18.3, 22.6)	6.6 (6.2, 7.0)	7.8 (6.7, 9.0)	12.6 (10.2, 15.1)
>10 to <20 cig/day	5.4 (4.4, 6.8)	3.2 (2.9, 3.4)	4.0 (3.2, 4.8)	1.4 (0.1, 3.0)
≥ 20 cig/day	14.9 (13.1, 16.9)	3.3 (3.0, 3.6)	3.3 (2.8, 3.8)	11.6 (9.8, 13.6)

[‡] Data are % (95% CI); [£] unstandardized weighted estimates are reported and the 95% CI was constructed using bootstrap method; [†] Age- and ethnoracial-standardized expected estimates based on women of the general population from CCHS; [¥] SPD: standardized prevalence difference (% (95% CI)); the 95% CI was constructed using MOVER algorithm; [a] Occasional smokers (<1 cigarette/day or <30 cigarettes/month); [b] Daily smokers (≥1 cigarettes/day or ≥30 cigarettes/month); [c] Because of missing values in variable intensity of cigarette smoking, the proportion of the first and second categories if different from the same categories in variable current cigarette smoking status, while the absolute numbers is the same.

3.3.3 Alcohol consumption

WLWH more frequently reported no alcohol consumption compared with the expected estimates (40.7% vs. 28.0%). The proportion of alcohol consumption categories among WLWH than expected estimates from standardized general population data was: 46.8% vs. 52.2% consumed alcohol ≤1 time/week, 7.0% vs. 12.9% consumed alcohol 2-3 times/week, and 5.5% vs. 6.9% consumed alcohol 4+ times/week. The monthly pattern of binge drinking in WLWH was: 15.4% vs. 30.6% for less than once/week (SPD -15.2%), and 4.6% vs. 3.9% for at least once/week (SPD 0.7%). The combination of these two categories showed that 20.0% of WLWH reported binge drinking at least once/month compared with 34.5% in women of the general population (**Table 3.3**).

Table 3.3: Comparison of Alcohol Consumption between Women with HIV (N=1,422) and Assumed HIV-Negative Women of the General Population (N=46,851)

	CHIWOS	CCHS estimates		SPD[¥]
		CCHS[£]	AER Std.[†]	
	(1)		**(2)**	**(1) - (2)**
Alcohol consumption frequency				
None (Never/none in specified time)	40.7 (38.2, 43.3)[‡]	24.5 (23.7, 25.4)	28.0 (25.4, 30.5)	12.7 (9.1, 1.4)
≤1 time a week	46.8 (44.2, 49.4)	51.3 (50.4, 52.1)	52.2 (49.6, 54.8)	-5.4 (-9.1, -1.7)
2-3 times a week	7.0 (5.7, 8.4)	15.1 (14.5, 15.7)	12.9 (11.5, 14.1)	-5.9 (-7.7, -3.9)
4+ times a week	5.5 (4.4, 6.8)	9.1 (8.7, 9.5)	6.9 (5.8, 8.1)	-1.4 (-3.0, 0.4)
Binge drinking categories [a]				
No alcohol consumed	41.0 (38.5, 43.7)	24.6 (23.8, 25.5)	28.0 (25.4, 30.6)	13.0 (9.4, 16.7)
Alcohol consumed, not binge	39.0 (36.4, 41.5)	40.3 (39.5, 41.1)	37.5 (34.9, 40.0)	1.5 (-2.1, 5.1)
Binge drinking less than once a week	15.4 (13.6, 17.4)	30.9 (30.1, 31.7)	30.6 (28.7, 32.4)	-15.2 (-17.8, -12.6)
Binge drinking at least once a week	4.6 (3.6, 5.9)	4.2 (3.9, 4.5)	3.9 (3.3, 4.4)	0.7 (-0.3, 2.1)

[‡] Data are % (95% CI); [£] unstandardized weighted estimates are reported and the 95% CI was constructed using bootstrap method; [†] Age- and ethnoracial-standardized expected estimates based on women od the general population from CCHS; [¥] SPD: standardized prevalence difference (% (95% CI)), and the 95% CI was constructed using MOVER algorithm; [a] CHIWOS measured the last-month pattern of binge drinking, while CCHS measured the last-year pattern of binge drinking.

3.3.4 Drug use

Last-month non-prescribed cannabis use in WLWH from BC was almost two times greater than last-year use of this drug from women of the general population in BC: 14.6% vs. 6.6% reported regular use (SPD 8.0%), and 18.1% vs. 6.1% reported occasional use (SPD 12.0%). The results of last 3 months use of illicit drug use compared with last-year use of these drugs showed a higher proportion of WLWH in BC reported cocaine or crack use: 16.8% vs. 0.1% for regular use (SPD 16.7%), and 8.2% vs. 1.5% for occasional use (SPD 6.7%), regular/occasional speed use (2.5% vs. 0.1%; SPD 2.4%), and regular/occasional heroin use (11.3% vs. 0.1%; SPD 11.2%) (**Table 3.4**).

Table 3.4: Comparing Illicit Drug Use between Women Living with HIV and Assumed HIV-Negative Women of the General Population[*].

Drug use [a]	CHIWOS	CCHS estimates		SPD[¥]
		CCHS[£]	AER Std.[†]	
	(1)		**(2)**	**(1) – (2)**
Non-prescribed cannabis use [b]				
Regular use [c]	14.6 (11.3, 18.7) [‡]	4.5 (3.4, 5.2)	6.6 (4.7, 8.6)	8.0 (4.1, 8.6)
Occasional use [d]	18.1 (14.4, 22.4)	7.1 (6.1, 8.1)	6.1 (4.9, 7.2)	12.0 (8.1, 16.5)
None [e]	67.3 (62.2, 72.1)	88.4 (87.2, 89.6)	87.3 (83.5, 91.1)	-20.0 (-26.3, -13.9)
Cocaine or crack use				
Regular use [f]	16.8 (13.2, 21.0)	0.1 (0.01, 0.2)	0.1 (0.00, 0.2)	16.7 (13.1, 20.9)
Occasional use [g]	8.2	0.7	1.5	6.7

	(5.78, 11.61)	(0.4, 1.0)	(0.2, 2.9)	(3.9, 10.3)
None (never or former)	75.0 (70.2, 79.2)	99.2 (98.8, 99.5)	98.4 (95.0, 101.7)	-23.4 (-29.2, -17.9)
Speed (amphetamine) use				
Regular/occasional use [f,g,h]	2.5 (1.3, 4.8)	0.1 (0.01, 0.2)	0.1 (0.00, 0.2)	2.4 (1.2, 4.7)
None (never or former)	97.5 (95.2, 98.68)	99.9 (99.8, 100.0)	99.9 (96.8, 100.0)[††]	-2.4 (-6.2, 0.9)
Heroin use				
Regular/occasional use [f,g,h]	11.3 (8.4, 15.1)	0.1 (0.02, 0.2)	0.1 (0.01, 0.2)	11.2 (8.3, 15.0)
None (never or former)	88.7 (84.9, 91.6)	99.9 (99.7, 100.0)	99.9 (96.8, 100.0)[††]	-11.2 (-16.1, -7.0)

[*] CHIWOS-BC (N=356) and CCHS-BC (N=7,698); [‡] Data are % (95% CI); [£] unstandardized weighted estimates are reported and the 95% CI was constructed using bootstrap method; [†] Age- and ethnoracial-standardized expected estimates based on women of the general population from CCHS; [¥] SPD: standardized prevalence difference (% (95% CI)), and the 95% CI was constructed using MOVER algorithm; [††] the upper limit was 102.96% but we made is to the maximum proportion 100.0%; [a] CCHS collected data for the period of last 12 months for all drugs, while CHIWOS collected data on cannabis use for last month and other drugs in last three months; [b] Any non-prescribed use of cannabis (i.e., non-medicinal, non-prescribed, self-medicating, or both medicinal and non-medicinal use simultaneously); [c] CCHS: every day or at least once a week, while it was measured as using regularly in CHIWOS; [d] CCHS: Occasional use (1-3 times a month or less than once a month), CHIWOS: occasional use (occasionally or used but not in the past 30 days); [e] No non-prescribed or medicinal cannabis use; [f] Regular use: at least once a week; [g] Occasional/episodic: less than once a week; [h] Regular and occasional use were merged in Amphetamine and Heroin use as the absolute "n" did not meet the minimum vetting guideline.

3.4. Discussion

We found that a considerable proportion of WLWH reported current cigarette smoking, were intensive cigarette smokers (i.e., ≥20 cigarettes/day), reported binge drinking, and reported regular/occasional use of non-prescribed cannabis, and other illicit drugs including crack or cocaine, speed, and heroin. We also provided evidence for an excess prevalence of cigarette

smoking and the use of non-prescribed cannabis, and other illicit drugs, but a lower to similar frequency of alcohol consumption, in WLWH compared to their age- and ethnoracial group-similar general population counterparts.

While a considerable difference was found between WLWH and their general population counterparts with regard to drug use and cigarette smoking, but not alcohol drinking, we acknowledge that these differences could in part be because of other uncontrolled population background characteristics. For example, prior studies have highlighted the contribution of socioeconomic factors (e.g., low income, unemployment) and mental health conditions to substance use among WLWH.[5] Moreover, HIV-specific factors such as HIV-related stigma may play a role in substance use as a maladaptive or avoidant coping strategy.[33] However, control of these in cross-sectional analysis can be problematic in ignoring potential mediation and creating artificially similar groups that obscure real differences that can result from age (or life stage) and from systemic discrimination and differential life options across ethnoracial groups.

Our findings were consistent with findings of the few available studies comparing WLWH with HIV-negative women. A higher proportion of cigarette smoking was found among WLWH in a 2015 US study (34.6% vs. 18.0% were current cigarette smokers; with an age-ethnoracial-education-poverty adjusted prevalence difference of 16.6%)[2] and a 2014 French study (32% regular tobacco smokers, with an age-education adjusted prevalence rate ratio of 1.32).[3] Consistent with previous research,[1] alcohol consumption was comparatively lower in WLWH than that in the general population; however, it was still one of the most prevalent substances reported by WLWH in the current study. The reason for the observed lower frequency of alcohol consumption among WLWH of the current study is unclear. Further research is needed to explore whether such lower frequency of alcohol use among WLWH is due to the higher use of

other drugs such as recreational cannabis use. Given the negative impacts of alcohol consumption on care and treatment outcomes,[34] our findings in line with other studies of women with HIV[35] suggest that there is a need for screening of alcohol drinking and targeted interventions within HIV care.

The comparison of our findings on illicit drug use with extant literature is difficult because there are few such comparison analyses specifically for WLWH. However, identifying a higher prevalence of drug use in individuals with HIV than the general population is relevant to the HIV setting, and suggests the need to ensure that factors that affect substance use among WLWH are identified and addressed, and that adequate resources are provided for addressing drug use in the context of HIV care. Limited descriptive studies have also indicated high prevalences of substance use in WLWH; for example, current cigarette smoking (56%) and concomitant use of other drugs in smokers (24.4% vs. 4.0% in nonsmokers)[12], past-year heavy/hazardous drinking over an 11-year follow-up period (ranged from 14% to 24%),[5] current marijuana use (from 21% to 14% over the 16-year follow-up period) and daily marijuana use (from 3.3% to 6.1% in all studied women).[36] Future research could examine which factors may contribute to WLWH using or avoiding substances, including discrimination, HIV-related stigma, intimate partner violence, and other factors that can lead to initiation or continuation of substance use. The identified substance use disparities, particularly smoking and illicit drug use, can help researchers explore pathways leading to greater vulnerability among WLWH.

Given the contribution of substance use to suboptimal HIV outcomes, considering the mixed evidence for the role of cannabis,[37,38] the high substance use prevalence identified in the current research has important implications for the clinical management of HIV.[12,39] This is particularly important as substance use oftentimes co-presents with other health-related problems

such as psychiatric comorbidities and socio-structural barriers, that interactively impact HIV outcomes in individuals with HIV including WLWH.[40-42] These findings highlight the need to make interventions available to women who use both drugs and antiretroviral therapy, particularly in cases where the substance use interferes with maintenance of effective HIV treatment.[34,43] Integration of substance use treatment services into HIV primary care settings may contribute to enhancing the quality of HIV care and care delivery.[9,39,44] Our findings also advocate for tailored, women-centred harm reduction strategies in which women's unique needs are effectively recognized,[45] and peer-driven interventions through which peers can also contribute to the care and treatment programs delivery.[46] Having access to pharmacologic and psychotropic substance use and harm reduction services through this model of care is essential to reduce use and harms of substance use.[6,7,9] To improve greater involvement and adherence to treatment, one recommendation is that such a model of care delivery also provides sustained follow-up with regular evaluations of HIV therapies to substance-using WLWH.[39,43,47]

This study had some limitations. CHIWOS recruited WLWH through Peer Research Associates (PRAs) – a non-random sampling design. Additionally, self-report data on substance use, a potentially stigmatizing behaviour, is subject to social desirability bias. In particular, this is of concern for data from the general population. However, this potential bias might have been mitigated in CHIWOS by using the PRAs, who also shared the experience of living with HIV. This was an attempt to build trust with WLWH, to allow for them to better contribute to the research in sharing their sensitive information.[24] Moreover, we compared the measure of substance use in WLWH with the *assumed* HIV-negative women of the general population. Because of small population estimates of WLWH in Canada – 97 per 100,000 females,[26] the inclusion of WLWH in the assumed HIV-negative group would not substantially change our

estimates. Furthermore, while CHIWOS collected data on cisgender (non-trans) women and trans women with HIV, CCHS does not contain data identifying trans women; therefore, it is both likely that there are also trans women in CCHS and it is impossible to adjust for gender identity.

In conclusion, substance use was prevalent among women living with HIV, with prevalences of cigarette smoking and illicit drug use in excess of what would be expected, but not of alcohol consumption and binge drinking. Due to their negative impacts on HIV outcomes, morbidity, and mortality, these results highlight the need for future research and programming to better understand factors that may contribute to substance use within the group of WLWH, and to intervene on these factors, or on health risk factors within HIV care settings. Future research may also be useful in identifying substance users through screening methods, in educating HIV care providers concerning screening for substance use problems, and in addressing specific causal pathways for use of substances and their impacts on HIV outcomes.

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4. Chapter 4: Patterns of social determinants of health associated with drug use among women living with HIV in Canada: a latent class analysis[1]

4.1. Introduction

Illicit drug use, particularly opioids and stimulants, is common among people living with HIV (PLWH). For example, 10%, 24%, and 39% of PLWH in a US study reported heroin, amphetamines, and cocaine use, respectively, by any administration route.[1] Although data on the prevalence of drug use among women living with HIV (WLWH) is limited, 28.6% of WLWH reported recent crack cocaine use, with 3.2% as persistent users.[2] In Canada, available evidence showed that 25.0% and 11.3% of WLWH reported recent crack cocaine and heroin use (by any route), respectively.[3]

Illicit drug use remains one of the most important factors influencing engagement in the HIV care cascade among individuals with HIV.[1,4-6] Much evidence has documented poorer HIV treatment outcomes among people who use drugs, particularly among WLWH.[5-11] For example, greater suboptimal combination antiretroviral therapy (cART) adherence was documented among WLWH who reported a history of drug use than among women who did not, or among men regardless of drug use.[7] Drug use also predicts increased risk of disease progression, HIV transmission, and mortality,[1,2,10] and continues to complicate HIV care and treatment efforts among PLWH.[12,13] Although active drug use has been shown to complicate the clinical management of individuals with HIV and common comorbidities such as hepatitis C, increasing evidence documents how marginalization and criminalization of people who use/inject drugs

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interferes with access and adherence to HIV medications.[14] Particular attention, therefore, needs to be given to such drug use practice throughout the course of HIV care and treatment among WLWH.

Although some determinants of illicit drug use are well documented (e.g., demographics, cognitive, behavioural),[15] few studies have explored the role of the social determinants of health (SDoH). The SDoH are the conditions (e.g., economic and social marginalization, and various forms of discrimination) in which people are born, work, live, and age, and the wider set of forces shaping the conditions of daily life that greatly contribute to health inequalities.[16] Greater adversities regarding these living conditions can lead to high levels of physiological and psychological stresses arising from coping with stressors.[16] For PLWH, HIV-related stigma in intersection with other social determinants (e.g., race and gender discrimination)[17] can result in coping behaviours such as illicit drug use[18] to help contend with worries and stresses,[19] which can in turn increase vulnerabilities to HIV-related health outcomes.[18,20-22]

Notably, multiple dimensions of SDoH tend to co-occur, and may cluster together into common combinations. Such concomitant determinants have been consistently treated as independent when studied in association with drug use. For example, previous studies have assessed the separate association of HIV stigma,[23] food insecurity,[24] unemployment,[25] and low social support[26] with drug use. However, there are limited data examining how clustering of these determinants is related to drug use. Such evidence is essential for developing HIV care and treatment programs to address potentially modifiable adversities and reduce their impacts on the lives of WLWH. Drawing on the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS),[27] we conducted a latent class analysis (LCA) to uncover underlying clusters of SDoH. LCA as a data reduction strategy classifies individuals into mutually exclusive

and exhaustive latent classes using multiple categorical observed variables.[28] LCA has been a useful technique for identifying population subgroups in different disciplines (e.g., substance using women at risk for HIV.[29] We then applied inverse probability weighting to address confounding and selection bias in examining the association of the clusters of SDoH with drug use.

4.2. Methods

4.2.1 Study sample

We used data from CHIWOS (www.chiwos.ca), a community-based cohort study. As previously described,[27] CHIWOS is a large cohort of WLWH (≥16 years; trans inclusive) residing in the Canadian provinces of British Columbia (BC), Ontario, and Quebec. WLWH (n=1,422) were interviewed during 2013-2015 (time-point 1) and after ~18-months (time-point 2; n=1,252). We considered 170 participants (11.9%) lacking time-point 2 data as *censored* (i.e., lost to follow-up). Participants were recruited through peers, HIV clinics, AIDS service or community-based organizations, word of mouth, and other methods.[30] Trained Peer Research Associates (PRAs) administered the survey through in-person interviews at clinics, community sites, or participants' homes, or via phone/Skype. Informed consent was obtained from all participants prior to the interview, consistent with the ethics protocol approved by Simon Fraser University, University of British Columbia/Providence Health, Women's College Hospital, and McGill University Health Centre.

4.2.2 Drug use

Recent drug use was defined as last three months at the first time-point and last six months at the second time-point, and included use of opioids (heroin, speedballs, Dilaudid, non-prescribed methadone, OxyContin/Oxycodone, morphine, Talwin & Ritalin) or stimulants (cocaine, crack,

crystal methamphetamine, amphetamine, MDA). The regular (daily or at least once/week) or episodic (less than once/week) use of these drugs was ascertained among those who reported any use. Due to small proportions in the episodic use category (i.e., ~1%), a binary outcome at time-point 2 was created: use of any vs. no drugs.

4.2.3 SDoH indicators

A set of potentially modifiable SDoH that have the potential to co-occur among WLWH were examined at time-point 1, including: racial discrimination, gender discrimination, enacted HIV stigma, perceived social support, barriers to access to care, food security, housing status, income level, employment status, education, recent sex work involvement, and recent incarceration. Included SDoH indicators: a) were measured at the first survey time-point, b) are potentially modifiable, c) were currently or recently experienced, and; d) align with the Canadian list of SDoH[19] (HIV-related stigma being an exception specific to PLWH). Selection of SDoH was limited to current or recent conditions to avoid the potential for collider stratification bias[31] that could be introduced in a selected (HIV-positive) sample by studying earlier social determinants that may have affected HIV status.

Racial discrimination was measured with the 8-item Everyday Discrimination Scale (current study α=0.96)[32]. In line with operationalization used in the prior research,[33] WLWH who reported discriminatory experiences due to their race (e.g., treated with less courtesy, respect) sometimes, frequently, or almost every day were considered as having experienced racial discrimination. The same scale (with the same definition) focusing on discriminatory mistreatments due to gender was used to measure *gender discrimination* (α=0.94). *Enacted HIV stigma* was measured using three items of Wright's abridged 10-item version of Berger's HIV Stigma Scale (α=0.85), measuring the extent to which WLWH experienced enacted/personalized

stigma toward PLWH.[34] Experience of HIV-related stigma was defined if WLWH reported any HIV-related discriminatory events with strongly agree/agree response options (i.e., been hurt by people's reaction, stopped socializing, or lost friends). *Social support* was examined by the 4-item Medical Outcome Study: Social Support Survey, measuring emotional-informational, tangible, affectionate, and positive social interaction supports (α=0.85). The overall mean score ranged from 1 to 5, with > 2 indicating poor social support availability.[35] *Difficulties in access to care* was assessed using the 12-item Barriers to Access to Care Scale, measuring barriers experienced due to geography/distance, medical and psychological service, community stigma, and personal resource (α=0.93). The overall mean severity scores ranged from 1 to 4, with $\geq$ 2 signifying severe/significant barriers.[21] Past-year experiences of *food security* were examined by three items: fears of running out of food; experiences of running out of food; and unaffordability of balanced meals, yielding an overall score ranging 1-6, with > 1 indicating food insecurity.[36] *Income level* was defined as low if participants reported having a yearly household income level < $20,000. Current *employment status* was categorized as unemployed (no income or income only from non-employment sources such as unemployment/welfare, dividends and interest, or pension) vs. employed (any paid job). Current *education level* was dichotomized as below high school vs. completed high school or more. Current housing status was also measured. Participants who reported residing in places such as a self-contained room, transition house, halfway house, safe house, or outdoors were considered as *unstable housing*. Past six months *sex work involvement* was also included, and defined as having been provided with money, drug, shelter, food, etc. in exchange for sex. Finally, any past year experience of *incarceration* was included as a structural-level determinant indicating social exclusion.

4.2.4 Covariates

The following covariates were hypothesized to be associated with either both SDoH clusters and drug use or only drug use: age (continuous); ethnoracial groups (white/Caucasian, African/Caribbean/Black, Indigenous, others); province (BC, Ontario, Quebec); city size (large, others); sexual orientation (heterosexual, LGBQ); relationship status (married/common-law/relationship, others); years living with HIV (<6 years, 6-14 years, > 14 years); cART status (optimal [≥ 95% adherence], suboptimal [< 95% adherence], not engaged in HIV treatment); ever diagnosed with a mental health condition; resilience (10-item Resilience Scale) ; any history of childhood sexual/physical violence; any experience of adulthood sexual/physical/verbal/action-limited violence; having been under the care of Child Protection Services or in foster care; and alcohol use (abstainers/low, moderate [1-7 drinks/week], heavy [> 7 drinks/week]). Drug use history before or at time-point 1 was also included to account for confounding by outcome history.[37] Missing values of covariates under the assumption of missing at random were singly imputed to reduce the loss of statistical power when computing inverse probability weights (IPW).[38]

4.2.5 Latent class analysis (LCA)

We used LCA to identify clusters of SDoH indicators. Under the assumption that all observed indicators are independent conditional on the latent variable, LCA aims to identify distinct groups of individuals with similar patterns within an unobserved categorical variable.[28] LCA was started with a two-class model and systematically increased to more classes (**S Table 4.1**). LCA provides both class membership probabilities and item-response probabilities condition on class membership to help interpret the final identified class (**Table 4.1**). The expectation–maximization (EM) algorithm with 5,000 iterations was employed to identify the best model

fit.[39] The selection of the best LCA model was informed by using goodness-of-fit indices, supporting statistics, and interpretability of class memberships. The following fit statistics were reported: log-likelihood, Akaike's information criterion (AIC), Bayesian information criterion (BIC), and sample-size-adjusted BIC (aBIC), and consistent AIC (CAIC).[40-42] Lower values of these criteria indicate better fit and parsimony. Two supporting statistics were also reported: Entropy as a measure of classification accuracy, with values approaching to 1 indicating better class separation,[43] and the percentage of seeds associated with the fitting models, with values close to 100% indicating they were unlikely to have hit the local maxima. For each model, the log-likelihood was replicated with 1,000 random starting values to avoid local maxima. Under the assumption of missing at random, LCA accounted for missing values of the SDoH indicators using the full information maximum likelihood estimation. LCA was conducted using SAS PROC LCA procedure.[44]

4.2.6 Models and estimations

We used inverse probability weights (IPW)[45,46] to account for confounding due to the presence of potentially imbalanced covariates across the SDoH clusters, and inverse probability censoring weights (IPCW) to account for prospective selection bias due to potentially non-random loss to follow-up/censoring (**S Table 4.2**). The product of these two weights yielded the final stabilized weights (**S Table 4.3**), producing a pseudo-population in which the independent variable and covariates are unassociated (**S Table 4.4**). In fitting models through IPW, we assumed correct specification of IPW models, conditional exchangeability, and positivity.[47]

4.2.7 Control of confounding using IPW

SDoH clusters were modeled using a multinomial logistic regression to estimate stabilized weights: the numerator was computed as the marginal probability of the SDoH clusters divided

by the denominator, which was computed as the probability that a participant was assigned to an SDoH cluster given the covariates and opioid/stimulant use history. These models were all performed among participants without censored information in time-point 2.

4.2.8 Control of selection bias using IPCW

Additionally, to account for any potential selection bias due to differential loss-to-follow-up at time-point 2, we estimated IPCW using logistic regression models: *numerator* was defined as the probability of not being censored given SDoH, and *denominator* was computed as the probability of not being censored given SDoH, covariates and opioid/stimulant use history.

4.2.9 Association of SDoH clusters with drug use

The association between SDoH clusters and any opioid/stimulant use was examined using generalized linear models with log link and Poisson distribution; crude and weighted risk ratios (RRs) and 95% confidence intervals (CIs) were reported. Further adjustment was made for imbalanced covariates after applying the IPW. These analyses were conducted using Stata 15.

4.2.10 Sensitivity analysis

We reported E-value to evaluate the extent to which residual (unmeasured) confounding might explain away the observed associations, and computed as: $E = RR^{*} + \text{sqrt}\{RR^{*} \times RR^{*} - 1\}$, where $RR^{*} = 1/RR$ for $RR < 1$.[48] E-value is a representation of the minimum strength of association that an unmeasured confounder would need to have with SDoH clusters and drug use to nullify the observed associations.

4.3. Results

4.3.1 SDoH classes

Prevalences for individual social determinants ranged from 6.3% (N = 82/1307) and 6.5% (N = 92/1419) for recent sex work involvement and incarceration to 71.8% (N = 1004/1398) and

77.8% (N = 1098/1412) for enacted HIV stigma and unemployment, respectively (**Table 4.1**). After considering LCA fit statistics and model interpretability, the four-class model was determined as the optimal number of classes (**S Table 4.1**). These four classes included WLWH with either none/least SDoH adversities (class 1 labeled as no/least SDoH adversities: N = 94 [6.6%]); WLWH who predominantly reported experiencing race and gender discrimination along with HIV-related stigma and barriers in access to care, but without economic hardship indicators (class 2 labelled as discrimination/stigma: N = 256 [18.0%]); WLWH who mainly reported food insecurity, low household income, and unemployment, accompanied with HIV-related stigma (class 3 labeled as economic hardship: N = 430 [30.2%]); and WLWH who experienced gender and race discrimination, HIV-related stigma, low social support, access to care difficulties, food insecurity, low income, and unemployment (class 4 labeled as most SDoH adversities: N = 642 [45.2%]).

Table 4.1: Class Membership Probabilities and Item-Response Probabilities of Social Determinants of Health (SDoH) from Latent Class Analysis among Women Living with HIV – CHIWOS (N=1,422).

SDoH measures		None/least SDoH (N = 94; 6.6%)[b]	Discrimination and Stigma (N = 256; 18.0%)	Economic hardship (N = 430; 30.2%)	Most SDoH adversities (N = 642; 45.2%)
Race discrimination (708/1408; 50.3%)[a]	No	0.00	0.40[c]	0.91	0.18
	Yes	0.00	**0.60**	0.09	**0.82**
	None[d]	<u>1.00</u>	0.00	0.00	0.00
Gender discrimination (818/1415; 57.1%)	No	0.00	0.33	0.91	0.04
	Yes	0.00	**0.67**	0.09	**0.96**
	None	<u>1.00</u>	0.00	0.00	0.00
Enacted HIV stigma	No	0.00	0.22	0.40	0.17

(1004/1398; 71.8%)	Yes	0.00	**0.78**	**0.60**	**0.83**
	None	1.00	0.00	0.00	0.00
Low social support	No	0.00	0.51	0.51	0.37
(722/1367; 52.8%)	Yes	0.00	0.49	0.49	**0.63**
	None	1.00	0.00	0.00	0.00
High barriers to access to	No	0.00	0.43	0.55	0.36
care	Yes	0.00	**0.57**	0.45	**0.64**
(725/1371; 52.8%)	None	1.00	0.00	0.00	0.00
Food insecurity	No	0.00	0.63	0.31	0.18
(907/1416; 64.1%)	Yes	0.00	0.37	**0.69**	**0.82**
	None	1.00	0.00	0.00	0.00
Low income	No	0.00	0.90	0.21	0.11
(901/1379; 65.3%)	Yes	0.00	0.10	**0.79**	**0.89**
	None	1.00	0.00	0.00	0.00
Unemployment	No	0.00	0.67	0.09	0.02
(1098/1412; 77.8%)	Yes	0.00	0.33	**0.91**	**0.98**
	None	1.00	0.00	0.00	0.00
Low education	No	0.00	1.00	0.83	0.75
(227/1415; 16.0%)	Yes	0.00	0.00	0.17	0.25
	None	1.00	0.00	0.00	0.00
Unstably housed	No	0.00	0.99	0.90	0.83
(152/1422; 10.7%)	Yes	0.00	0.01	0.10	0.17
	None	1.00	0.00	0.00	0.00
Recent sex work practice	No	0.00	0.99	0.95	0.90
(82/1307; 6.3%)	Yes	0.00	0.01	0.05	0.10
	None	1.00	0.00	0.00	0.00
Recent incarceration	No	0.00	1.00	0.96	0.88
(92/1419; 6.5%)	Yes	0.00	0.00	0.04	0.12
	None	1.00	0.00	0.00	0.00

[a] (n/N; %) indicating the prevalence of the SDoH indicators under the study; [b] Class membership probabilities; [c] Item-response probabilities, indicating the probability of experiencing a SDoH indicator for each identified latent

class; [d] We categorized each SDoH measure into three categories: No: indicating either did not have/experience this determinant, Yes: indicating either living/experiencing this determinant, None: indicating either did not experience any of these 12 determinants or experienced only one (i.e., least). Item response probabilities of "Yes" category ≥ 0.50 are bolded, and item response probabilities of "None" category with 100% are underlined. The "None" category was added to produce a distinct class named "None/least SDoH adversities" to ease interpretation of the latent classes and reduce LCA model complexity.

4.3.2 Participants' characteristics

WLWH were an average of 42.8 [SD 10.6] years of age, with 584 (41.1%) members of the white ethnoracial group, 1237 (87.3%) heterosexual, 689 (48.5%) single, 552 (40.2%) living with HIV for 6-14 years, 863 (70.0%) self-reporting optimal cART adherence; 819 (62.7%) and 1057 (80.4%) reported exposure to violence as children and adults, respectively, 573 (40.7%) reported a mental health diagnosis, and 140 (10.1%) were heavy alcohol users. The distributions of these covariates across the SDoH clusters are presented in **Table 4.2**.

Table 4.2: Characteristics of Women Living with HIV (WLWH) across the Social Determinants of Health (SDoH) Classes – CHIWOS Time-point 1, 2013-2015 (N = 1,422).

Variables	Overall	SDoH classes				
		None/least adversities	Discrimination/ stigma	Economic hardship	Most adversities	P-value[b]
Age, yr[d] (mean [SD])	42.8 [10.6]	39.2 [10.3]	43.5 [10.6]	42.9 [11.5]	43.1 [10.0]	0.007
Ethno-racial group						<0.001
White/Caucasian	584 (41.1)[a]	58 (61.7)	97 (37.9)	219 (50.9)	210 (32.7)	
African/Caribbean/Black	418 (29.4)	23 (24.5)	109 (42.6)	123 (28.6)	163 (25.4)	
Indigenous	318 (22.3)	7 (7.4)	29 (11.3)	60 (14.0)	222 (34.6)	
Other	102 (7.2)	6 (6.4)	21 (8.2)	28 (6.5)	47 (7.3)	
Province						<0.001
Ontario	717 (50.4)	50 (53.2)	131 (51.2)	235 (54.6)	301 (46.9)	
British Columbia	356 (25.0)	13 (13.8)	49 (19.1)	65 (15.1)	229 (35.7)	
Quebec	349 (24.6)	31 (33.0)	76 (29.7)	130 (30.2)	112 (17.5)	
Living in large cities	1169 (82.2)	83 (88.3)	203 (79.3)	345 (80.2)	538 (83.8)	0.106
Bing heterosexual	1237 (87.3)	85 (90.4)	237 (93.3)	395 (91.9)	520 (81.4)	<0.001
Relationship status						<0.001
Single (non-married)	689 (48.5)	40 (42.6)	100 (39.1)	201 (46.7)	348 (54.4)	
Married/common-law	454 (32.0)	44 (46.8)	103 (40.2)	134 (31.1)	173 (27.0)	
Others	277 (19.5)	10 (10.6)	53 (20.7)	95 (22.1)	119 (18.6)	
Years living with HIV						0.001

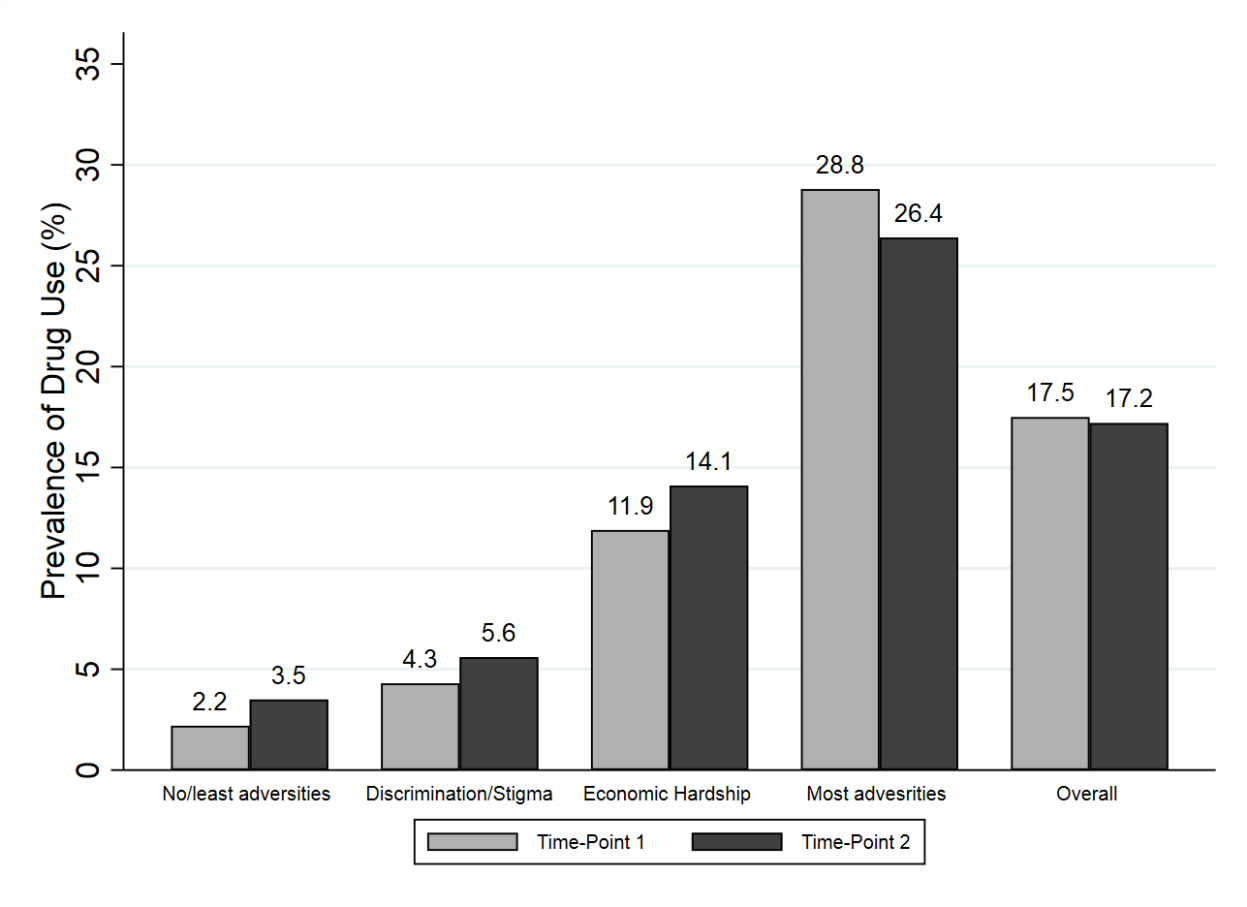
< 6 years	345 (25.1)	23 (25.0)	40 (15.7)	128 (31.4)	154 (24.8)	
6-14 years	552 (40.2)	35 (38.0)	118 (46.7)	140 (34.3)	259 (41.8)	
> 14 years	477 (34.7)	34 (37.0)	96 (37.8)	140 (34.3)	207 (33.4)	
Taking HIV treatment						0.001
Yes, optimal (≥ 95%)	863 (70.0)	65 (69.9)	163 (64.7)	279 (65.0)	356 (55.5)	
Yes, suboptimal (< 95%)	312 (22.0)	12 (12.9)	52 (21.4)	74 (17.2)	172 (26.8)	
Not engaged in treatment	240 (17.0)	16 (17.2)	35 (13.9)	76 (17.7)	113 (17.6)	
Mental health diagnosis	573 (40.7)	26 (28.0)	93 (36.6)	134 (31.6)	320 (50.3)	<0.001
Resiliency (below median)[c]	662 (47.1)	22 (23.66)	104 (40.9)	172 (40.6)	364 (57.4)	<0.001
Childhood violence	819 (62.7)	34 (38.6)	138 (56.8)	211 (53.8)	436 (74.7)	<0.001
Adulthood violence	1057 (80.4)	52 (59.1)	189 (77.5)	284 (71.9)	532 (90.5)	<0.001
Child development events	326 (23.0)	10 (10.6)	33 (13.0)	74 (17.3)	209 (32.7)	<0.001
Heavy alcohol use						0.132
Abstainers/low (< 1 drink/week)	956 (69.1)	64 (68.8)	174 (68.5)	302 (71.1)	419 (68.1)	
Moderate (1-7 drinks/week)	288 (20.8)	22 (23.7)	60 (23.6)	88 (20.7)	118 (19.2)	
Heavy (> 7 drinks/week)	140 (10.1)	7 (7.5)	20 (7.9)	35 (8.2)	78 (12.7)	
Drug use history[d]						
Before study entry	234 (16.8)	3 (3.2)	10 (3.9)	48 (11.24)	173 (27.5)	<0.001
At entry (time-point 1)	244 (17.5)	2 (2.2)	11 (4.3)	50 (11.9)	181 (28.8)	<0.001

[a] Data are presented as N(%) unless specified; [b] P-values are for the chi-square test for categorical covariates and one-way ANOVA for continuous covariates; [c] Scores ranged 10-70, with higher scores indicating increased resilience (median=64); [d] Opioid/stimulant use histories before and at time-point 1.

4.3.3 SDoH clusters and drug use

Overall, opioid/ stimulant use at time-points 1 and 2 were respectively reported by 244 (17.5%) and 212 (17.2%.). Drug use at time-point 2 was reported by 143 (26.4%) among WLWH with most SDoH adversities, with 53 (14.1%), 13 (5.6%) and 3 (3.5%) for economic hardship, discrimination/stigma, and no/least SDoH classes, respectively (**Figure 4.1**). The crude regression analysis demonstrated that WLWH in the no/least SDoH adversities, discrimination/stigma, and economic hardship classes had significantly lower likelihood of opioid/stimulant use than WLWH in the most SDoH adversities class. Compared with the most SDoH adversities class, weighted analysis showed that WLWH in no/least SDoH class were at 87% decreased risk of drug use (RR 0.13, 95% CI: 0.03, 0.58), while an association was not observed for other classes. Additionally, WLWH in the no/least SDoH class were at decreased risk of drug use compared to WLWH in the economic hardship class (RR 0.13, 95% CI: 0.03, 0.63) and discrimination/stigma class (RR 0.15; 95% CI: 0.03, 0.78) (**Table 4.3**).

Figure 4.1: Prevalence of Drug Use According to the Social Determinants of Health (SDoH) Classes Obtained from Latent Class Analysis (LCA) – CHIWOS.



Illicit drugs included a) Stimulants: cocaine, crack (crack cocaine), crystal, speed (amphetamine) and MDA; and b) Opioids: heroin, speedballs (heroin+ cocaine), Dilaudid (hydromorphone), non-prescription use of methadone, OxyContin/Oxycodone, morphine, Talwins & Ritalin. These drugs were measured at baseline (time-point 1, 2013-15) and in ~18 month follow up (time-point 2; 2015-17). Analytic sample size for these prevalences was 1,395 at time-point1 and 1,236 at time-point 2.

Table 4.3: Inverse Probability Weighted Estimates of the Association of the Social Determinants of Health (SDoH) Classes with Drug Use among Women Living with HIV (WLWH) – CHIWOS[a]

	Observed estimates				E-value for the observed estimates [c]	
SDoH classes[c]	Crude RR[b] (95% CI)	P-value	Weighted RR (95% CI)	P-value	Weighted RR	Upper CI
Economic hardship class vs. Most SDoH adversities	0.53 (0.40, 0.71)	<0.001	0.95 (0.67, 1.34)	0.760	---	---
Discrimination/stigma class vs. Most SDoH adversities	0.21 (0.12, 0.37)	<0.001	0.82 (0.44, 1.52)	0.539	---	---
None/least adversities class vs. Most SDoH adversities	0.13 (0.04, 0.40)	<0.001	**0.13 (0.03, 0.58)**	0.008	14.86	2.84
Discrimination/stigma class vs. Economic hardship	0.40 (0.22, 0.71)	0.002	0.87 (0.44, 1.68)	0.678	---	---
None/least adversities class vs. Economic hardship	0.24 (0.07, 0.76)	0.015	**0.13 (0.03, 0.63)**	0.011	14.86	2.55
None/least adversities class vs. Discrimination/stigma	0.61 (0.18, 2.1)	0.440	**0.15 (0.03, 0.78)**	0.024	11.81	1.88

[a] N = 1,236 in crude analysis and N= 1,225 in weighted analysis; [b] RR: risk ratio (95% confidence intervals: CI); [c] This is a sensitivity analysis evaluating the extant to which an unmeasured confounder would explain away the exposure-outcome estimates observed for the association between the SDoH classes and drug use. E-value was check for the observed point estimate and the upper 95% CI that is close to the null RR = 1.

The sensitivity analysis suggested that these associations were relatively robust to potential unmeasured confounding. For instance, for the observed RR: 0.13 for drug use among those with no/least SDoH adversities versus those with most adversities, an unmeasured confounder correlated with both exposure and outcome by RRs of ~14.86-fold each, above and beyond the measured confounders, would explain away the observed association, but weaker confounding would not. Such an E-value for the upper 95% limit of the same association was 2.84-fold (**Table 4.3**).

4.4. Discussion

In our study of data from a large prospective cohort of WLWH in Canada, we observed that most WLWH reported experiencing multiple forms of a set of mutually reinforcing SDoH. We identified two partially overlapped SDoH clusters of discrimination/stigma and economic hardship as well as one cluster containing most of the SDoH adversities. Most notably, we found that the prevalence of self-reported opioid/stimulant use was approximately seven times higher in WLWH who experienced the most SDoH adversities than those experiencing no/least adversity (26.4% vs. 3.5%). WLWH with no/least adversity were substantially less likely to report drug use at ~18 months follow up compared with WLWH experiencing an accumulation of social disadvantages.

Overall, the high prevalence of socio-structural adversities among WLWH is consistent with existing knowledge that women experience substantial SDoH vulnerabilities and multiple forms of these adversities.[49,50] The majority of the SDoH indicators were well-distinguished across the SDoH classes using LCA analysis, except for low education, unstable housing, sex work involvement, and incarceration. That these four determinants were less distinctive may be

due to their relatively low proportions, likely resulted in a low overall impact on drug use in the current sample of WLWH.

We documented that the clustered classes of multiple SDoH adversities were associated with drug use. Notably, no difference was observed in the risk of drug use for the two classes of discriminations/stigma and economic hardship compared with the class with most SDoH adversities and also the same risk of drug use was estimated when WLWH in the no/least class were compared with WLWH in these two classes. Such findings may help shed light on the processes that generate and reinforce well-documented syndemics of HIV and substance use, by showing the role that each specific cluster of SDoH may play in initiation/continuation of drug use. Our results suggest that improving modifiable social determinants may be crucial to addressing this syndemic.[51] Harm reduction and treatment interventions need to seriously consider the important role of multiple SDoH – regardless of their types. Drug treatment programs that mainly focus on behaviour change interventions may result in limited impact if no additional efforts are made to change the social environments of drug users.[52]

Our findings may also have implications for HIV care and treatment programs by illuminating the association of current social determinants with illicit drug use, which has been shown to create challenges within the HIV care cascade. Prior evidence has demonstrated how income level,[53] HIV stigma,[22] and food insecurity increase vulnerabilities to suboptimal cART adherence by limiting access to HIV care and treatment services, and affecting individuals' health seeking behaviours. Illicit drug use, e.g., crack cocaine, also impacts HIV clinical care through the same mechanism of HIV treatment interruptions.[2,10,11,54] Individually or combined, these factors can threaten the benefits accompanied with early HIV treatment initiation and the commitments toward eliminating the HIV pandemic. Paying particular attention to these

interlinked social and drug use determinants should be a key priority in efforts to improve HIV medical care for WLWH, and merits continued and thorough investigation. Given the impacts of these SDoH adversities and risk practices on HIV care and treatment outcomes, these findings indicate a need for regular assessment of these factors and targeted support for women with greater needs within routine HIV care,[55] which if addressed holistically, may reduce the likelihood of suboptimal HIV clinical outcomes.

While this study took advantage of CHIWOS as the largest community-based research cohort of WLWH in Canada, it had some limitations. First, non-random sampling of the participants may limit the generalizability and interpretation of our findings. Second, we relied on self-reported drug use, which may be subject to social desirability bias; however, participants were interviewed by PRAs who also experienced living with HIV (and in some cases, using drugs), and this may have limited such bias. Third, although unmeasured confounding is a source of bias in observational research, our sensitivity analysis showed that relatively strong unmeasured confounding would be required to nullify the observed associations.

The current research has several strengths despite these limitations: First, we used data from a nationwide large sample of WLWH. Second, our research extends the relatively limited extant knowledge on drug use among women with HIV. Third, our research contributes to theoretical development through examining the inclusion of detailed individual-level data of current and modifiable social determinants as leading stressors in the target population's daily life. Fourth, we demonstrated how these determinants cluster together using LCA, a probability-based technique that provides a better insight into the underlying clusters of the individual SDoH indicators given the concurrent occurrence of these determinants. Fifth, IPW was used to account

for both confounding and selection bias. Finally, the survey had a high retention rate (88%) after 18 months of follow-up.

Despite a growing body of evidence on the independent associations between social determinants and drug use, less focus has been put on ways these determinants overlap, or on their clustering impacts on drug use. The complex relationships between the SDoH indicators, the documented (individual) associations with barriers to care, and stigma that surrounds both drug use and many aspects of social adversity suggest that HIV care programs will need to make intentional efforts to ensure that patients have full access to optimal care across the HIV care cascade. Our findings support the targeted assessment of multiple social determinant and drug use vulnerabilities; HIV-specific and women-centered care models have good potential to create the kind of low-stigma environment that would allow for these issues to be both assessed and addressed.[56] Developing evidence-based treatment for drug dependence, including harm reduction strategies, requires a recognition of the role of social determinants of health. Individuals with these socio-structural adversities in intersection with drug use may continue to experience greater challenges with regard to HIV treatment adherence and HIV outcomes; therefore, the continued support for individuals with greater vulnerabilities is required.

4.5. Supplementary Tables

S Table 4.1: Comparison of Goodness-of-fit Measures for Different Class Models (N=1,422)

Model	LL[a]	AIC[b]	BIC[c]	CAIC[d]	Entropy	% seeds[e]
1-class	-12363.0	10080.9	10207.2	10231.2	1.000	100%
2-class	-8582.2	2569.1	2826.9	2875.9	1.000	100%
3-class	-8271.3	1997.4	2386.7	2460.7	0.843	98.4%
4-class[f]	*-8030.0*	*1564.9*	*2085.6*	*2184.6*	*0.831*	*93.5%*
5-class	-7966.5	1487.8	2140.0	2264.0	0.819	35.0%
6-class	-7922.1	1449.0	2232.7	2381.7	0.814	15.0%
7-class	-7889.8	1434.5	2349.7	2523.7	0.745	32.4%

[a] Log-Likelihood (LL); [b] Akaike information criterion (AIC); [c] Bayesian information criterion (BIC); [d] Consistent AIC (CAIC), [e] Percentage of seeds associated with best fitted model (% seeds); [f] 4-class model had the lowest BIC and CAIC. Moving forward to model with more classes, entropy suggested lower classification accuracy (e.g., ~10% reduction from 4-class to 7-class). In addition, the 4-class model had a higher percentage of seeds associated with best fitted model (i.e., increased confidence that the best solution was achieved even though it is not a fit criterion). Fit indices/statistics align with model interpretability suggested the 4-class model provided a better fit with plausible distribution of the sample within each class.

S Table 4.2: Characteristics of Women Living with HIV (WLWH) who were Lost to Follow-up (i.e., Censored), CHIWOS, 2013-2017

Variables	Not Lost to follow up (N = 1252)	Lost to follow up (N = 170)	P-value
SDoH classes			0.057
Class 1: No/least SDoH adversities	88 (7.03)	6 (3.53)	
Class 2: Discrimination/Stigma	232 (18.53)	24 (14.12)	
Class 3: Economic adversities	381 (30.43)	49 (28.82)	
Class 4: Most SDoH adversities	551 (44.01)	91 (53.53)	
Age, yr[d] (mean [SD])	42.9 [10.61]	42.2 [10.34]	0.430
Ethno-racial group			0.062
White/Caucasian	515 (41.13)	69 (40.59)	
African/Caribbean/Black	380 (30.35)	38 (22.35)	
Indigenous	272 (21.73)	46 (27.06)	
Other	85 (6.79)	17 (10.00)	
Province			0.018
Ontario	637 (50.88)	80 (47.06)	
British Columbia	299 (23.88)	57 (33.53)	
Quebec	316 (25.24)	33 (19.41)	
Living in large cities	1029 (82.19)	140 (82.35)	0.958
heterosexual	1095 (87.81)	142 (83.53)	0.116
Relationship status			0.596
Single (non-married)	612 (48.92)	77 (45.56)	
Married/common-law	394 (31.49)	60 (35.50)	
Others	245 (19.58)	32 (18.93)	
Years living with HIV			0.648
< 6 years	310 (25.49)	35 (22.15)	
6-14 years	487 (40.05)	65 (41.14)	

> 14 years	419 (34.46)	58 (36.71)	
Taking HIV treatment			0.012
Yes, optimal (≥ 95%)	759 (60.91)	104 (61.54)	
Yes, suboptimal (< 95%)	264 (21.19)	48 (28.40)	
Not engaged in treatment	223 (17.90)	17 (10.06)	
Mental health diagnosis	499 (40.21)	74 (44.58)	0.282
Resiliency (below median)	568 (45.81)	94 (56.97)	0.007
Childhood violence	708 (61.51)	111 (71.15)	0.019
Adulthood violence	918 (79.07)	139 (90.26)	0.001
Child development events	269 (21.55)	57 (33.73)	<0.001
Heavy alcohol use			0.011
Abstainers/low (< 1 drink/week)	865 (70.44)	94 (59.12)	
Moderate (1-7 drinks/week)	242 (19.71)	46 (28.93)	
Heavy (> 7 drinks/week)	121 (9.85)	19 (11.95)	
Stimulant/opioid use			
Before study entry	187 (15.19)	47 (28.31)	<0.001
At entry (time-point 1)	193 (15.70)	51 (30.72)	<0.001

S Table 4.3: Distributions of the Estimated Weights for the Classes of the Social Determinants of Health (SDoH), Censoring, and both, CHIWOS, Time-point 1, 2013-2015

	Mean (SD)	Percentiles				
		5th	25th	50th	75th	95th
Stabilized weights for SDoH weights						
Class 1	0.90 (1.30)	0.16	0.26	0.46	0.95	3.21
Class 2	0.96 (0.82)	0.39	0.54	0.74	1.04	2.20
Class 3	1.00 (0.67)	0.50	0.63	0.80	1.12	2.26
Class 4	0.99 (0.60)	0.48	0.60	0.81	1.18	2.01
Overall	0.98 (0.73)	0.43	0.58	0.78	1.13	2.18
Stabilized weights for censoring weights						
Overall	0.99 (0.08)	0.91	0.94	0.98	1.02	1.14
Stabilized weights for final weights						
Class 1	0.89 (1.38)	0.15	0.26	0.45	0.93	3.18
Class 2	0.97 (0.86)	0.39	0.53	0.73	1.02	2.30
Class 3	1.02 (0.75)	0.47	0.62	0.78	1.13	2.35
Class 4	0.97 (0.55)	0.50	0.62	0.81	1.15	1.89
Overall	0.98 (0.76)	0.43	0.58	0.77	1.12	2.12

S Table 4.4: Inverse-Probability Weighted Estimates of the Parameters of a Marginal Structural Model for the Association of the Classes of the Social Determinants of Health (SDoH) on Drug Use among Women Living with HIV (WLWH), CHIWOS, Canada, 2013-2017

	SDoH classes[a]		
Variables	No/least SDoH adversities	Discrimination/ stigma	Economic adversities
Age, yr (mean)	0.99 (0.95, 1.02)	0.99 (0.97, 1.01)	1.00 (0.98, 1.01)
Ethno-racial groups			
White/Caucasian	1	1	1
Indigenous	1.01 (0.29, 3.46)	0.91 (0.5, 1.66)	0.88 (0.56, 1.38)
African/Caribbean/Black	0.75 (0.36, 1.56)	0.87 (0.57, 1.32)	0.96 (0.67, 1.38)
Other	0.58 (0.18, 1.85)	0.98 (0.48, 1.99)	0.99 (0.53, 1.86)
Study province			
Ontario	1	1	1
British Columbia	0.61 (0.21, 1.78)	0.63 (0.39, 1.02)	1.05 (0.69, 1.59)
Quebec	0.77 (0.35, 1.67)	0.90 (0.56, 1.45)	1.00 (0.69, 1.43)
Living large size cities	1.08 (0.42, 2.74)	1.11 (0.70, 1.76)	0.96 (0.63, 1.48)
Heterosexual	0.60 (0.14, 2.56)	1.65 (0.86, 3.14)	1.22 (0.76, 1.95)
Relationship status			
Single (non-married)	1	1	1
Married	0.84 (0.38, 1.85)	0.81 (0.53, 1.25)	1.07 (0.74, 1.56)
Others	0.89 (0.31, 2.55)	0.78 (0.49, 1.26)	1.02 (0.68, 1.53)
Years living with HIV			
< 6 years	1	1	1
6-14 years	1.22 (0.49, 3.05)	0.88 (0.52, 1.49)	0.91 (0.62, 1.34)
> 14 years	1.53 (0.68, 3.48)	0.89 (0.52, 1.52)	0.95 (0.63, 1.41)
Taking HIV treatment			

Yes, optimal	1	1	1
Yes, suboptimal	0.57 (0.23, 1.42)	1.11 (0.66, 1.87)	1.02 (0.67, 1.55)
Not in treatment	0.75 (0.32, 1.78)	0.97 (0.55, 1.70)	0.89 (0.59, 1.36)
Mental health diagnosis	1.44 (0.66, 3.18)	0.82 (0.55, 1.23)	0.94 (0.68, 1.31)
Resiliency (below median)	0.48 (0.22, 1.03)	0.90 (0.6, 1.34)	0.97 (0.71, 1.34)
Childhood violence	1.02 (0.51, 2.03)	0.89 (0.59, 1.34)	0.95 (0.69, 1.32)
Adulthood violence	0.71 (0.33, 1.53)	0.90 (0.55, 1.45)	0.92 (0.62, 1.37)
Childhood development events	0.67 (0.22, 2.02)	0.98 (0.56, 1.70)	0.96 (0.63, 1.45)
Heavy alcohol use			
Abstainers/low (< 1 drink/week)	1	1	1
Moderate (1-7 drinks/week)	1.55 (0.55, 4.34)	0.98 (0.62, 1.57)	0.87 (0.58, 1.30)
Heavy (> 7 drinks/week)	0.30 (0.12, 0.79)[b]	1.68 (0.79, 3.55)	0.97 (0.57, 1.67)
Stimulant/opioid use			
Before study entry	0.95 (0.17, 5.38)	0.84 (0.37, 1.90)	0.88 (0.55, 1.41)
At entry (time-point 1)	0.89 (0.16, 5.06)	0.72 (0.32, 1.58)	0.95 (0.61, 1.50)

[a] Base class in multinomial logistic regression was most SDoH adversities; [b] Further adjustment for this imbalanced covariate resulted in no changes in the regression estimates presented in Table 3.

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5. Chapter 5: A Latent Class Analysis of the Social Determinants of Health Impacting Heavy Alcohol Consumption among Women Living with HIV in Canada: The Canadian HIV Women's Sexual and Reproductive Health Cohort Study[1]

5.1. Introduction

Heavy alcohol consumption is prevalent among individuals living with HIV, including women.[1-3] For example, a study conducted in the United States (US) over an 11-year follow-up period found that almost half of women living with HIV (WLWH) reported any past-year alcohol consumption, with 14% to 24% reporting heavy/hazardous drinking,[1] defined as ≥ 4 drinks per occasion or > 7 drinks/week.[4] Research in Canada has documented that 20% (i.e., 15.4% less than once a week and 4.6% weekly) of WLWH reported any past-month binge drinking, defined as ≥ 4 drinks per occasion,[5] compared to 34.5% (i.e., 30.6% less once a week and 3.9% weekly) from general population women of similar ages/ethnoracial backgrounds.[3]

While less frequent in WLWH than the general population,[3] heavy alcohol use has been shown to be negatively associated with outcomes along the HIV treatment cascade. For example, Monroe et al. in a US longitudinal study found that heavy drinkers and frequent binge drinkers were respectively associated with inferior retention in HIV care and lower visit adherence.[6] Research on WLWH has also documented the impact of heavy drinking and poor HIV outcomes; for example, Barai et al. in a secondary analysis of data collected in a US randomized control

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trial found heavy drinking as a barrier to achieving viral suppression,[7] appearing through alteration of virus infectivity, immune response, tissue injury and inflammatory markers.[8-10] In addition, heavy drinking accounts for considerable mortality among WLWH; e.g., Neblett et al. in a US longitudinal cohort of WLWH found that heavy drinking independently increased the risk of earlier death by 40% (aHR = 1.40).[11] Indeed, a better recognition of heavy drinking has implications for HIV care and treatment. Further, the identification of such prevalent but modifiable risk-taking practices is essential to improve the health and wellbeing of WLWH, who now represent almost one-quarter of all new HIV diagnoses in Canada.[12]

While extant research has shown the association of increased heavy drinking with sociodemographic factors (e.g., age and race/ethnicity) as well as psychological, and treatment or clinical factors (e.g., viral load and CD4 indictors),[1,11,13-16] less has been explored through a social determinants of health (SDoH) framework. SDoH are living conditions in which people are born, live, work, and age,[17] and represent structural causes of health problems.[17,18] SDoH are particularly important among WLWH as an array of socio-structural adversities such as low income, food insecurity, low social support, stigma and discrimination have been reported.[19,20] Approaches informed by an SDoH framework may examine such daily living stressors that contribute to WLWH's likelihood of initiating or continuing heavy/hazardous drinking as a coping behaviour. This framework underscores the complex dynamic of social, economic and structural factors that have the potential to cluster together; a key feature of these determinants that has been methodologically less taken into account.

In the present study, we explored the association between SDoH and heavy alcohol use among WLWH in Canada. As SDoH tend to co-occur in particular combinations,[20] we examined the concomitant patterns of these determinants using latent class analysis (LCA). We then

explored the association of the clustered SDoH with heavy drinking. This research is informed by an SDoH framework contending that upstream socio-structural determinants share or influence individuals' health,[17] as well as a syndemics framework referring to disease-social condition interactions that synergistically influence the health of a population within the context of persistent social inequalities.[21] Understanding the unique (distinct) clusters of social determinants through which heavy drinking may be impacted and/or intervened on can help address alcohol use among WLWH.

5.2. Methods

5.2.1 Study sample

We used data from the community-based Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS). As previously described,[22,23] CHIWOS enrolled WLWH aged ≥16 years, including transgender women, residing in the provinces of British Columbia (BC), Ontario, or Quebec. A total sample of 1,422 were interviewed during 2013-2015 (time-point 1), and 1,252 after ~18-months (2016-17, time-point 2). Participants who had died or did not participate in time-point 2 were considered as *censored* (i.e., lost to follow-up; N = 170; 11.9%). Participants were recruited from HIV clinics, community-based organizations, peers, and online networks. The survey was administered via trained peer research associates (PRAs) through face-to-face interviews at clinics, community sites, participants' homes, or via phone/Skype.[23] CHIWOS was approved by the Research Ethics Boards of Simon Fraser University, University of British Columbia/Providence Health, Women's College Hospital and McGill University Health Centre.

5.2.2 Alcohol use measures

Alcohol use measures at time-point 2 were considered as the study outcomes when investigating its association with SDoH measured at time-point 1. A standard drink was defined as having a 341 ml (12 oz.) bottle of 5% alcohol beer, cider or cooler, or a 142 ml (5 oz.) glass of 12% alcohol wine, or a 43 ml (1.5 oz.) (single shot) serving of liquor or spirits. Two measures of alcohol consumption were defined according to the definitions from the available recommendation:[4,5]

Weekly alcohol use: The average quantity of drinks per week was computed by multiplying last-year frequency of alcohol use (with five response options: never, monthly or less, 2-4 times a month, 2-3 times a week, 4 or more times a week) by quantity of alcohol consumed on a typical drinking day (with five response categories: 1-2, 3-4, 5-6, 7-9, 10 or more). We used the midpoint for response options. We then created a three-category measure: nondrinking or low drinking (< 1 drink/week), moderate drinking (1-7 drinks/week), and heavy drinking (> 7 drinks/week).

Binge drinking: Past-month *heavy* binge drinking (i.e., ≥ 6 drinks on one single occasion) at least once/month was measured and categorized into three categories: non-drinking or non-binge drinking, infrequent binge drinking (< 1/month), or frequent binge drinking (≥ 1/month). The typical threshold for binge drinking among women is 4 or more drinks;[5] however, having a more conservative measure of two more drinks over the typical binge drinking threshold has been found to be of value in capturing adequately the nature of problem drinking practice in other studies.[24]

5.2.3 SDoH indicators

The following 12 potentially modifiable current or recent SDoH indicators measured at time-point 1 were examined: race discrimination, gender discrimination, enacted HIV stigma, social support, barriers to access to care, food security, housing status, employment status, education, income level, recent sex work involvement, and recent incarceration. In this study, we only included the current/recent SDoH indicators to avoid the potential for spurious correlation and biased estimation known as collider stratification bias.[25] Such bias can be introduced in studies of selected populations (here, WLWH) if they investigate earlier exposures (here earlier social determinants such as childhood events) that may have affected study inclusion/exclusion criteria (here HIV status).

We separately measured *racial discrimination* and *gender discrimination*, defined as any discriminatory mistreatments due to race and gender, using the 8-item Everyday Discrimination Scale.[26] Consistent with its operationalized definition,[27] WLWH who reported (sometimes, frequently, or almost everyday) having discriminatory experiences due to their race and gender were considered as having experienced race discrimination and gender discrimination, respectively. Three items of Wright's shortened version of Berger's HIV Stigma Scale were used to measure *enacted HIV stigma* (i.e., been hurt by people's reaction, stopped socializing, or lost friends), indicating the extent to which participants faced mistreatment due to their HIV status.[28] Participants who reported any HIV-related discriminatory events with strongly agree/agree response options were considered as having experienced HIV-related stigma. A 4-item Medical Outcome Study: Social Support Survey[29] was used to gauge *perceived social support*, measuring emotional-informational, tangible, affectionate, and positive social interaction supports. The overall possible mean score ranged from 1-5, with scores > 2 indicating poor social support

availability.[30] *Barriers to Access to Care* was measured using a 12-item scale.[31] Overall possible mean severity scores ranged from 1-4, with scores ≥ 2 indicating severe/significant barriers.[32] *Food insecurity* over the past 12 months was assessed using three items: fears of running out of food; experiences of running out of food; and unaffordability of balanced meals. The sum of these items yielded an overall score ranged 1-6, with scores > 1 indicating food insecure.[33] Other SDoH indicators included *yearly household income level* (less than $20,000 vs. $20,000 or more), current *employment status* (unemployed [e.g., no income or income from non-employment sources such as employment insurance/compensation/welfare, dividends and interest, or pension plan] vs. employed [i.e., having any paid jobs]), current *education level* (below high school vs. completed high school), current *housing status* (unstable [e.g., residing in a self-contained room, transition house, halfway house, safe house, or outdoors] vs. stable housing), any *sex work involvement* in the last six months (Yes, No), and any history of *incarceration* in the last year (Yes, No).

5.2.4 Covariates

Covariates with potential association with either both SDoH classes and alcohol consumption measures or only alcohol consumption measures were considered, including: age (continuous; with its linear and quadratic forms in the model); ethnoracial groups (white, African/Caribbean/Black, Indigenous, other); city size (large, others); study province (Ontario, BC, Quebec); sexual orientation (heterosexual, LGBQ); relationship status (single (non-married), married/common-law, others); years living with HIV (<6 years, 6-14 years, > 14 years); antiretroviral therapy status (optimal [≥ 95% treatment adherence], suboptimal [< 95% treatment adherence], not engaged in treatment); ever being diagnosed with a mental health condition by a care provider (Yes, No); resilience measured using the 10-item version of the Resilience Scale,[34]

ranging 10-70, with higher scores implying increased resilience, dichotomized at its median; any history of childhood sexual/physical violence (Yes, No); any experience of adulthood sexual/physical/verbal/action-limited violence (Yes, No); having been under the care of Child Protection Services or in foster care (Yes, No); last-year cigarette smoking history (never/former, occasional/regular); last-month non-prescribed cannabis use (never/former, occasional/regular), last three months any non-prescribed/illicit opioid and/or stimulant use (Yes, No), ever used alcohol counseling services (Yes, No).

5.2.5 Latent class analysis (LCA)

We conducted LCA to identify the clusters of SDoH assessed at time-point 1. LCA as a data reduction strategy is a probabilistic model-based clustering technique to detect unobserved but homogenous patterns of the observed indicators within an unobserved categorical measure. LCA identifies such latent variable under the assumption that all observed indicators are independent given the latent variable (i.e., the latent variable is the reason that observed indicators are correlated).[35] The expectation–maximization (EM) algorithm with 5,000 iterations was used to find the best model fit.[36] We started LCA with a 2-class model and progressively increased (**S Table 5.1**), for each the log-likelihood was replicated with 1,000 random starting values to increase the confidence that the best identified model solution is the true maximum likelihood solution. Therefore, we reported the percentage of seeds associated with best fitting model, with higher values indicating being unlikely to hit the local maxima. While we predominantly relied on the interpretability of class memberships, the following fit statistics were also reported to help obtain the best model: log-likelihood, Akaike's information criteria (AIC), Bayesian information criteria (BIC), and sample-size-adjusted BIC (aBIC), and consistent AIC (CAIC),[37-39] with their lower values implying better goodness-of-fit and parsimony. Entropy as a measure of

classification accuracy was also reported (varied from 0 to 1), with higher values suggesting clearer separation/distinction among the latent classes.[35]

As shown in (**S Table 5.1**), we proposed the 4-class model as the best fitting model of the SDoH classes among WLWH. The observed prevalence of each item as well as item-response probabilities (Yes category only) condition on class membership of the 4-class model are illustrated in Supplementary Figure 1. These four classes included: WLWH who experienced none or only one SDoH adversity (class 1, labeled as none/least SDoH adversities; 6.6%); WLWH who predominantly reported experiencing racial discrimination, gender discrimination and HIV-related stigma, accompanied by experiencing barriers in access to care without economic hardship experiences (class 2, labeled as discrimination/stigma group; 17.9%); WLWH who mainly reported food insecurity, low household income, and unemployment without stigma/discrimination (class 3, labeled as economic hardship group; 31.6%); and WLWH who experienced gender and racial discrimination, HIV-related stigma, low social support, greater difficulties access to care, food insecurity, low income, and unemployment (class 4, labeled as most SDoH adversities; 43.9%). After identification of the fitting model, each participant was assigned to the SDoH latent classes in which they had the greater posterior probability. LCA accounted for missing values using the full information maximum likelihood estimation under the assumption of missing at random. We conduced LCA using the SAS PROC LCA procedure.[35]

5.2.6 Models and estimations

Inverse probability weights (IPW) was used to account for confounding bias due to the potentially imbalanced covariates across the SDoH classes. We also used inverse probability

censoring weights (IPCW) to account for prospective selection bias due to potentially non-random loss to follow-up (**S Table 5.2**).

Covariate selection: Consistent with recommendations,[40] measured covariates that were potentially associated with the study outcomes were considered. To account for confounding by outcome history, we also included alcohol use measures at time-point 1.[41] Missing values of covariates considered for generating the weights were singly imputed under the assumption of missing at random to reduce the loss of statistical power.[42]

Control of confounding using IPW: We generated stabilized weights using multinomial logistic regression models: the numerator was computed as the marginal probability of the SDoH classes (accounting for imbalanced proportions of the SDoH classes) divided by the denominator which was computed as the probability that a participant assigned to a SDoH class conditioning on the measured covariates. These models were performed among WLWH without censored information in time-point 2.

Control of selection bias using IPCW: We first created a binary measure indicating censored individuals at time-point 2. Then, IPCW using binary logistic regression model was obtained: the numerator was defined as the probability of not being censored given SDoH classes, and the denominator was calculated as the probability of not being censored given SDoH and the study covariates.[43]

Final stabilized weight: We created the final stabilized weight using the product of IPW and IPCW. The distribution of the weights across the SDoH classes is presented in (**S Table 5.3**). Under the following assumptions: correct specification of IPW models, conditional exchangeability, and positivity,[44] the final weight removes the association between SDoH classes, as the main independent variable, and the study covariates[43] (**S Table 5.4**).

Association of SDoH classes with alcohol use measures: The association between SDoH classes and alcohol use measures was examined using multinomial logistic regression models as the alcohol use outcomes had more than two categories. We then estimated crude and weighted relative-risk ratios (RRR) and 95% confidence intervals (CI). Further adjustment was made for history of the study outcomes. Additionally, a sensitivity analysis was conducted to evaluate the extent to which unmeasured confounding would explain away the observed associations. To do this, we computed the E-values as: $E = RRR + \text{sqrt}\{RRR \times RRR - 1\}$, where RRR referred to the significant observed estimates. We replaced RRR with $RRR^{*} = 1/RRR$ for those estimates less than the null (RRR = 1).[45] E-value for RRR provides values below, equal to or above the null, representing the minimum strength of the association between unmeasured confounders with SDoH clusters and/or alcohol use to nullify the observed associations. These analyses were done using Stata 15.

5.3. Results

5.3.1 Participants' characteristics

Characteristics of study participants enrolled in time-point 1 can be seen in **Table 5.1**. The mean age was 42.8 [SD 10.6] years old. The largest category identified as white (41.1%), while 29.4% identified as African/Caribbean/Black, 22.3% as Indigenous, and 7.2% as other. The majority reported their sexual orientation as heterosexual (87.3%). About one-third (32%) reported being in a relationship, married, or common-law; 40.2% reported living with HIV for 6-14 years; and 70.0% reported optimal HIV treatment adherence. Childhood and adulthood violence were reported by 62.7% and 80.4%, respectively. Ever having a mental health diagnosis was reported by 40.7%. The distribution of these covariates across the SDoH classes is also presented in **Table 5.1**.

Table 5.1: Characteristics of Women Living with HIV Overall and Stratified by Social Determinants of Health (SDoH) Classes, CHIWOS Survey – Time-point 1

Variables at time-point 1	Overall	SDoH classes at time-point 1				
		None/least adversities	Discrimination/ stigma	Economic hardship	Most adversities	P-value[b]
N	1,422 (100)	94 (6.6)	256 (18.0)	430 (30.2)	642 (45.2)	---
Age, yr (mean [SD])	42.8 [10.6]	39.2 [10.3]	43.5 [10.6]	42.9 [11.5]	43.1 [10.0]	0.007
Ethno-racial identity						<0.001
White	584 (41.1)[a]	58 (61.7)	97 (37.9)	219 (50.9)	210 (32.7)	
African/Caribbean/Black	418 (29.4)	23 (24.5)	109 (42.6)	123 (28.6)	163 (25.4)	
Indigenous	318 (22.3)	7 (7.4)	29 (11.3)	60 (14.0)	222 (34.6)	
Other	102 (7.2)	6 (6.4)	21 (8.2)	28 (6.5)	47 (7.3)	
Province						<0.001
Ontario	717 (50.4)	50 (53.2)	131 (51.2)	235 (54.6)	301 (46.9)	
British Columbia	356 (25.0)	13 (13.8)	49 (19.1)	65 (15.1)	229 (35.7)	
Quebec	349 (24.6)	31 (33.0)	76 (29.7)	130 (30.2)	112 (17.5)	
Living in large cities	1169 (82.2)	83 (88.3)	203 (79.3)	345 (80.2)	538 (83.8)	0.106
Being heterosexual	1237 (87.3)	85 (90.4)	237 (93.3)	395 (91.9)	520 (81.4)	<0.001
Relationship status						<0.001
Single (non-married)	689 (48.5)	40 (42.6)	100 (39.1)	201 (46.7)	348 (54.4)	
Married/common-law	454 (32.0)	44 (46.8)	103 (40.2)	134 (31.1)	173 (27.0)	

Others	277 (19.5)	10 (10.6)	53 (20.7)	95 (22.1)	119 (18.6)	
Years living with HIV						0.001
< 6 years	345 (25.1)	23 (25.0)	40 (15.7)	128 (31.4)	154 (24.8)	
6-14 years	552 (40.2)	35 (38.0)	118 (46.7)	140 (34.3)	259 (41.8)	
> 14 years	477 (34.7)	34 (37.0)	96 (37.8)	140 (34.3)	207 (33.4)	
Taking treatment						0.001
Yes, optimal adherence (≥ 95%)	863 (70.0)	65 (69.9)	163 (64.7)	279 (65.0)	356 (55.5)	
Yes, suboptimal adherence (< 95%)	312 (22.0)	12 (12.9)	52 (21.4)	74 (17.2)	172 (26.8)	
Not engaged in treatment	240 (17.0)	16 (17.2)	35 (13.9)	76 (17.7)	113 (17.6)	
Mental health diagnosis	573 (40.7)	26 (28.0)	93 (36.6)	134 (31.6)	320 (50.3)	<0.001
Low resiliency (below median)[c]	662 (47.1)	22 (23.66)	104 (40.9)	172 (40.6)	364 (57.4)	<0.001
Childhood violence	819 (62.7)	34 (38.6)	138 (56.8)	211 (53.8)	436 (74.7)	<0.001
Adulthood violence	1057 (80.4)	52 (59.1)	189 (77.5)	284 (71.9)	532 (90.5)	<0.001
Child development events	326 (23.0)	10 (10.6)	33 (13.0)	74 (17.3)	209 (32.7)	<0.001
Cigarette smoking (regular/occasional)	616 (43.7)	15 (16.1)	65 (25.5)	176 (41.1)	360 (56.7)	<0.001
Non-prescribed cannabis use (regular/occasional)	264 (18.9)	7 (7.7)	34 (13.4)	75 (17.7)	148 (23.6)	<0.001
Drug use[d]	244 (17.5)	2 (2.2)	11 (4.3)	50 (11.9)	181 (28.8)	<0.001
Received alcohol counseling	3 (3.2)	24 (9.4)	60 (14)	201 (31.3)	3 (3.2)	<0.001
Weekly alcohol use						0.132

Abstainers to low (<1 drink)	956 (69.1)	64 (68.8)	174 (68.5)	302 (71.1)	419 (68.1)	
Moderate (1 to 7 drinks)	288 (20.8)	22 (23.7)	60 (23.6)	88 (20.7)	118 (19.2)	
Heavy (>7 drinks)	140 (10.1)	7 (7.5)	20 (7.9)	35 (8.2)	78 (12.7)	
Binge drinking						0.037
Non-drinkers/no binge drinking	1107 (81.9)	73 (79.4)	214 (85.3)	348 (85.5)	472 (78.5)	
Infrequent (< 1 per month)	14 (1.0)	1 (1.1)	4 (1.6)	1 (0.3)	8 (1.3)	
Frequent (≥ 1 per month)	230 (17.0)	18 (19.6)	33 (13.2)	58 (14.3)	121 (20.1)	

[a] Data are presented as N (%) unless specified; [b] P-values are for the chi-square test for categorical covariates and one-way ANOVA for continuous covariates; [c] Scores ranged 10-70, with higher scores indicating increased resilience (median = 64); [d] Last three months any non-prescribed/illicit opioid and/or stimulant use measured.

5.3.2 Weekly alcohol use

Overall, moderate (1-7 drinks/week) and heavy (>7 drinks/week) alcohol use at time-point 2 were reported by 20.1% and 10.5%, respectively. Heavy alcohol use at time-point 2 was reported by 6.8% among WLWH in no/least SDoH adversities, 10.2% among WLWH in discrimination/stigma class, 8.8% among economic hardship class, and 12.6% among WLWH in the most SDoH adversities class (**Table 5.2**).

Table 5.2: Alcohol Consumption Measures (Study Outcomes) Overall and Across the Social Determinants of Health (SDoH) Classes among Women Living with HIV, CHIWOS Survey

Alcohol use measures at time-point 2	Overall	SDoH classes at time point 1				
		None/least adversities	Discrimination/ stigma	Economic hardship	Most adversities	P-value
N	1237	88	231	378	540	---
Weekly alcohol use[*]						0.006
Abstainers to low (<1 drink)	858 (69.4)	55 (62.5)	156 (67.5)	282 (74.6)	365 (67.6)	
Moderate (1 to 7 drinks)	249 (20.1)	27 (30.7)	54 (23.4)	65 (17.2)	103 (19.1)	
Heavy (>7 drinks)	130 (10.5)	6 (6.8)	21 (9.1)	31 (8.2)	72 (13.3)	
Binge drinking[b,*]						0.001
Non-drinkers/no binge drinking	952 (77.5)	70 (79.6)	183 (79.2)	309 (82.4)	390 (72.9)	
Infrequent (< 1 per month)	155 (12.6)	15 (17.1)	33 (14.3)	32 (8.5)	75 (14)	
Frequent (≥ 1 per month)	122 (9.9)	3 (3.4)	15 (6.5)	34 (9.1)	70 (13.1)	

[a] Data are presented as N (%); [b] Heavy binge drinking at time-point 2 was defined as having 6 or more drinks in one single occasion; * P-value < 0.05, indicating that the distribution of both alcohol consumption measures is significantly different across the SDoH classes.

Our results showed no crude associations between SDoH classes and heavy weekly alcohol consumption. However, the weighted regression analysis demonstrated that WLWH in no/least SDoH adversities had lower likelihood of weekly heavy alcohol use than WLWH in discrimination/stigma class (RRR = 0.10; 95% CI: 0.02, 0.68), economic hardship class (RRR = 0.18; 95% CI: 0.03, 1.04; not significant), and most SDoH adversities class (RRR = 0.11; 0.02, 0.62). While crude associations showed an increased likelihood of moderate weekly alcohol consumption among WLWH in the no/least SDoH adversity in comparison with other three classes, no significant association was observed in the weighted analyses (**Table 5.3**).

Table 5.3: The Association of Social Determinants of Health (SDoH) Classes on Weekly Alcohol Use using Inverse-Probability Weighting Analysis among Women Living with HIV in Canada, CHIWOS Survey

	Moderate use (1-7 drinks per week)[a]		Heavy use (> 7 drinks per week)[a]	
SDoH classes at time-point 1	Crude estimates RRR (95% CI)[b]	IPW estimates RRR (95% CI)	Crude estimates RRR (95% CI)	IPW estimates RRR (95% CI)
Economic hardship vs. most adversities	0.82 (0.58 ,1.16)	*0.66 (0.43, 1.01)*	0.56 (0.36 ,0.87)	0.61 (0.32, 1.13)
P-value	0.253	*0.060*	0.011	0.120
Discrimination/stigma vs. most adversities	1.23 (0.84 ,1.79)	1.04 (0.59, 1.84)	0.68 (0.41 ,1.15)	1.09 (0.39. 3.03)
P-value	0.291	0.866	0.151	0.863
No/least adversities vs. most adversities	1.74 (1.04 ,2.9)	0.39 (0.09, 1.62)	0.55 (0.23 ,1.33)	**0.11 (0.02, 0.62)**
P-value	0.033	0.200	0.187	**0.013**
Discrimination/stigma vs. economic hardship	1.50 (1.00 ,2.26)	1.56 (0.87, 2.83)	1.22 (0.68 ,2.20)	1.79 (0.64, 4.95)
P-value	0.052	0.135	0.499	0.262
No/least adversities vs. economic hardship	2.13 (1.25 ,3.63)	0.59 (0.14, 2.45)	0.99 (0.40 ,2.49)	*0.18 (0.03, 1.04)*
P-value	0.005	0.473	0.987	*0.056*
No/least adversities vs. discrimination/stigma	1.42 (0.81 ,2.47)	0.38 (0.08, 1.64)	0.81 (0.31 ,2.11)	**0.10 (0.02, 0.68)**
P-value	0.217	0.196	0.667	**0.019**

[a] Base Group in Multinomial Logistic Regression: Abstainers to Low [<1 drink/week]); [b] RRR: relative-risk ratio (95% confidence intervals: CI); [c] Italicized estimates indicate having a p-value less than 0.10; [d] Bold estimates indicate having a p-value less than 0.05.

5.3.3 Binge drinking

Overall, infrequent (<1/month) and frequent (≥1/month) binge drinking at time-point 2 were reported by 12.6% and 9.9%, respectively. Frequent binge drinking was reported by 3.4% among WLWH in no/least SDoH adversities, 7.2% among WLWH in discrimination/stigma class, 9.6% among economic hardship class, and 12.3% among WLWH in the most SDoH adversities class (**Table 5.2**). WLWH in no/least SDoH adversities class were shown to have a lower likelihood of frequent binge drinking than WLWH in discrimination/stigma class (RRR 0.02; 95% CI: 0.002, 0.21), economic hardship class (RRR = 0.03; 95% CI: 0.01, 0.24), and most SDoH adversities class (RRR = 0.02; 95% CI: 0.002, 0.13). Furthermore, the likelihood of infrequent binge drinking was lower among WLWH in no/least SDoH adversities class than those in discrimination/stigma and the most SDoH adversities classes (**Table 5.4**).

Table 5.4: The Association of the Classes of Social Determinants of Health (SDoH) on Binge Drinking using Inverse-Probability Weighting Analysis among Women Living with HIV in Canada, CHIWOS Survey

	Binge drinking < 1 per month[a]		Binge drinking ≥ 1 per month[a]	
SDoH classes at time-point 1	Crude estimates RRR (95% CI)[b]	IPW estimates RRR (95% CI)	Crude estimates RRR (95% CI)	IPW estimates RRR (95% CI)
Economic hardship vs. most adversities	0.53 (0.34, 0.83)	0.75 (0.35, 1.59)	0.61 (0.39, 0.94)	0.56 (0.29, 1.10)
P-value	0.006	0.456	0.028	0.097
Discrimination/stigma vs. most adversities	0.93 (0.60, 1.46)	1.57 (0.76, 3.22)	0.45 (0.25, 0.82)	0.70 (0.28, 1.70)
P-value	0.777	0.217	0.009	0.432
No/least adversities vs. most adversities	1.11 (0.60, 2.05)	**0.20 (0.04, 0.99)**	0.23 (0.07, 0.77)	**0.02 (0.002, 0.13)**
P-value	0.728	0.050	0.018	< 0.001
Discrimination/stigma vs. economic hardship	1.74 (1.03, 2.92)	2.09 (0.81, 5.39)	0.74 (0.39, 1.40)	1.23 (0.46, 3.26)
P-value	0.036	0.126	0.363	0.671
No/least adversities vs. economic hardship	2.06 (1.06, 4.02)	0.26 (0.04, 1.44)	0.38 (0.11, 1.30)	**0.03 (0.01, 0.24)**
P-value	0.032	0.127	0.126	0.001
No/least adversities vs. discrimination/stigma	1.18 (0.60, 2.32)	**0.12 (0.02, 0.69)**	0.52 (0.14, 1.86)	**0.02 (0.002, 0.21)**
P-value	0.614	0.017	0.317	0.001

[a] Base Group in Multinomial Logistic Regression: Non-Drinkers/No Binge Drinking; [b] RRR: relative-risk ratio (95% confidence intervals: CI); [c] Italicized estimates indicate having a p-value less than 0.10; [d] Bold estimates indicate having a p-value less than <0.05.

5.3.4 Sensitivity analysis

The sensitivity analysis reflected that our observed associations were relatively robust to potential unmeasured confounding. For example, for the observed RRR: 0.11 for heavy weekly alcohol consumption among WLWH in the no/least SDoH adversities class versus the most SDoH adversities class, an unmeasured confounder correlated with both exposure and outcome by RRRs of ~17.6-fold each, above and beyond the measured confounders, would explain away the observed association, but weaker confounding would not. Such an E-value for the upper 95% limit of the same comparison (Upper CI = 0.62) was 2.6-fold. The E-values for the significant observed associations were reported in (**S Table 5.5**).

5.4. Discussion

We explored the pattern of alcohol consumption measures and their association with four SDoH classes in a diverse cohort of WLWH in Canada. We found that 10.5% of WLWH reported heavy weekly alcohol use at enrollment and 9.9% reported frequent binge drinking at ~18 months follow up, with greater proportion among WLWH who experienced multiple forms of SDoH adversities than those with no/least SDoH adversity. We also documented that WLWH with no/least SDoH adversity were less likely to report heavy alcohol consumption relative to WLWH experiencing either discrimination/stigma or economic hardship or suffering from the most SDoH adversities. These findings can inform intervention strategies to advance health among WLWH.

Our research contributes to the literature in several ways. Firstly, we found that a large proportion of WLWH reported experiencing specific forms of socio-structural adversities including economic hardship and stigma/discrimination, or multiple types of disadvantages. Secondly, this study adds to the current understanding of how social determinants clustered

together and such clustering increased the likelihood of heavy drinking among WLWH. Thirdly, we documented that the risk of alcohol use did not change much (vs. no/least SDoH class) whether a women reported experiencing primarily stigma/discrimination, primarily economic hardship, or the most SDoH adversities. These findings may indicate that in addressing heavy drinking, it is important to consider the role that any form of SDoH inequities play in shaping such risk-taking practice. This is particularly important as heavy drinking has been shown to be a significant predictor of mortality among WLWH of the same cohort in Canada.[22] Overall, our findings suggest that WLWH continue to experience a high level of stress as a result of social and structural inequalities, contributing to elevated risk of alcohol consumption.[46,47]

While it is difficult for us to compare our findings directly with prior research, these findings are in line with the extant literature, implying that a greater level of social adversity is associated with increased likelihood of heavy drinking among WLWH.[1,13,14] Previous studies have mostly reported the independent impact of individual social factors (either modifiable or non-modifiable ones) on alcohol use. For example, Cook et al. in a longitudinal study identified unemployment and low education as the independent predictors of heavy alcohol consumption among WLWH.[1] They also found the independent effect of low education (but not employment or race/ethnicity) on higher odds of heavy drinking in a trajectory analysis.[13] In 2018, Kelso-Chichetto et al. found an association between alcohol consumption trajectories and race/ethnicity, but not with annual income levels among WLWH.[14] Concentrating on modifiable social factors, we found a significant association of the clustered SDoH on heavy drinking among WLWH. While our estimates relied on a set of SDoH indicators gathered on only one time-period, future research could conduct a trajectory analysis to assess the stability of these social determinants over time in association with behavioural and HIV treatment outcomes.

Our study had some limitations. First, CHIWOS used a purposive, nonrandom sampling approach that may have oversampled WLWH receiving care, who may have different characteristics such as sociodemographic or socio-structural vulnerabilities than other WLWH. In turn, CHIWOS also oversampled WLWH experiencing intersecting forms of marginalization such as sex work and substance use to mitigate sampling bias.[22] Second, data on both alcohol use and social determinants were gathered via self-report, and are subject to social desirability and recall biases (particularly the past-year frequency and quantity of alcohol use). However, the survey was administered by PRAs who are also WLWH,[22] to build trust with participants in sharing their information.[23]

Despite these limitations, this study has several notable strengths. We included a large sample of WLWH with diverse ethno-racial identities and social-economic experiences, which may provide a better picture of the target population beyond only those in clinical settings. Second, this research enhances understanding of the clustered SDoH and their association with heavy alcohol use. Third, a large proportion of the study sample remained in the follow-up survey, allowing for assessment of study outcomes which makes temporality between SDoH classes and alcohol use measures clear. Fourth, use of LCA including 12 SDoH indicators allowed for data reduction and a clearer presentation of the impact of the clustered SDoH on the study outcomes. This underscores the interdependent nature of the SDoH beyond their independent impacts.

5.4.1 Conclusion

Approximately one out of ten WLWH from the CHIWOS cohort met criteria for heavy drinking and frequent binge drinking, with higher likelihood among those experiencing overlapping forms of SDoH adversities. Our findings suggest that multiple forms of SDoH adversities – regardless

of their types – can substantially impact the initiation/continuation of heavy drinking. In the current era where viral suppression is achieved and an improved survival is expected among individuals who have access to HIV medications and are on treatment and in care,[48,49] adversities regarding socioeconomic and structural determinants as well as behavioural factors (heavy drinking) may undermine the efforts of the management of HIV. Effective interventions aiming to target WLWH who drink at heavy levels should also consider the substantial contribution of socio-structural barriers that WLWH inequitably experience in their daily life. While integration of harm reduction approach into HIV care through the women-centered care model may be considered as an approach in addressing heavy drinking and social barriers,[50] more evidence-based research is needed to determine the effectiveness of such interventions. Our findings highlight the urgency to address SDoH for interventions to be fully beneficial for WLWH who involve in heavy drinking.

5.5. Supplementary Tables and Figures

S Table 5.1: Comparison of Goodness-of-fit Measures for Different Class Models (N=1,422)

Model	LL[a]	AIC[b]	BIC[c]	CAIC[d]	Entropy	% seeds[e]
1-class	-12363.0	10080.9	10207.2	10231.2	1.000	100%
2-class	-8582.2	2569.1	2826.9	2875.9	1.000	100%
3-class	-8271.3	1997.4	2386.7	2460.7	0.843	98.4%
4-class[f]	*-8030.0*	*1564.9*	*2085.6*	*2184.6*	*0.831*	*93.5%*
5-class	-7966.5	1487.8	2140.0	2264.0	0.819	35.0%
6-class	-7922.1	1449.0	2232.7	2381.7	0.814	15.0%
7-class	-7889.8	1434.5	2349.7	2523.7	0.745	32.4%

[a] Log-Likelihood (LL); [b] Akaike information criterion (AIC); [c] Bayesian information criterion (BIC); [d] Consistent AIC (CAIC), [e] Percentage of seeds associated with best fitted model (% seeds); [f] 4-class model had the lowest BIC and CAIC. Moving forward to model with more classes, entropy suggested lower classification accuracy (e.g., ~10% reduction from 4-class to 7-class). In addition, the 4-class model had a higher percentage of seeds associated with best fitted model (i.e., increased confidence that the best solution was achieved even though it is not a fit criterion). Fit indices/statistics align with model interpretability suggested the 4-class model provided a better fit with plausible distribution of the sample within each class.

S Table 5.2: Characteristics of Women Living with HIV who were Lost to Follow-up (i.e., Censored), CHIWOS, 2013-2017

Variables at time-point 1	Not Lost to follow up (N = 1252)	Lost to follow up (N = 170)	P-value[b]
SDoH classes			0.057
Class 1: No/least SDoH adversities	88 (7.03)[a]	6 (3.53)	
Class 2: Discrimination/Stigma	232 (18.53)	24 (14.12)	
Class 3: Economic adversities	381 (30.43)	49 (28.82)	
Class 4: Most SDoH adversities	551 (44.01)	91 (53.53)	
Age, yr (mean [SD])	42.9 [10.61]	42.2 [10.34]	0.430
Ethno-racial group			0.062
White	515 (41.13)	69 (40.59)	
African/Caribbean/Black	380 (30.35)	38 (22.35)	
Indigenous	272 (21.73)	46 (27.06)	
Other	85 (6.79)	17 (10.00)	
Province			0.018
Ontario	637 (50.88)	80 (47.06)	
British Columbia	299 (23.88)	57 (33.53)	
Quebec	316 (25.24)	33 (19.41)	
Living in large cities	1029 (82.19)	140 (82.35)	0.958
Heterosexual	1095 (87.81)	142 (83.53)	0.116
Relationship status			0.596
Single (non-married)	612 (48.92)	77 (45.56)	
Married/common-law	394 (31.49)	60 (35.50)	
Others	245 (19.58)	32 (18.93)	
Years living with HIV			0.648
< 6 years	310 (25.49)	35 (22.15)	
6-14 years	487 (40.05)	65 (41.14)	

> 14 years	419 (34.46)	58 (36.71)	
Taking treatment			0.012
Yes, optimal adherence (≥ 95%)	759 (60.91)	104 (61.54)	
Yes, suboptimal adherence (< 95%)	264 (21.19)	48 (28.40)	
Not engaged in treatment	223 (17.90)	17 (10.06)	
Mental health diagnosis	499 (40.21)	74 (44.58)	0.282
Low resiliency[c] (below median)	568 (45.81)	94 (56.97)	0.007
Childhood violence	708 (61.51)	111 (71.15)	0.019
Adulthood violence	918 (79.07)	139 (90.26)	0.001
Child development events	269 (21.55)	57 (33.73)	<0.001
Cigarette smoking (regular/occasional)	516 (41.4)	100 (60.2)	<0.001
Non-prescribed cannabis use (regular/occasional)	226 (18.4)	38 (23.0)	0.150
Drug use[d]	193 (15.7)	51 (30.7)	<0.001
Received alcohol counseling	234 (18.7)	54 (31.8)	<0.001
Weekly alcohol use			0.011
Abstainers to low (<1 drink)	865 (70.4)	94 (59.1)	
Moderate (1 to 7 drinks)	242 (19.7)	46 (28.9)	
Heavy (>7 drinks)	121 (9.8)	19 (11.9)	
Binge drinking			<0.001
Non-drinkers/no binge drinking	997 (83.6)	110 (69.2)	
Infrequent (< 1 per month)	12 (1.0)	2 (1.3)	
Frequent (≥ 1 per month)	183 (15.3)	47 (29.6)	

[a] Data are presented as N (%) unless specified; [b] P-values are for the chi-square test for categorical covariates and one-way ANOVA for continuous covariates; [c] Scores ranged 10-70, with higher scores indicating increased resilience (median = 64); [d] Last three months any non-prescribed/illicit opioid and/or stimulant use measured.

S Table 5.3: Distributions of the Estimated Weights for the Classes of the Social Determinants of Health (SDoH), Censoring, and both, CHIWOS, Time-point 1, 2013-2015

	Mean (SD)	Percentiles				
		5th	25th	50th	75th	95th
Stabilized weights for SDoH weights						
Class 1[a]	0.97 (2.50)	0.12	0.20	0.43	1.00	2.26
Class 2	1.01 (1.04)	0.39	0.51	0.72	0.98	3.19
Class 3	0.99 (0.67)	0.48	0.61	0.79	1.11	2.16
Class 4	0.99 (0.61)	0.48	0.58	0.80	1.16	2.19
Overall	0.99 (0.97)	0.41	0.57	0.78	1.12	2.25
Stabilized weights for censoring weights						
Overall	1.00 (0.08)	0.91	0.94	0.98	1.02	1.15
Stabilized weights for final weights						
Class 1	1.01 (2.90)	0.12	0.21	0.43	0.99	2.17
Class 2	1.04 (1.16)	0.38	0.51	0.71	1.03	3.3
Class 3	1.00 (0.75)	0.45	0.62	0.78	1.13	2.24
Class 4	0.97 (0.55)	0.51	0.61	0.78	1.12	2.01
Overall	0.99 (1.06)	0.40	0.58	0.76	1.09	2.17

[a] Class 1: No/least SDoH adversities; Class 2: Discrimination/Stigma; Class 3: Economic adversities; Class 4: Most SDoH adversities

S Table 5.4: Inverse-Probability Weighted Estimates of the Parameters of a Marginal Structural Model for the Association of the Social Determinants of Health (SDoH) Classes on Alcohol Use Measures among Women Living with HIV, CHIWOS, Canada, 2013-2017

	SDoH classes[a]		
Variables	No/least SDoH adversities	Discrimination/ stigma	Most SDoH adversities
Age, yr (mean)	0.97 (0.93, 1.01)[b]	0.99 (0.97, 1.01)	1 (0.99, 1.02)
Ethno-racial groups (Ref: White)			
Indigenous	2.07 (0.45, 9.6)	1.08 (0.58, 2.03)	0.88 (0.56, 1.39)
African/Caribbean/Black	0.94 (0.43, 2.03)	0.86 (0.56, 1.32)	0.95 (0.66, 1.37)
Other	0.63 (0.18, 2.21)	1.04 (0.43, 2.53)	0.96 (0.52, 1.78)
Study province (Ref: Ontario)			
British Columbia	0.35 (0.1, 1.23)	0.62 (0.36, 1.07)	0.99 (0.65, 1.52)
Quebec	0.53 (0.19, 1.47)	0.91 (0.54, 1.52)	0.99 (0.69, 1.42)
Living large size cities	1.79 (0.62, 5.14)	1.18 (0.73, 1.92)	0.97 (0.63, 1.47)
Heterosexual	0.27 (0.05, 1.55)	1.37 (0.62, 3.02)	1.19 (0.74, 1.89)
Relationship status (Ref: Single)			
Married	0.74 (0.23, 2.37)	0.76 (0.48, 1.2)	1.03 (0.71, 1.49)
Others	0.67 (0.17, 2.62)	0.64 (0.39, 1.04)	1.05 (0.71, 1.58)
Years living with HIV (Ref: < 6 yrs)			
6-14 years	2.23 (0.64, 7.72)	0.85 (0.48, 1.51)	0.9 (0.62, 1.32)
> 14 years	1.76 (0.78, 3.97)	0.81 (0.46, 1.44)	1.01 (0.68, 1.52)
Taking treatment (Ref: Yes, optimal)			
Yes, suboptimal	0.45 (0.12, 1.64)	1.28 (0.74, 2.21)	1.05 (0.68, 1.6)

Not in treatment	0.6 (0.2, 1.77)	1 (0.53, 1.89)	0.87 (0.57, 1.31)
Mental health diagnosis	1.62 (0.49, 5.4)	0.82 (0.53, 1.28)	0.96 (0.69, 1.33)
Low resiliency[c] (below median)	0.32 (0.11, 0.91)	1.01 (0.66, 1.55)	0.96 (0.7, 1.32)
Childhood violence	1.15 (0.42, 3.14)	1.08 (0.71, 1.63)	0.97 (0.7, 1.33)
Adulthood violence	0.73 (0.26, 2.06)	0.99 (0.6, 1.62)	0.91 (0.61, 1.36)
Childhood development events	0.42 (0.11, 1.57)	1.22 (0.68, 2.17)	0.96 (0.64, 1.45)
Cigarette smoking (regular/occasional)	1.11 (0.29, 4.22)	1.2 (0.77, 1.84)	0.97 (0.71, 1.34)
Non-prescribed cannabis use (regular/occasional)	0.44 (0.12, 1.63)	1.19 (0.66, 2.14)	0.8 (0.54, 1.18)
Drug use[d]	2.12 (0.32, 13.91)	0.77 (0.34, 1.73)	0.9 (0.57, 1.4)
Received alcohol counseling	2.16 (0.39, 11.9)	1.53 (0.84, 2.78)	0.79 (0.5, 1.25)
Heavy alcohol use (Ref: Abstainers/low)			
Moderate (1-7 drinks/week)	2.39 (0.53, 10.74)	1.23 (0.71, 2.11)	0.84 (0.56, 1.27)
Heavy (> 7 drinks/week)	0.3 (0.09, 0.93)	1.66 (0.76, 3.67)	1.09 (0.63, 1.89)
Binge drinking (Ref: Non-drinkers/no binge drinking)			
Less than once per month	9.36 (1.18, 74.31)	0.46 (0.17, 1.22)	0.54 (0.23, 1.26)
At least once per month	0.59 (0.26, 1.34)	1.41 (0.76, 2.63)	0.93 (0.59, 1.46)

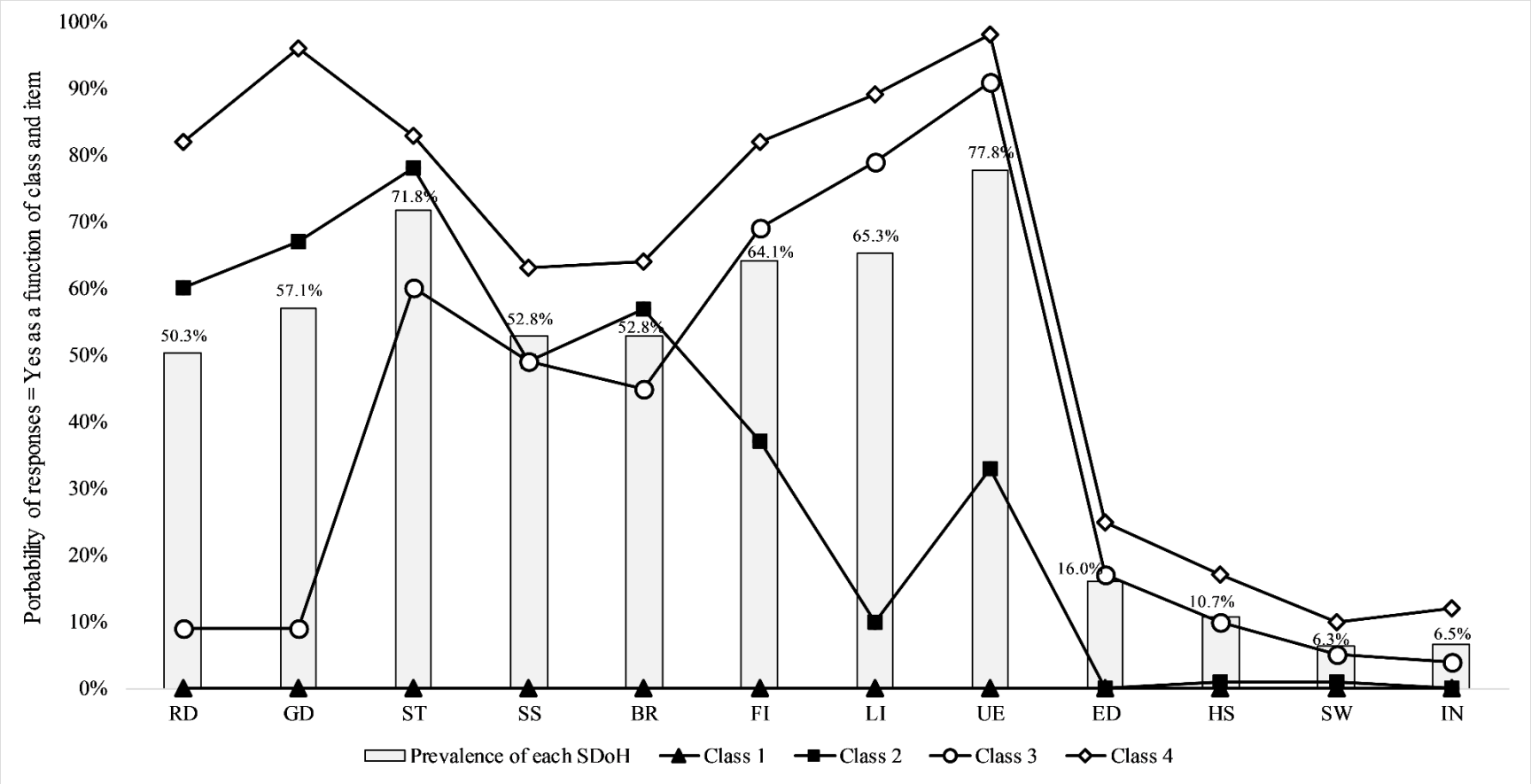
[a] Base group in multinomial logistic regression was "the most SDoH adversities"; [b] Data are presented as relative-risk ratio (RRR) and 95% confidence intervals (CI); [c] Scores ranged 10-70, with higher scores indicating increased resilience (median = 64); [d] Last three months any non-prescribed/illicit opioid and/or stimulant use measured.

S Table 5.5: Sensitivity Analysis of the Magnitude of Potential Unmeasured Confounding that Would Totally Explain Away the Observed [Significant] Association from the Inverse Probability Weighting Analysis between the Classes of the Social Determinants of Health (SDoH) and Alcohol Use Measures

SDoH Clusters	E-value for point estimate	E-value for CI close to the null	E-value for point estimate	E-value for CI close to the null
	Moderate weekly alcohol use[a]		Heavy weekly alcohol use[a]	
No/least adversities vs. most adversities	---[c]	---	17.6	2.6
No/least adversities vs. discrimination/stigma	---	---	19.5	2.3
	Infrequent binging (< 1/month)[b]		Frequent binging (≥ 1/month)[b]	
No/least adversities vs. most adversities	9.5	1.1	99.5	14.9
No/least adversities vs. economic hardship	---	---	66.1	7.8
No/least adversities vs. discrimination/stigma	16.1	2.3	99.5	9.0

[a] Base group: nondrinking or low (< 1 drink per week); [b] Base group: Non-drinkers/no binge drinking; [c] The sensitivity analysis was not done for these estimates as the 95% CIs of their observed point estimate crossed the null RRR = 1.

S Figure 5.1: Prevalence and Item-Response Probabilities (= Yes) for each Social Determinant of Health (SDoH) Obtained from Latent Class Analysis with four Classes among Women Living with HIV– CHIWOS (n=1,422)



RD: Racial Discrimination, GD: Gender Discrimination, ST: HIV-related Stigma, SS: Perceived Social Support, BR: Barriers to Access to Care, FI: Food Insecurity, LI: Low Household Income, UE: Unemployment, ED: Low Education, HS: Unstable Housing; SW: Recent Sex Work Involvement, IN: Recent Incarceration;
Class 1 (6.6%): none/least SDoH adversities (the assigned probability for this class was 0), Class 2 (17.9%): a group who mainly experienced discrimination/stigma, Class 3 (31.6%): a group who mainly experienced economic hardship, Class 4 (43.9%): a group of WLWH who experienced most SDoH adversities.

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6. Chapter 6: Integrated Discussion

This last chapter reviews key findings of this research derived from the four peer-reviewed published papers (Chapters 2-5), the implications of these findings for the HIV care and treatment and health outcomes of women living with HIV, and highlight future research.

6.1. Summary of key findings

Drawing on the cross-sectional data from the largest cohort study of women with HIV in Canada (CHIWOS, time-point 1, 2013-2015), we found that a high proportion of women with HIV reported experiencing social and structural adversities and low quality of life (Chapter 2) as well as substance use (Chapter 3). In comparison with Canadian women of similar ages/ethnoracial backgrounds (CCHS, 2013-14), a higher proportion of women with HIV reported living with poverty (measured by annual personal income) and food insecurity, experienced social exclusion (measured by poor perceived social support, and racial and gender discriminations), recorded lower quality of life (measured using a single-item self-assessment of overall health status) (all in Chapter 2), as well as reported substance use including intensive cigarette smoking, non-prescribed cannabis use, crack-cocaine, speed ,and heroin use (but not alcohol use) (Chapter 3).

Analysis of the longitudinal data of women with HIV (CHIWOS, time-point 1 and 2, 2013-17) also showed that a substantial proportion of women with HIV reported experiencing multiple forms of a set of potentially modifiable social determinants of health (SDoH). Latent class analysis (LCA) identified four distinct SDoH subgroups, consisting of one small cluster of women with HIV who reported no or least SDoH adversities, two unique clusters including discrimination/stigma and economic hardship, and one single cluster containing multiple forms of social adversities (Chapters 4 and 5). Additional analyses also showed that self-reported opioid/stimulant use (Chapter 4) and heavy alcohol drinking (Chapter 5) were significantly less

likely to be reported among women living with HIV who reported none/least SDoH than among women in other three SDoH clusters, regardless of the type of SDoH adversities. These findings suggested the substantial contribution of the clusters of SDoH adversities to illicit drug use and heavy drinking among women with HIV.

6.2. Socio-structural adversities

As described, women with HIV were found to experience a high prevalence of individual SDoH adversities (Chapter 2). They also reported experiencing these adversities in excess of what would be expected from the assumed HIV-negative general population of women. While direct comparison of these determinants between individuals with HIV, including women, and the general population is challenging due to limited comparability of population-based data on the indicators of SDoH owing to differences in equity measurements as well as general data quality and availability,[1] the current research documented that women with HIV inequitably experienced greater barriers or difficulties in their daily life in excess of what would be expected. These findings underscore the importance of the recognition of the social, economic and structural barriers accounting for health inequities among women, which not only exacerbate the vulnerability of them to an elevated risk of HIV infection,[2] but also, in turn, among women who are living with HIV, have the potential to negatively impact their ability to optimally navigate the HIV care and treatment programs.

These findings suggest that to improve the health and well-being of women with HIV, programs should focus on interventions addressing inequalities that women frequently face. To do this, the ongoing collection and quality measurement of SDoH indicators across either surveillance systems or care and treatment programs is necessary.[1] Having more comprehensive data on all aspects of health indicators, with the addition of SDoH measures, would enable health

care providers to identify the burden of SDoH adversities, gain a broader and more complete picture of HIV epidemiology, and then address (i.e., through developing structural interventions) these underlying causes of HIV and health conditions. The CDC emphasizes that without the collection of all relevant SDoH indicators, a large proportion of HIV data is incomplete in the context of broader population health, and adds that the increased understanding of SDoH data "may lend more credibility to the science of SDH, and prevention efforts will be able to use and execute more contextually appropriate initiatives to reduce health disparities and promote health equity."[1] Furthermore, identifying such underlying causes is required to be also considered as one of the main priorities of the extant HIV programs. In this regard, future research should pay additional attention to how such underlying determinants can be better integrated into the current priorities of HIV programs.[3] In addition to the current focus on the provision of better HIV care and treatment services, practitioners and public health experts should also strive to ameliorate the socio-structural adversities that individually (e.g., stigma alone) or in combination (e.g., stigma and discrimination) continue to result in poor health outcomes among affected people. Improved data collection on the SDoH indicators may help healthcare providers recognize the leading role of these barriers and reduce some of these adversities, such as stigma,[1,4-6] that these individuals may frequently encounter in their life.

Addressing SDoH inequalities among women is particularly important as women face greater vulnerability to discriminatory social, economic, and political processes,[7-9] resulting in greater health inequalities.[1] Our findings in support of the current evidence suggest that experiencing a high degree of SDoH adversities may explain the potential pathways by which women with HIV experience inequalities in their health outcomes, and support possible interventions to address the gaps in such health inequalities.[10] In addition to their elevated

vulnerability to HIV infection, women experience socioeconomic inequalities that pose additional challenges to their HIV care and treatment programs.[11] It is believed that a better understanding of these adversities, for example, stigma, is of paramount public health importance and the foundation for the development of programs in addressing these adversities and their resultant health inequalities.[11] Consistent with extant evidence, our findings support structural interventions, referring to public health interventions that improve health through changing the structural factors – which are aspects of the social, economic, and physical environment – within which health or health outcomes are produced and reproduced.[12] Frieden believes that interventions focusing on socio-structural levels (e.g., socioeconomic factors) tend to be more effective as these interventions cover a broader portion of society and require less individual effort, and can help obtain optimal public health benefits.[13]

The SDoH adversities are largely the result of the unjust distribution of power and resources, indicating the important role of policy in addressing these adversities.[5,14,15] Therefore, understanding these leading adversities (i.e., barriers) can help inform healthcare providers where women interrupt their HIV care along the cascade.[16] Our findings also suggest that, in addition to approaches to prevent, control and manage HIV on the individual (e.g., behavioural) level factors, it is important to seek strategies to address the underlying social and structural contributors of health inequalities, such as food insecurity, lack of or low education, HIV stigma, and discrimination, which have negative impacts on HIV outcomes.[4]

A growing body of evidence has shown that the SDoH adversities (e.g., food insecurity,[17] under-housing,[18] gender-related factors,[19] and stigma[20,21]) have been substantially associated with poor HIV outcomes (e.g., low treatment adherence). This may indicate that the SDoH that are sensitive indicators of women's capacity have the potential to impede them prioritizing their

health care needs over such survival needs. Therefore, if the goal in the current era of effective HIV treatment is to help individuals with HIV achieve optimum cART outcomes,[10,22,23] addressing these key social and structural barriers should be considered as one of the main priorities of HIV programs. Evidence has supported that reducing the burden of these daily life challenges or hardships can also help improve HIV outcomes. For example, Martinez et al. in a 12-month prospective clinical trial showed that household food assistance and nutrition education programs positively improved HIV treatment adherence (defined as on-time prescription refills).[24] With regard to HIV stigma and discrimination, additional research is required to better understand other pathways through which these barriers can influence subsequent behaviours, health and well-being. Evidence suggests that interventions such as skill building through peer coaching, education programs to provide a better understanding of the diseases/infection, and connecting them with community resources and peers, may help affected individuals overcome stigma and discrimination and improve their engagement in healthcare process.[25-28] Economic hardship, particularly low annual personal and household income and food insecurity, were significantly higher among women with HIV versus HIV-free women of the general population, indicating the need for economic strengthening for women with HIV to promote utilization of HIV care services.

6.3. Clustered social determinants

A key feature of the social determinants is that they tend to co-occur.[29] Therefore, studying social determinants individually may miss the co-occurring patterns of these determinants. For example, those living with income insecurity are more likely to be exposed to food insecurity, or those experiencing racial discrimination and/or HIV-related stigma might be at a higher likelihood of having lower social support. There has been a growing interest in this phenomenon

to identify opportunities for impactful strategies dealing with health-related behaviours.[ex.30,31] Some studies have analyzed the co-occurrence of these determinants through the count of the total number or types of social determinants.[32] While such additive methods can help provide information on the burden of the social determinants, they strongly rely on the assumption of homogeneity in the co-presence of these determinants in a population.[30] However, the use of model-based complex analytical approaches, such as latent class analysis (LCA), can help provide valuable insights into the complexity of these determinants. In addition, such approaches can help researchers determine individual indicators of these determinants within the identified clusters. Further, instead of analyzing these determinants separately in association with a health outcome, LCA helps explore the impact of clustering of these determinants.

In the current study, our analyses and findings showed that women reported experiencing complex adversities characterized by social, economic, and structural determinants of health. LCA analyses demonstrated that social determinants are clustered together and create unique classes/groups of adversities. Of the four identified SDoH classes, three classes exhibited a *combination* of two or more SDoH adversities. While the majority of the study sample reported experiencing multiple forms of adversities (i.e., class 4), we were able to identify two more clear/distinct classes of SDoH adversities including stigma/discrimination and economic hardship that have been the key barriers to prevention as well as care and treatment of HIV infection from the beginning of its epidemic. In particular, our findings indicated that multiple forms of discriminatory behaviours had the potential to cluster together (i.e., racial discrimination, gender discrimination, and HIV-related stigma). Findings also showed that multiple indicators of economic difficulties were clustered in one unique group. Further, these two unique classes together tended to cluster and created a more complex class of SDoH (i.e.,

class 4), which might indicate that the unique clusters of stigma/discrimination and economic hardship can both independently in their unique clusters and jointly together account for the majority of health inequalities. These findings also suggest the need to consider multiple social, economic and structural adversities when analyzing and reporting the severity (e.g., prevalence) of these determinants and recognizing their detrimental impacts on health outcomes. Examining one single indicator may not properly characterize the daily living experiences of underserved individuals such as women with HIV, who typically report experiencing multiple adversities. [ex.33]

Identifying the patterns of these determinants and examining their grouped/clustered impact not in separation but in combination has implications for health inequalities reduction and health promotion programs. The use of such analytic approaches aiming at the identification of the latent patterns of social determinants can help in the contextualization of the clustered determinants, as their co-occurrence as well as synergistic impacts may contribute to more intense adverse health outcomes than if they were experienced (or treated in the analysis) alone. Moreover, programs targeting multiple determinants (i.e., addressing multiple social, economic, and structural adversities) would have the potential for a greater impact on public health relative to the strategies that only address one single adversity. For example, in addressing housing instability among vulnerable populations, considering other vulnerabilities such as food insecurity and/or economic pressure is critical. Assessing the pattern of these determinants can also help prioritize most vulnerable individuals for better support.

6.4. Substance use among women with HIV

Significant efforts have been made over time to reduce adverse clinical and health outcomes among individuals with HIV in Canada.[34] Evidence has suggested that people with HIV, particularly those in resource-rich nations such as Canada,[35-37] have or are approaching a normal

life expectancy (i.e., that is almost equivalent to that of HIV-uninfected individuals) if they receive appropriate cART treatment.[34,37-41] Such considerable change in the profile of HIV may give rise to the greater experience of chronic health conditions among these individuals.[42] Evidence has also supported such elevated burden of chronic conditions among people receiving HIV treatment versus their HIV-free counterparts.[35,43,44] Aside from the intersection of aging and HIV infection itself that negatively impact the overall health of these individuals, identifying and addressing other potential challenges that these individuals continue to experience in gaining a healthy state remains essential.[35] Substance use is one such potential barrier contributing to a lower survival or quality of life of individuals with HIV compared with individuals without HIV and it needs to be carefully studied and addressed among these individuals,[37,45] particularly among women, a population with limited resources available on their social and behavioural factors.[46]

As described in the Introduction Chapter, the detrimental contribution of substance use to the elevated poor HIV treatment outcomes and mortality among individuals with HIV has been well documented.[34,42,46-64] Prior research documented that individuals who were involved in substance use were at elevated risk for suboptimal linkage to and retention in HIV care, HIV treatment adherence, AIDS-related illness and mortality.[42,46,63-66] Substance use is of paramount importance in ongoing concentration for the management of HIV infection. Literature suggests that a considerable proportion of non-AIDS-related causes are now the prevailing cause of mortality among these individuals, yet many of these causes have a strong link with substance use.[42]

Our findings suggesting a high prevalence of substance use in the study population have implications for HIV care and treatment programs in the current era of Treatment as Prevention

(TasP). These findings may indicate that behavioural barriers yet remain as one of the main challenges in the management of HIV among women with HIV. These risk-taking practices may also explain the variations/gaps in the elevated non-AIDS comorbidities and mortality of individuals with HIV, women in particular, over their counterparts in the general population. As substance use has the potential to interrupt every step along the cascade, our findings emphasize that the effectiveness of HIV care and treatment services may rely on how these risk-taking barriers are effectively addressed.

Evidence has extensively highlighted the need for developing care models where, in addition to addressing HIV-related care and treatment, substance use is routinely assessed. Raposeiras-Roubín et al. (2017) believe that the awareness within the health system with respect to the elevated risks posed by substance use on causes of mortality among individuals with HIV is suboptimal.[67] Dawson-Rose et al. (2017) noted that while primary care clinics are the best setting to offer screening and interventions for substance use, few HIV clinics routinely assess substance use. These authors added that implementation of standard practice for screening substance use in HIV primary care clinics is necessary.[68] Nijhawan et al. (2008) believe that substance use should be discussed without alienating substance users in the context of a trusting provider-patient relationship.[69] It has been emphasized that healthcare providers should ensure that the overarching goal of substance use interventions is to maintain individuals in HIV care,[69,70] and better manage the HIV/AIDS complications.[42] Interventions, either behavioural (e.g., counselling for tobacco use cessation,[71] or a case management intervention model for alcohol and illicit drug use[72]), pharmacological (e.g., nicotine patches[71] and Vaporised nicotine products[73] for cigarette smoking cessation, lamotrigine for crack cocaine users,[74] buprenorphine and methadone maintenance therapy for illicit drug users[75-77]), or psychosocial (e.g., contingency

management treatment for opioids and cocaine[78]) interventions/supports for individuals with HIV involving in substance use should become a priority in routine HIV care services. The integration of these interventions warrants further investigation for the management of the use of various substances.

Existing research proposed multiple models for integration of HIV care and substance use interventions, such as[69,77] i) *a primary care model*, through which the HIV treatment provider prescribes the substitution therapy; ii) *an on-site specialist model*, through which a substance use specialist prescribes the substance use interventions; iii) *a hybrid model*, through which an on-site specialist prescribes the initial induction therapy of the substance use intervention and the HIV care provider prescribes its maintenance phase; iv) *a drug treatment model*, through which both HIV care and substance use services are provided in a substance use clinic setting, v) *directly administered antiretroviral therapy (DAART)*, is another integrated care that through which substance using individuals with HIV receive supervised doses of HIV treatment in a substance use clinic setting,[69,79-81] and vi) *patient-centered model of care*, in which individuals with HIV receive diverse health-related services, including harm reduction programs, in a friendly environment setting[28,42,67] are offered for maintaining individuals with HIV optimally engaged in care, and for meeting national and global goals of HIV treatment.[82] Similar to the latter form of model of HIV care, gender-matched-centered model of care has also been proposed. For example, a women-centered model of HIV care[83,84] and a women-centered harm reduction approach[85,86] have been identified as promising models for addressing women's comprehensive care needs.[84,87-90] Consistent with extant research,[28,42,67,84] our findings advocate for developing women-centered models of care where, in addition to providing multiple healthcare services, women with HIV can also have access to harm reduction and substance use

intervention programs. In the Canadian context, O'Brien et al. (2017) underlined that a women-centered approach to HIV care is essential for guiding policy and practice to promote the health and clinical outcomes for women with HIV.[84] These researchers additionally pointed out that given gaps in care and inequalities in health, models/approaches that address the care priorities of women living with HIV "must be incorporated into care delivery to ensure that women's comprehensive care needs are met and to enable diverse populations to benefit equally from health care advances."

6.5. Social determinates give rise to elevated risk of substance use

Our research added to the literature demonstrating high prevalences of substance use among women with HIV. While the prevalences of all studied substances were high, the prevalence of illicit drug use and cigarette smoking, in particular, were in excess of what would be expected from the background HIV-negative women (Chapter 2). Our additional analyses using latent class analysis (LCA) identified distinct subgroups (clusters) of women with HIV characterized by a set of potentially modifiable social and structural determinants. These analyses showed that a substantial proportion (93.4%) of study participants reported experiencing two or more types of SDoH adversities (classes 2-4). Furthermore, our findings demonstrated that illicit drug use and drinking patterns among women with HIV were socio-structurally distributed, such that women who experienced less social adversities were less likely to report using these substances than those in other three classes who experienced distinct levels of SDoH adversities. Future research should identify and explore interventions addressing social determinants among women with HIV.

Several theoretical frameworks can help guide our understanding of potential pathways through which the SDoH clusters increase the risk of substance use. Our research is also

centrally informed by a *social determinants of health (SDoH) framework*, highlighting that political, economic and cultural drivers impact socioeconomic status/position, which in turn shapes SDoH impacting health and well-being,[4,5,91] and influencing health inequities. This framework mostly focuses on the upstream determinants of health such as education, occupation, income, housing status, social support, stigma and discrimination. In the context of HIV and substance use, this framework has been used to emphasize that socio-structural determinants play a pivotal role in risk-taking behaviours[2,92,93] and poor HIV outcomes,[94-96] resulting in health inequalities. Informed by these theoretical frameworks, our findings imply that the overlapping/clustering social determinants have the potential to severely constrain the ability of women with HIV to effectively respond to behaviour change strategies. A *syndemics theory* can also support these findings. This model links multiple social and structural adversities to co-occurring and synergistic health epidemics that disproportionately affect vulnerable populations, and magnify the negative impact of disease interaction.[97-99] This model highlights the contribution of the excess burden of "entwined and mutually enhancing health problems" to the health inequalities,[97] fueled by social, economic and structural inequities.[98,99] Applications of this theory to HIV studies have mostly concentrated on factors that synergistically contribute to HIV risk among vulnerable populations.[100,101] A special form of this theory is known as the *SAVA syndemic*, referring to the clustering of substance use, violence and HIV/AIDS among marginalized populations such as women of color living with HIV.[102] This model explicitly advocates for socio-structural interventions that more effectively address the intersecting issues of substance use, structural adversities such as violence, and poor outcomes which necessitate systemic work to target the underlying conditions perpetuating health inequities among marginalized populations.[101,102] In accordance with a *self-medication model*,[103] our findings may

also indicate that women with HIV initiate or continue substance use (e.g., alcohol use) as a coping strategy to alleviate their daily stressors. This model underscores behavioural coping as a potentially relevant mediator for the association between multiple social adversities and substance use.[63,104] Consistent with this model, Wardell et al. (2018) in a longitudinal analysis in Canada showed that greater HIV-related stigma, as a key and relevant SDoH in the context of HIV, predicted increased maladaptive strategies for coping (e.g., self-blame, denial), and that maladaptive coping mediated the prospective associations between HIV-related stigma and alcohol use severity.[92]

HIV research has extensively accentuated the contribution of social determinants to both the distribution of HIV infection (i.e., as the drivers of HIV infection) and poor HIV outcomes (i.e., among those who are living with HIV). Research has also highlighted interventions addressing social determinants of HIV infection and substance use among affected individuals as the most effective interventions in addressing poor outcomes and then reducing health inequalities.[69,105-107] For example, Wolitski et al. (2010) in a randomized controlled trial assessed the longitudinal effects of a structural intervention (i.e., rental assistance on the housing status) on the health and risk behaviours of homeless and unstably housed people with HIV, and showed that the receipt of stable housing significantly reduced risk-taking behaviours, improved access to care, increased adherence to treatment, and improved self-reported physical and mental health (e.g., depression and perceived stress).[108] These studies indicate that if HIV care programs viewed the patients as a whole, including their social determinants,[109] improved outcomes would be achieved.[84] This is particularly of the essence among women with HIV who are unjustly occupied in the socioeconomically disadvantaged position.[84,110-112] Research in Canada, in line with international research, has noted that these leading determinants, even though essential to

addressing barriers of HIV care, are challenging to properly address in health care settings since many of these determinants (e.g., housing, poverty) lie beyond the purview of the health care system.[84,113,114] O'Brien et al. (2017), however, believe that strategies such as interdisciplinary teams and revised prescription financing policies that address socioeconomic hardship may help bring greater attention to socio-structural barriers that have negative impacts on women's care-seeking behaviours, HIV outcomes, and overall health.[84] In this regard, it is imperative to continue to educate and advocate for all healthcare professionals to acknowledge socio-structural factors giving rise to poor health.[84,113,115]

Our findings indicate that, in addition to the efforts in increasing the number of individuals receiving cART treatment, the successful management of HIV requires making greater efforts in addressing the social barriers as well as substance use through the integration of health care services. Undoubtedly, substantial advances have been achieved in HIV care and treatment programs, and subsequently substantial reductions have been made in HIV morbidity and mortality; however, treatment alone does not appear to help end the HIV epidemic. Such prevalent clustering co-occurring conditions and/or adversities pose a "*complex problem*" for patients as well as healthcare providers and health systems that seek to provide coordinated care to them.[116,117] The complexity in care has been referred to individuals with multiple co-morbid medical *and* behavioural health conditions whose care is complicated by social factors (e.g., poverty) and health system factors (e.g., segregated medical and behavioural healthcare programs).[116] Grembowski et al. (2014) developed a conceptual model and defined *complexity in care* as the misalignment between patient needs and the services available for them (i.e., need-service gap), highlighting the need for care systems to address *dynamic* or *complex* conditions and incorporating social, economic, and physical conditions as *contextual factors* that influence

patient needs and services delivery.[117] In the face of such multiple co-occurring health, behavioural, and socio-structural adversities that have also been identified in the present study among women with HIV, research supports that the integration of services that address multiple services such as substance use treatment, psychosocial support, counselling, and HIV care might bring about improved health outcomes.[69,118] While addressing each service can help improve care when applied individually, a multidisciplinary strategy such as a gender-focused HIV care strategy, where various health care needs are considered may better address the comprehensive needs of women with HIV.[69,84,119,120] *Women-centred interventions* have become an emerging model for the provision of the comprehensive health care needs of women.[83-85,88,118] For example, Carter et al. (2013) in a comprehensive review explored the concept of women-specific HIV/AIDS services, as a complex and multidimensional model, and identified the key dimensions of such model. According to this review, this approach to care is conceptualized to, for example, create an atmosphere of safety, respect and acceptance; facilitate interaction among peers; facilitate meaningful access to care through the provision of social and supportive services; provide gender-, culture- and HIV-sensitive training to health and social care providers; provide women's social economic needs/supports such as transportation assistance, and food; conduct gendered HIV/AIDS research.[83] Ellsberg et al. (2015) in a review study recommended women-centered programs as one key intervention to reduce women's risk of further victimization and promote their health and wellbeing through providing a combination of strategies such as psychosocial support, advocacy and counselling, and home visitation.[118] These interventions are closely consistent with the principle of the Greater Involvement of People Living with HIV/AIDS (GIPA), a critical principle to halting and reversing the HIV epidemic, which has been formalized to support a greater involvement of individuals with HIV at all levels

(e.g., policy, programming, care, research) and advocate for their rights.[121] Due to the particular social environment where women with HIV face these adversities (i.e., gendered nature of these adversities), our findings advocate for further research to identify more culturally tolerated, women-focused interventions and assess their effectiveness if the care programs are to better address health inequalities among women, particularly women in greater needs such as substance users.[83,119,120,122]

This part of our analysis and findings also adds to the body of evidence supporting that social determinants are highly inter-correlated,[29] a key feature of these determinants that has not been well taken into account in the analyses of the social determinants with health outcomes. Extant research has commonly treated these determinants as independent factors in the assessment of their impacts on the subsequent health outcomes. While this approach has implications for HIV care and treatment strategies on how to overcome the adversities with each determinant, future research should take the co-occurrence nature of these determinants into account. Such analysis has implications for HIV care in a way that any care models should address multiple adversities of women with HIV.

6.6. Future research and directions

Further research should 1) focus on the reproducibility of the identified latent classes in populations with different sociodemographic backgrounds and HIV-related clinical characteristics to see whether similar classes are found and how they contribute to substance use as well as other health outcomes, 2) identify the predictors of the SDoH latent classes, 3) explore the SDoH latent classes over time using other mixture models such as latent transition analysis (LTA),[123] 4) longitudinally investigate the association of the SDoH latent classes with health outcomes (e.g., substance use, HIV outcomes) among women with HIV, and 5) develop

conceptual and analytic strategies to explore how modifiable and non-modifiable SDoH can be modelled together to capture a detailed picture of the indicators of SDoH among individuals with HIV. In such models, it is important to assess how non-modifiable SDoH (such as gender, ethnoracial status) can modify the impact of modifiable SDoH on health outcomes, or how these modifiable factors may explain (i.e., transmit the impact) the relationship between non-modifiable SDoH and health outcomes; 6) seek and identify culturally tailored, women-specific interventions in addressing multiple forms of women's needs, particularly social adversities and substance use; and 7) promote linkages between substance use treatment programs and HIV care, that can be evaluated in the women-centered model of care.

6.7. References

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7. Appendices

Appendix A: A brief description of latent class analysis and procedures

We used latent class analysis (LCA) to determine latent classes/subgroups of women with HIV with distinct profiles with regard to the social determinants of health (SDoH) based on 12 observed categorical indicators including racial discrimination, gender discrimination, enacted HIV stigma, perceived social support, barriers to access to care, food security, housing status, income level, employment status, education, recent sex work involvement, and recent incarceration. LCA is a data-driven probabilistic model commonly used to identify the levels of the categorical latent variables representing classes (groups) with similar profiles based upon conditional probabilities. LCA uses the expectation-maximization (EM) algorithm[1] – an iterative, maximum-likelihood estimation approach, to estimate the unknown parameters.[2] The maximum number of iterations was set to 5000 (the default number in SAS LCA procedure) in the EM estimation procedure for the replication of the log-likelihood value to ensure that a best-fit solution is obtained. As an iterative approach, EM algorithm begins with a set of starting values and proceeds with a series of steps of parameter estimation and re-estimation iterations until [some] designated criterion is reached. As an attempt to avoid suboptimal estimates produced by local maxima of the likelihood function, multiple random sets of starting values (i.e., in the present study, 1000 random starting values) was used.

We started LCA with a 2-class model and systematically increased to an 8-LCA model to examine the LCA solutions. Model interpretability along with the following goodness-of-fit indices or/and information criteria were considered to choose the best number of latent classes: Log-Likelihood, Akaike information criterion (AIC), Schwarz Bayesian information criterion (BIC), Consistent AIC (CAIC), and [relative] Entropy. Lower values for the AIC, BIC and CAIC

imply better model fit, while higher entropy reflects better classification or class distinction, with approaching 100% indicating clear delineation or better separation of latent classes (varied between 0 to 1).[3,4] In addition, we reported the *percentage of seeds associated with best fitting model* as a diagnostic information on the random starting value process; higher percentages indicate that the model appears to be well-identified (i.e., highly unlikely to have hit local maxima).

Missing data

In LCA, where the latent class membership is always missing, manifest indicators used to estimate the latent classes may also come with missing values. Under the assumption of missing at random (MAR) – even though this assumption is sometimes ignored,[5] LCA computes LCA parameters accounting for missing values of observed indicators (here, SDoH indicators) typically by maximum-likelihood estimation using the EM algorithm so that all available information are used to estimate the best model,[2] except for those participants with full missing data for all observed indicators (Note: participants with missing values for the study outcomes in Chapter 4 and 5 were excluded from the associational analyses between clustering SDoH and substance use.

EM algorithm

As explained above, LCA estimates unknown parameters using the expectation-maximization (EM) algorithm[1] which is maximum-likelihood estimation approach with iteration when some parts of the data is missing; e.g., the hidden classes,[2] in each iteration two steps of the E-step and M-step is followed. The iterative process between the E-step and M-step aims to generate a sequence of parameter estimates that converges reliably to a local or global maximum of the

likelihood function.[5] The first step is computed using the expected value of the log of the likelihood function, given the observed data and the initial parameter estimates (i.e., sometimes called starting values)[6] which can be specified either by the researchers (if there is enough evidence knowing the distribution of these parameters – called user-specified starting values)[7] or randomly. In the current research, random starting values (referring to any positive integer value) were specified. SAS program starts with the default starting value of 1/NCLASS for Gamma [γ] parameters, where NCLASS refers to the number of classes specified to estimate the class membership probabilities – unknown or hidden classes. One issue with the specification of the random starting values is that some starting values may bring about local solutions that are not reflecting the global maximum of the likelihood. In such case and to avoid this happen, multiple sets of starting values were specified and the solution with the best likelihood was chosen.[7] The second step, the M-step, the algorithm maximizes the function to give new values of the parameter estimates, replaces the initial estimates of the starting values by the updated/new estimates of the parameters, and then returns to the first step (E step). This process (algorithm) iteratively continues until changes in either the parameter estimates or log-likelihood function reach some predefined level of precision (convergence criterion default set to 0.000001) in which the iteration halts.

Parameters

LCA estimates two sets of parameters:[7] 1) *class membership probabilities* (i.e., called as Gamma [γ] parameters), representing the probabilities that each participant falls into each class. For each participant, the sum of these probabilities across estimated classes equals one (i.e., 100%); and 2) *class-specific item-response probabilities* (i.e., called as Rho [ρ]), representing the probabilities of each indicator predicting the class memberships. The Rho (ρ) parameters express the

correspondence between the observed items and the latent classes. We did not include covariates predicting class membership probabilities into the model. Instead, we adjusted for covariates in a separate regression model after identifying the best fitting model in this step. This is called a three-step approach through which investigators examine the association between the best-fitted latent categorical variable and a distal outcome variable after class membership has already been determined.[8,9] In comparison with the approach in which LCA process and regression models are combined in a joint model, the multi-step approach (i.e., conducing LCA and regression analyses separately) may attenuate associations; however, the multi-step approach allows the researchers to run multivariable regression analysis adjusted for a large set of covariates. In the presence of having numerous covariates required to be adjusted for the association of the latent classes and the distal outcomes, adjustment process may affect the CLA structure in the one-step approach, while it is unlikely to occur in the multi-step approach.[9,10]

LCA models use *distributional assumptions* to estimate classes, by which the measure of *distance* in LCA is provided. For example, with binary items – which will be treated as outcomes in the process of LCA, such distributional assumptions must follow a binary-outcome distribution: a) items are assumed to be independent within each class, b) items are assumed to be distributed marginally as Bernoulli. This distribution has two possible outcomes: a) Y=1 ("success") occurs with probability ρ and Y=0 ("failure") occurs with probability *1 minus* ρ, where $0 < \rho < 1$. In the present study, success meant experiencing an SDoH adversity and failure meant not experiencing that SDoH adversity. We also added another category to the SDoH indicators indicting that individuals either experienced none of the 12 SDoH indicators or only one of these indicators. This additional step helped create a better reference group representing

those who wither experienced none of the 12 SDoH adversities or only one of them, labeled as those who none/least SDoH adversity. Each indicator has a probability function as follows:

$$f(y) = \begin{cases} 1-\rho & for\ y = 0 \\ \rho & for\ y = 1, \end{cases}$$

alternatively as,

$$f(y) = (\rho_i)^y (1-\rho_i)^{(1-y_i)}$$

For example, if we assume that Y = 1 representing that a women experienced food insecurity, and Y = 0 indicating no experience of food insecurity. Our sample tells us that the probability of women with HIV with food insecurity is approximately 64%. So, ρ is 64%; therefore, P (Y=1) = 0.64 and P(Y=0) = 0.36. The same likelihood function will be obtained as follow:

If Y=1, the likelihood is: $p(y_i = 1) = (0.64)^1(1-0.64)^{(1-1)} = 0.64, or\ 64\%$

and, if Y=0, the likelihood is: $p(y_i = 0) = (0.64)^0(1-0.64)^{(1-0)} = 0.36, or\ 36\%$

These illustrations show that the likelihood function of the statistical distribution provided the likelihood of an event occurring (i.e., SDoH indicator as an outcome variable). Put differently, in the case of discrete-outcome variables, the likelihood of an event is the same as the probability of the event occurring.

As mentioned above, one of the assumptions is independence between items/outcomes within each class. To make this simple, let's think about another item, experiencing enacted HIV-related stigma. If we take a sample, the probability of having experienced stigma is approximately 72% (ρ_2=72%). Under assumption of independence of these two items (outcomes), the probability of occurring both food insecurity and experiencing HIV stigma is the product of the probability of the occurrence of each adversity separately:

$$P(Y_1 = 1, Y_2 = 1) = (\rho_1 \times \rho_2) = 0.64 \times 0.72 = 0.46$$

Generally, the likelihood of any set of outcomes when no predictors included can be expressed as:

$$P(Y_J = y_J) = \prod_{j=1}^{J} \rho_j^{y_j}(1-\rho_j)^{(1-y_j)}$$

LCA models are special cases of more general models called *Finite Mixture Models*.[11,12] A finite mixture model expresses the distribution of a set of outcome variables, Y, as a function of the sum of weighted distribution likelihoods. More generally, a finite mixture model can be expressed as:

$$f(Y) = \sum_{c=1}^{C} \gamma_c f(Y|c)$$

This is the conditional distribution of Y given c which is a sequence of independent Bernoulli variables. For example, for two observed indicators (Y_1 and Y_2), we can express the LCA model as:

$$f(Y) = \sum_{c=1}^{C} \gamma_c f(Y_1|c) f(Y_2|c)$$

where, γ_c is the probability of class c, $(Y_1|c)$is the probability of occurring Y_1 in class c (which is a conditional probability), and $(Y_2|c)$ is the probability of occurring Y_2 in class c (a conditional probability). More generally, an LCA for the response vector of J variables (j = 1, . . . , J) with C classes (c = 1, . . . ,C) when no predictors of class membership included can be expressed as:

$$f(y_i) = \sum_{c=1}^{C} \gamma_c \prod_{j=1}^{J} \rho_{jc}^{yij}(1-\rho_{jc})^{1-y_{ij}}$$

where, i refers to observations, γ_c (Gamma) is the probability that an individual is a member of SDoH class/group c, y_{ij} is the observed response of individual i to the item j, ρ_{jc} is the

probability of a positive response to item j (i.e., experiencing an SDoH indicator) from an individual from class c.

LCA assumes that all observed indicators are independent given a class, called as *local independence*. By this, any association between observed variables/items is accounted for only by the presence of the latent class. Put differently, the latent class is the reason that variables are correlated; this is why indicators within classes are assumed to be independent (*local independence*). SAS tests this assumption using a chi-square test when the indicators as included in the models as binary; however, in the present study, we used three-category SDoH measures and then skipped this test and assumed that the estimated latent classes were locally independent.

Software

We used PROC LCA (https://methodology.psu.edu),[13] a SAS procedure for latent class analysis, using using *% macro alc*. We also used a user-defined macro code named *%macro it* to produce the summary statistics of all requested models. In addition, *%itemresponseplot* and *%identificationplot* macros were used to produce plots assisting in the evaluation of models. Details of these macros are described by Berglund.[14] Parameters were estimated by maximum likelihood using the expectation maximization (EM) algorithm. LCA used a baseline-category multinomial logistic regression (as we included three-category SDoH indicators) to predict latent class membership.

Model evaluation

To select the best fitting model, in addition to the interpretability of the classes, we relied on information criteria obtained from parsimony indices: 1) log-likelihood = -2ln(L), where ln(L) is the log-likelihood of the model; 2) Akaike information criterion (AIC) = -2ln(L) + 2p, where p is

the number of estimated model parameters; 3) Schwarz Bayesian information criterion (BIC) = -2ln(L) + p*ln(N), where N is the total number of observations; 4) consistent AIC (CAIC) with CAIC = -2ln(L) + p * (1 + ln(N)). The convergence method was set to the maximum absolute deviation (convergence criterion default set to 0.000001).

SAS procedure for LCA analysis

```
/* Import csv into SAS */
libname sdh "F:\Statistical analysis - Objective 2\Wave 2 and 1 - Merged -
      SDH analysis\SAS\LCA 12";
proc import out=sdh.SdhfromCSV12
      datafile = "F:\Statistical analysis - Objective 2\Wave 2 and 1 - Merged
      - SDH analysis\SDH variables12.csv" dbms=csv replace; getnames=yes;
      dataraw=2;
run;

/* Creating three-category indicators from the binary SDoH indicators */
data Sdh.LCAanalysis12;
      set Sdh.SdhfromCSV12;
      array zzz stigma bacs edu food house income racism sexism socsup
            unemploy sexwork prison;
            do over zzz;
            zzz = zzz +1;
      end;
run;


/* Contents and frequencies */
proc contents;
run;
proc freq data = Sdh.LCAanalysis12;
      tables stigma bacs edu food house income racism sexism socsup unemploy
      sexwork prison;
run;


/* LCA analysis from starting with one LCA-model, increased to eight */
/*Step A: Use %macro alc to run several LCA models (i.e., 1 to 8)*/
%macro alc (nc);
proc lca data=Sdh.LCAanalysis12 outest=Sdh.outests1&nc
outpost=Sdh.outposts1&nc;
      id part_id;
      title2 "LCA analysis with 12 SDH indicators";
```

```
      nstarts 1000;
      nclass &nc;
      items stigma bacs edu food house income racism sexism socsup unemploy
            sexwork prison;
      categories 3 3 3 3 3 3 3 3 3 3 3;
      seed 100000000;
      rho prior=1;
      cores 1;
run;
%mend alc;
%alc(1); %alc(2); %alc(3); %alc(4); %alc(5); %alc(6); %alc(7); %alc(8);


/* Step 2: Use %macro it to summarize Model Fit Comparisons of 8 models */
%macro it (nc);
      data Sdh.outests1&nc;
      set Sdh.outests1&nc;
      nclass=&nc;
run;
%mend;
%it(1); %it(2); %it(3); %it(4); %it(5); %it(6); %it(7); %it(8);
/*Then concatenating the output datasets of 8 models to produce a summary
data set called allfit_alc using PROC PRINT */
data Sdh.allfit_alc;
      set Sdh.outests11 - Sdh.outests18;
run;
proc print;
run;
proc print data=Sdh.allfit_alc noobs label;
      title "Model fits for variables";
      label nclass="# classes" log_likelihood="LL" degrees_of_freedom="DF";
      var nclass LOG_LIKELIHOOD DEGREES_OF_FREEDOM G_SQUARED AIC BIC CAIC
            ABIC ENTROPY;
run;
/* The above code creates a table with all model fit statistics of the 8 LCA
models.*/
/* The best (optimal) LCA fitted model was obtained in this step. */


/* Model with 4 classes was chosen as the best LCA model */
/* Two evaluation tools are used to assist in model selection*/
/* The "item response" and "model identification" plots are produced using
the %itemresponseplot and %identificationplot macros */
%INCLUDE "C:\Users\Mostafa\Desktop\Proc LCA\SAS Graphics
Macros\LcaGraphicsV2\LcaGraphicsV2 (1).sas";
proc lca data=Sdh.LCAanalysis12
            outpost=Sdh.posts1_4c_alc
            outseeds=Sdh.outseeds_4c_alc
            outparam=Sdh.outparm_4c_alc
```

```
            outstderr=Sdh.outstderr_4c_alc;
            id part_id;
            title2 "LCA analysis test data with 4 classes";
            nclass 4;
            nstarts 1000;
            items stigma bacs edu food house income racism sexism socsup
unemploy sexwork prison;
            categories 3 3 3 3 3 3 3 3 3 3 3;
            seed 262169154;
            rho prior=1;
            cores 1;
run;
%itemresponsePlot(ParamDataset=Sdh.outparm_4c_alc);
%IdentificationPlot(SeedsDataset=Sdh.outseeds_4c_alc);

proc freq data=Sdh.outposts14;
tables best / plots=freqplot(type=barchart scale=percent);
run;

proc format;
value bestf 1='Most SDH adversities' 2='none/least SDH' 3='Economic hardship'
4='Stigma/discrimination' ;
run;
/* This order was changed in the process of analysis with */
proc freq data=Sdh.outposts14;
tables best / plots=freqplot(type=barchart scale=percent);
format best bestf.;
run;
* Export into Stata;
proc export data=Sdh.outposts14 outfile= "F:\Statistical analysis - Objective
2\Wave 2 and 1 - Merged - SDH analysis\SAS\LCA 12\SAStoSTATA12.dta";
run;
```

SAS Output for a 4-LCA model

```
                    The SAS System        12:53 Tuesday, August 7, 2018  10
                                  LCA analysis SDH data

                Data Summary, Model Information, and Fit Statistics (EM Algorithm)


Number of subjects in dataset:        1422
Number of subjects in analysis:       1422
Number of measurement items:            12
Response categories per item:            3 3 3 3 3 3 3 3 3 3 3 3
Number of groups in the data:            1
Number of latent classes:                4

NOTE: A data-derived prior was applied to the rho parameters to help
      avoid parameter estimates on boundary values of zero and one.

Rho starting values were randomly generated (seed = 100000000).
```

No parameter restrictions were specified (freely estimated).

Seed selected for best fitted model: 1165345913
Percentage of seeds associated with best fitted model: 93.70%

The model converged in 78 iterations.

Maximum number of iterations: 5000
Convergence method: maximum absolute deviation (MAD)
Convergence criterion: 0.000001000

==========
Fit statistics:
==========

Log-likelihood:	-8030.01
G-squared:	1366.87
AIC:	1564.87
BIC:	2085.59
CAIC:	2184.59
Adjusted BIC:	1771.10
Entropy:	0.83
Degrees of freedom:	531341

Test for MCAR

Log-likelihood:	-7346.58
G-squared:	1283.90
Degrees of freedom:	2921792

Class membership probabilities: Gamma estimates (standard errors)

Class:	1	2	3	4
	0.4345	0.0661	0.3083	0.1911
	(0.0214)	(0.0066)	(0.0225)	(0.0170)

Item response probabilities: Rho estimates (standard errors)

Response category 1: (this section was omitted by the authors)

.
.

Response category 2

Class:	1	2	3	4
stigma :	**0.8317**	0.0018	**0.6048**	**0.7800**
	(0.0170)	(0.0044)	(0.0263)	(0.0293)
bacs :	**0.6384**	0.0014	0.4509	**0.5696**
	(0.0219)	(0.0038)	(0.0268)	(0.0346)
edu :	0.2477	0.0004	0.1683	0.0059
	(0.0187)	(0.0021)	(0.0199)	(0.0099)
food :	**0.8185**	0.0017	**0.6880**	0.3707
	(0.0184)	(0.0042)	(0.0259)	(0.0365)
house :	0.1701	0.0003	0.0980	0.0146
	(0.0160)	(0.0017)	(0.0154)	(0.0085)
income :	**0.8893**	0.0017	**0.7943**	0.1004
	(0.0178)	(0.0043)	(0.0254)	(0.0370)
racism :	**0.8234**	0.0013	0.0948	**0.5967**
	(0.0248)	(0.0038)	(0.0278)	(0.0375)
sexism :	**0.9604**	0.0015	0.0864	**0.6734**
	(0.0198)	(0.0040)	(0.0393)	(0.0366)
socsup :	**0.6265**	0.0014	0.4909	0.4996
	(0.0217)	(0.0038)	(0.0268)	(0.0354)
unemploy :	**0.9814**	0.0020	**0.9132**	0.3264
	(0.0101)	(0.0047)	(0.0170)	(0.0441)
sexwork :	0.1068	0.0002	0.0464	0.0091
	(0.0137)	(0.0013)	(0.0119)	(0.0078)
prison :	0.1204	0.0002	0.0398	0.0013
	(0.0138)	(0.0014)	(0.0106)	(0.0070)

Response category 3 (this section was omitted by the authors)

.
.

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Appendix B: CHIWOS's Data Sharing Agreement

MShokoohi copy

WCHRI
WOMEN'S COLLEGE HOSPITAL
Health care for women REVOLUTIONIZED

women's college research institute

Principles of Collaboration and Data Sharing Agreement
For the Canadian HIV Women's Sexual and Reproductive Health Cohort Study

CHIWOS

Created December 22nd 2015 -
By the Women and HIV Research Program

Background & Mandate:

- The Canadian HIV Women's Reproductive Health Cohort Study (CHIWOS) is a nation-wide community-based research longitudinal cohort study that enrolled over 1,400 women living with HIV from British Columbia, Ontario and Quebec to answer questions on their health delivery and outcomes; there is a plan to enroll an additional 400 women living with HIV from Saskatchewan and Manitoba into the cohort.
- The CHIWOS data is houses at Women's College Hospital (WCH) by the Women and HIV Research Program (WHRP).

Purpose of the Principles of Collaboration and Data Sharing Agreement:

- This document summarizes the principles that will guide the collaboration of and agreement for CHIWOS data sharing between any investigator, student or organization (i.e. collaborator) and between CHIWOS and WHRP who houses the CHIWOS data at WCH.

Mission, guiding frameworks and values that guide CHIWOS and therefore this collaboration:

- CHIWOS is guided by a mission statement and a set of guiding frameworks and values. These same principles are to be met by the collaborator of this agreement.

Mission: CHIWOS is committed to creating new knowledge that will be used to support women living with HIV in Canada to achieve optimal health and wellbeing through meaningfully involving them in every stage of the research process by providing a safe, innovative, and transformational research environment.

Guiding Frameworks:

- Women-specific Community-Based Research
- Critical Feminist Approach
- Intersectionality
- Anti-Oppression and Anti-Racism
- Social Justice and Human rights
- MIWA: Meaningful Involvement of Women living with HIV
- GIPA: Greater Involvement of Persons living with HIV/AIDS
- OCAP: Ownership, Control, Access, and Possession

Values:

- Integrity
- Respect
- Accountability
- Inclusivity
- Equity
- Partnership and Collaboration
- Empowerment
- Social Action

Principles of Collaboration and Data Sharing Agreement

For the Canadian HIV Women's Sexual and Reproductive Health Cohort Study

Signatures

- By signing this Collaboration and Data Sharing Agreement, each agent in the partnership agrees to comply with the terms and conditions set out in this agreement.

Name:

08-06-2016
Date (DD-MMM-YYYY)

Collaborator

Dr. Mona Loutfy,
Nominated Principal Applicant, CHIWOS
Director, Women and HIV Research Program

08-JUNE-2016
Date (DD-MMM-YYYY)

Appendix C: CCHS's Microdata Research Contract

(3 pages out of 17 pages are presented here)

Contract number: 17-SSH-UWO-5075

APR 0 4 2017

MICRODATA RESEARCH CONTRACT

(Hereinafter referred to as the "Contract")

BETWEEN:

HER MAJESTY THE QUEEN IN RIGHT OF CANADA, as represented by the Minister responsible for Statistics Canada,

(Hereinafter referred to as "Statistics Canada"),

AND:

Mostafa Shokoohi ; University of Western Ontario

Greta Bauer ; University of Western Ontario

(Hereinafter referred to as Researcher(s))

Each a "Party" and collectively referred to as "Parties".

Recitals

1. Statistics Canada requires the services of the Researcher(s) to perform Special Services of statistical research and analysis, as described herein, pursuant to the *Statistics Act* R.S.C. 1985 chapter S-19;

2. The performance of these Special Services requires that the Researcher(s) has/have access to the Information in Appendix D;

3. Subsection 5(3) of the *Statistics Act* provides that any persons retained under contract to perform Special Services for the Minister pursuant to the *Statistics Act*, and the employees and agents of those persons shall, for the purposes of the *Statistics Act*, be deemed to be employed under the *Statistics Act* while performing those services;

4. Subsection 6(1) of the *Statistics Act* provides that any person deemed to be employed pursuant to the *Statistics Act* shall, before entering on his/her duties, take and subscribe the oath or solemn affirmation contained in that subsection;

5. To perform these services and to have access to confidential information, the Researcher(s) must become Deemed Employee(s) of Statistics Canada, and is/are required to take the Oath of Secrecy and must adhere to Statistics Canada's security and confidentiality requirements;

6. Pursuant to section 13 of the Act, documents or records (Administrative Data) maintained in any department or in any municipal office, corporation, business or organization can be obtained and brought into Statistics Canada for the purpose of this Contract. All Administrative Data required for the purpose of this Contract must be listed in Appendix 'G';

7. (Keep if Administrative Data Provider is a provincial government or institution) Paragraph 19 (1)(c) of the Privacy Act provides that head of a government institution

IN WITNESS WHEREOF, this Contract has been executed on behalf of:

FOR STATISTICS CANADA:

Director, Microdata Access Division Print Name

Witness Print Name

DATED at Ottawa, Province of Ontario, this 11 day of 04 (month) 2017 (year).

FOR THE PRINCIPAL RESEARCHER AND CO-RESEARCHER(S):

Principal Researcher [sign here] Print Name

Witness [sign here] Print Name

DATED at London (location), this 28 day of March (month) 2017 (year).

Co- Researcher [sign here] Print Name

Witness [sign here] Print Name

DATED at London (location), this 31 day of March (month) 2017 (year).

(Complete for all deemed employees signing contract)

APPENDIX F
CONFLICT OF INTEREST DECLARATION FORM

Deemed Employees are required to conduct themselves in accordance with the *Values and Ethics Code for the Public Sector*, including taking all possible steps to prevent and resolve any real, apparent or potential conflicts of interests between their official responsibilities and their private affairs in favour of the public interest.

As a Deemed Employee of Statistics Canada, I acknowledge that I have read the *Values and Ethics Code for the Public Sector*, that I will not undertake any projects in the future that would benefit from my access to any confidential data as a result of this contract, and I further declare that I will comply with the code and that:

✓ I have no conflicts to declare, or

__ I may have a conflict and will complete the "Confidential Report" as required.

Signature of Deemed Employee	Printed Name of Deemed Employee	Date
		2017,03,28

✓ I have no conflicts to declare, or

__ I may have a conflict and will complete the "Confidential Report" as required.

Signature of Deemed Employee	Printed Name of Deemed Employee	Date
		31 March 2017

__ I have no conflicts to declare, or

__ I may have a conflict and will complete the "Confidential Report" as required.

Signature of Deemed Employee	Printed Name of Deemed Employee	Date

(Complete for all deemed employees signing contract)

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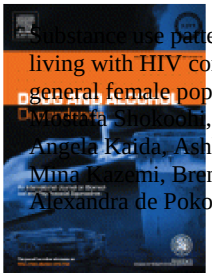

Title: Substance use patterns among women living with HIV compared with the general female population of Canada

Author: Mostafa Shokoohi, Greta R. Bauer, Angela Kaida, Ashley Lacombe-Duncan, Mina Kazemi, Brenda Gagnier, Alexandra de Pokomandy, Mona Loutfy

Logged in as: Mostafa Shokoohi

The University of Western Ontario

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Publisher: Elsevier

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Appendix E: CHIWOS and CCHS surveys

A. CHIWOS

A1) Detailed CHIWOS Wave 1 Survey, English format, can be found here:

http://www.chiwos.ca/wp-content/uploads/2014/08/CHIWOS-May-13-2014-En.pdf

A2) Detailed CHIWOS Wave 2 Survey, English format, can be found here:

http://www.chiwos.ca/wp-content/uploads/2012/04/CHIWOS-Wave-2-Survey-2016.02.12-EN_clean.pdf

B. CCHS

Detailed Canadian Community Health Survey (CCHS; 2013) is accessible here:

http://www23.statcan.gc.ca/imdb/p3Instr.pl?Function=getInstrumentList&Item_Id=152567&UL=1V&

Selected list of variables in both CHIWOS and CCHS used in objectives 1a and 1b

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
Demographic variables			
Sex (SEX)	SEX_Q01, DHH_SEX If necessary, ask: (**Is [respondent name] male or female?**) 1 Male [**will be excluded**] 2 Female (DK, RF are not allowed)	**S1-Q2b. What gender do you currently live as in your day-to-day life?** *Select one.* Man **[if only selection, end interview]** Woman Sometimes man, sometimes woman Third gender, or something other than male or female Don't know Prefer not to answer	This will be used for limiting the study on only females/women including trans women. We exclude the estimates for men in the CCHS data.
Age	ANC_Q03 **What is ^YOUR1 age?** |_|_|_| Age in years	ANC_Q03 , ANC_03 **What is ^SPECRESPNAME's age?** |_|_|_| Age in years Age will be a categorical variable and will be used for the adjustments	This will be used to standardize the prevalences Limit the study to only those people aged ≥16. **Age categories:** 16-25 26-35 36-45

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
			46-55 56+
Ethnic – race	SDC_Q4A To which ethnic or cultural groups did ^YOUR2 ancestors belong? (For example: French, Scottish, Chinese, East Indian) SDC_4B 01 Canadian SDC_4B 02 French SDC_4C 03 English SDC_4D 04 German SDC_4E 05 Scottish SDC_4F 06 Irish SDC_4G 07 Italian SDC_4H 08 Ukrainian SDC_4I 09 Dutch (Netherlands) SDC_4J 10 Chinese SDC_4K 11 Jewish SDC_4L 12 Polish SDC_4M 13 Portuguese SDC_4N 14 South Asian (e.g. East Indian, Pakistani, Sri Lankan) SDC_4T 15 Norwegian SDC_4U 16 Welsh SDC_4V 17 Swedish SDC_4P 18 First Nations (North American Indian) SDC_4Q 19 Métis SDC_4R 20 Inuit SDC_4S 21 Other - Specify	S1-Q7. What do you consider to be your racial and/or ethnic background? Select all that apply. Aboriginal person living in Canada (e.g., First Nations, Métis, and Inuit) Indigenous Person from a country outside of Canada Black African (e.g., Nigerian, Somali) Black Caribbean (e.g., Haitian) Black Other (e.g., Black Canadian) Caucasian/White Chinese or Taiwanese Filipino Japanese Korean Latin American (e.g., Chilean, Costa Rican, Mexican) South Asian (e.g., Indian, Bangladeshi, Pakistani, Punjabi, and Sri Lankan) Southeast Asian (e.g.,Cambodian, Laotian, Malaysian, Vietnamese) Arab (e.g., Egyptian, Kuwaiti, and Libyan) West Asian (e.g. Iraqi, Isreali, Lebanese, Afghani, Iranian) Central Asian (e.g., Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan) Multiple races / Multiracial / "Mixed" Other, please specify: _____ Don't know Prefer not to answer	This will be used to standardize the prevalences **Ethnoracial groups:** Indigenous White African, Caribbean, Black (ACB), Other ethnicities

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	DK, RF Go to SDC_C04B And SDC_Q4B_1, SDC_41 ^ARE_C ^YOU1 an Aboriginal person, that is, First nations, Métis or Inuk (Inuit)? First Nations includes Status and Non-Status Indians. 1 Yes 2 No DK, RF SDC_N4B_2 (^ARE_C ^YOU1 First Nations, Métis or Inuk (Inuit)?) SDC_42A 1 First Nations (North American Indian) SDC_42B 2 Métis SDC_42C 3 Inuk (Inuit) DK, RF SDC_Q4C you may belong to one or more racial or cultural groups on the following list. Are you? SDC_43A 01 White SDC_43C 02 South Asian (e.g., East Indian, Pakistani, Sri Lankan, etc.) SDC_43B 03 Chinese SDC_43D 04 Black SDC_43E 05 Filipino SDC_43F 06 Latin American SDC_43H 07 Arab SDC_43G 08 Southeast Asian (e.g., Vietnamese, Cambodian, Malaysian, Laotian, etc.) SDC_43I 09 West Asian (e.g., Iranian, Afghan, etc.) SDC_43K 10		

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	Korean SDC_43J 11 Japanese SDC_43M 12 Other - Specify DK, RF		
Province	ADM_D3A Ontario British Columbia Québec	Provinces: Ontario British Columbia Québec	This will be used to limit the study to only the people of these three provinces Ontario British Columbia Québec Participants with on-reserve status will be excluded from the analytic sample.
Behavioural variables			
Alcohol use (ALC)			
Definition of a standard drink	Now, some questions about ^YOUR2 alcohol consumption. When we use the word 'drink' it means: - one bottle or can of beer or a glass of draft - one glass of wine or a wine cooler - one drink or cocktail with one and a half ounces of liquor.	A standard drink was considered to be contained 13.45 grams of pure alcohol or the equivalent of 0.6 ounces (oz) of 100% alcohol and was defined as: 341 ml (12-oz) bottle of 5% alcohol "beer, cider or cooler", 142 ml (5-oz) glass of 12% alcohol "wine", and 43 ml (1.5-oz) serving of "liquor or spirits".	

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
Alcohol frequency	Question identifier: ALC_Q1, ALC_1 During the past 12 months, that is, from one year ago to yesterday, have you had a drink of beer, wine, liquor or any other alcoholic beverage? 1 Yes 2 No DK, RF Question identifier: ALC_Q2, ALC_2 During the past 12 months, how often did you drink alcoholic beverages? 1 Less than once a month 2 Once a month 3 2 to 3 times a month 4 Once a week 5 2 to 3 times a week 6 4 to 6 times a week 7 Every day DK, RF Variable: more than 3 times a week, 2-3 times a week, once a week, once a month and others (less than once a month or never)	S6-Q1 How often in the last year have you had a drink containing alcohol? Never Monthly or less 2-4 times a month 2-3 times a week 4 or more times a week DK PNTA	a) Alcohol use in last year: Yes No b) <u>alcohol drinking frequency</u> 4 or more times a week 2-3 times a week 2-4 times a months Monthly or less None
Binge drinking	ALC_Q3, ALC_3 How often in the *past 12* months have you had BINGE DRINK (=4 for women) or more drinks on one occasion? 1 Never 2 Less than once a month 3 Once a month 4 2 to 3 times a month 5 Once a week 6 More than once a week DK, RF	S6Q3. Considering all types of alcoholic beverages (e.g., wine, beer, etc), have you had 4 or more drinks on any one single occasion in the *past month*? • Yes • No S6Q4. How many times in the past month have you had 4 or more drinks on any one single occasion? Indicate number of times: _____ 0 = 0 1 = 1 2 - 9 = 2 10 - 19 = 3	*Non-binge drinkers (monthly)*: those who responded NO to S6Q3 (in CHIWOS) AND those who responded Never to ALC-Q3 (in CCHS); *Light binge drinkers (monthly)*: those who responded Yes to S6Q3 but reported 0 to S6Q4 or reported 1 to S6Q4 (CHIWOS) AND those who responded once a month or less than once a month to ALC-Q3 (in CCHS).

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
		20 or more = 4	*Moderate binge drinkers (monthly)*: those who reported 2-3 times per month to S6Q4 (CHIWOS) AND those who reported 2 to 3 times a month to ALC-Q3 (in CCHS). *Heavy binge drinkers (monthly)*: those who reported 4 or more times per month to S6Q4 (CHIWOS) AND those who reported once a week or more than once a week to ALC-Q3 (in CCHS).
Smoking (SMK)			
Current status of cigarette smoking	Question identifier: SMK_Q202, SMK_202 At the present time, do you smoke cigarettes every day, occasionally or not at all? 1: Daily 2: Occasionally 3: Not at all 8: RF 9: DK Variable: regular users (daily), occasional user, other options	S6-Q5. What is your cigarette (tobacco) smoking history? I am currently a regular smoker I smoke occasionally I am a former smoker I have never been a smoker DK PNTA	a) smoke cigarette currently Yes No b) Current pattern of cigarette smoking regular or daily occasionally others (never, former)
Number of cigarette per day or month	Question identifier: SMK_Q204, SMK_204 How many cigarettes do you smoke each day now? NO: ….. Variable: an ordinal variable will be created based on pack per day	S6-Q6. How many cigarettes do you normally smoke? Indicate number of cigarettes ….. per day/or per month Indicate number of packs: …. Per day / or per moth	Number of cigarettes per day: This will be an ordinal variable such as: 20+ cigarette/day 16-20 cigarette/day 11-15 cigarette/day 6-10 cigarette/day 1-5 cigarette/day None
Social determinants			
Food security	FSC_Q010, FSC_010 Which of the following statements best describes the food eaten in your household in the past 12 months, that is, since	S1-Q22. Which of the following statements best describes the food eaten in your household in the past 12 months, that is since [current month] of last year? Select	Q1) **Last year household food eaten status**: Enough /the kind wanted Enough /not kind wanted Sometimes/often not

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	current month of last year? 1. You and other household members always had enough of the kinds of food you wanted to eat. 2 you and other household members had enough to eat, but not always the kinds of food you wanted. 3 Sometimes you and other household member did not have enough to eat. 4 Often you and other household members didn't have enough to eat. DK, RF	one. - In the past 12 months, you and other household members always had enough of the kinds of food you wanted to eat - In the past 12 months, you and other household members had enough to eat, but not always the kinds of food you want - Sometimes you and other household members did not have enough to eat - Often you and other household members didn't have enough to eat - Don't know - Prefer not to answer	have enough Q2-4) **Description of food situations** Often true=2, sometimes true=1, never true =0; Score range 0 to 6 Food secure 0-1 / food insecure 2-6
	FSC_Q020, FSC_020 You and other members worried that food would run out before you got money to buy more. Was that often true, sometimes true, or never true in the past 12 months? 1 Often true 2 Sometimes true 3 Never true DK, RF	S1-Q23. In the past 12 months, you and other household members worried that food would run out before you got money to buy more. 1 Often true 2 Sometimes true 3 Never true PNTA	
	FSC_Q030, FSC_030 The food that you and other members bought just didn't last, and there wasn't any money to get more. Was that often true, sometimes true, or never true in the past 12 months? 1 Often true 2 Sometimes true 3 Never true DK, RF	S1-Q23. In the past 12 months, the food that you and other household members bought just didn't last, and there wasn't any money to get more. 1 Often true 2 Sometimes true 3 Never true PNTA	
	FSC_Q040, FSC_040 You and other members couldn't afford to eat balanced meals. In the past 12 months was that often true, sometimes true, or never true? 1 Often true 2 Sometimes true 3 Never true DK, RF	S1-Q23. In the past 12 months, you and other household members couldn't afford to eat balanced meals. 1 Often true 2 Sometimes true 3 Never true PNTA	

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
Household income	INC_Q5A Can you estimate in which of the following groups your household income falls? Was the total household income in the past 12 months...? 1 Less than $50,000 including income loss 2 $50,000 and more INC_Q5B, INC_5B Please stop me when I have read the category which applies to ^YOUR1 household. Was it...? 1 Less than $5,000 2 $5,000 to less than $10,000 3 $10,000 to less than $15,000 4 $15,000 to less than $20,000 5 $20,000 to less than $30,000 6 $30,000 to less than $40,000 7 $40,000 to less than $50,000 DK, RF	S1-Q11a. How much does your household make in a year, before taxes (i.e., household gross yearly income)? Less than $10,000 $10,000 to $19,999 $20,000 to $29,999 $30,000 to $39,999 $40,000 to $49,999 $50,000 to $59,999 $60,000 to $69,999 $70,000 to $79,999 $80,000 to $99,999 $100,000 or more Don't know / Prefer to estimate by month Prefer not to answer S1-Q11b. If unable to answer gross yearly household income, prompt for gross monthly income: Indicate gross monthly income in dollars: __	Base on the definitions used for LICO: Less than 20,000 ≥ 20,000 20,000 is not the exact cut point, but it is the closest cut off point. This will be adjusted based on the number of dependents.
	INC_Q5C, INC_5C Please stop me when I have read the category which applies to your household. Was it...? 1 $50,000 to less than less than $60,000 2 $60,000 to less than less than $70,000 3 $70,000 to less than less than $80,000 4 $80,000 to less than less than $90,000 5 $90,000 to less than less than $100,000 6 $100,000 to less than less than $150,000 7 $150,000 and over DK, RF		
Personal income	INC_Q8B Can you estimate in which of the following groups ^YOUR1 personal income falls? Was ^YOUR1 total	S1-Q12a. How much do you make in a year, before taxes (i.e., personal gross yearly income)? Less than $10,000	Base on the definitions used for LICO: Less than 20,000 ≥ 20,000

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	personal income in the past 12 months...? 1 Less than $30,000 including income loss 2 $30,000 and more INC_Q8C, INC_8C Please stop me when I have read the category which applies to you Was it...? 1 Less than $5,000 2 $5,000 to less than $10,000 3 $10,000 to less than $15,000 4 $15,000 to less than $20,000 5 $20,000 to less than $25,000 6 $25,000 to less than $30,000 DK, RF	$10,000 to $19,999 $20,000 to $29,999 $30,000 to $39,999 $40,000 to $49,999 $50,000 to $59,999 $60,000 to $69,999 $70,000 to $79,999 $80,000 to $99,999 $100,000 or more Don't know / Prefer to estimate by month Prefer not to answer S1-Q12b. If unable to answer gross yearly household income, prompt for gross monthly income: Indicate gross monthly income in dollars: __	20,000 is not the exact cut point, but it is the closest cut off point
	INC_Q8D, INC_8D Please stop me when I have read the category which applies to you Was it...? 01 $30,000 to less than $40,000 02 $40,000 to less than $50,000 03 $50,000 to less than $60,000 04 $60,000 to less than $70,000 05 $70,000 to less than $80,000 06 $80,000 to less than $90,000 07 $90,000 to less than $100,000 08 $100,000 and over DK, RF		
Race and gender discrimination	EDS_Q005, EDS_005 In your day-to-day life, how often do any of the following things happen to you? You are treated with less courtesy or respect than other people are. 1 At least once a week 2 A few times a month	S5-Q2. These next questions ask about your experiences of racism. Please think carefully, and do your best to answer each question Q1) You are treated with less courtesy Q2) You are treated with less respect Almost everyday	We found five matched questions on contents and wordings. These items will be summed up to create a new continuous variable. The range of scale for CCHS will be 5-25, whereas it will be 6-30 in CHIWOS. We will combine two items

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	3 A few times a year 4 Less than once a year 5 Never DK, RF	Frequently Sometimes Not that often Almost never Never	of "not that often" and "almost never" in CHIWOS to create a single item conceptually close to the item of "less than once a year" in CCHS. By doing this, both scales will have matched ranges from 5 to 25.
	EDS_Q010, EDS_010 In your day-to-day life, how often do any of the following things happen to you? You receive poorer service than other people at restaurants or stores. 1 At least once a week 2 A few times a month 3 A few times a year 4 Less than once a year 5 Never DK, RF	S5-Q2. These next questions ask about your experiences of racism. Please think carefully, and do your best to answer each question Q3) You receive poorer service Almost everyday Frequently Sometimes Not that often Almost never Never	
	EDS_Q015, EDS_015 In your day-to-day life, how often do any of the following things happen to you? People act as if they think you are not smart. 1 At least once a week 2 A few times a month 3 A few times a year 4 Less than once a year 5 Never DK, RF	S5-Q2. These next questions ask about your experiences of racism. Please think carefully, and do your best to answer each question Q4) People act as if you are not as smart Almost everyday Frequently Sometimes Not that often Almost never Never	
	EDS_Q020, EDS_020 In your day-to-day life, how often do any of the following things happen to you? People act as if they are afraid of you. 1 At least once a week 2 A few times a month 3 A few times a year 4 Less than once a year 5 Never DK, RF	S5-Q2. These next questions ask about your experiences of racism. Please think carefully, and do your best to answer each question Q5) People act as if they are afraid of you Almost everyday Frequently Sometimes Not that often Almost never Never	
	EDS_Q025, EDS_025 In your day-to-day life, how often do any of the following things happen to	S5-Q2. These next questions ask about your experiences of racism. Please think carefully, and do your best to answer	

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	you? You are threatened or harassed. 1 At least once a week 2 A few times a month 3 A few times a year 4 Less than once a year 5 Never DK, RF	each question Q6) You are threatened or harassed Almost everyday Frequently Sometimes Not that often Almost never Never Point: the questionnaire in the CHIWOS has two more questions in this section, but CCHS does not. Then, We will remove these two in the analysis to make balance in terms of the questions	
	EDS_Q030 What do you think the reasons might be for you to have had these experiences? Was it... EDS_030A 01 Your race EDS_030B 02 Your gender DK, RF	Important point: In the CHIWOS, participants were explicitly asked these questions regarding their race discrimination and these questions once again repeated to sex discrimination (assumed to be gender discrimination). However, in the CCHS, participants were asked these questions first and then were asked the reason for such experiences that gender and race are among those reason. Then, these questions will be summed to calculate the scores for only those who reported the reasons for race and gender. Those who did not report these experiences for both race and gender separately, we will assign the least possible score for them. Additionally, in CHIWOS, trans participants were asked questions regarding discrimination in relation to their gender, whereas cisgender women were asked about discriminating in relation to being a woman. This will be considered in the analysis.	
	EDS_Q035, EDS_035 Of the reasons you just mentioned, which one do you think is the main		

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	reason? 01 Your race 02 Your gender DK, RF		
Social support			
A) SS- emotional/informational	SPS_Q06, SPS_06 There is a trustworthy person I could turn to for advice if I were having problems. 1 Strongly agree 2 Agree 3 Disagree 4 Strongly disagree DK, RF	S9-Q4 (1) Someone to turn to for suggestions about how to deal with a personal problem All of the time Most of the time Some of the time A little of the time None of the time DK PNTA	a) We will sum these four items and create a new continuous variable. Total score with current version range: 4-20 (in CHIWOS) and 4-16 (in CCHS) obtained by summing each item. We will combine "most of the time" and "some of the time" in the CHIWOS study and create four-point-Likert scale. The new construct will have a range from 4 to 16, matched with CCHS data.
B) SS- Tangible support	SPS_Q01, SPS_01 There are people I can depend on to help me if I really need it. 1 Strongly agree 2 Agree 3 Disagree 4 Strongly disagree DK, RF	S9-Q4 (2) Someone to help with daily chores if you were sick All of the time Most of the time Some of the time A little of the time None of the time DK PNTA	
C) SS- affectionate support	SPS_Q08, SPS_08 I feel a strong emotional bond with at least one other person. 1 Strongly agree 2 Agree 3 Disagree 4 Strongly disagree DK, RF	S9-Q4 (3) Someone to love and make you feel wanted All of the time Most of the time Some of the time A little of the time None of the time DK PNTA	
D) SS- positive social interaction	SPS_Q02 , SPS_02 There are people who enjoy the same social activities I do. 1 Strongly agree 2 Agree 3 Disagree 4 Strongly disagree DK, RF	S9-Q4 (4) Someone to do something enjoyable with All of the time Most of the time Some of the time A little of the time None of the time DK PNTA	
Housing status	SDC_Q7A, DHH_OWN Now a question about the dwelling in which you live. Is this dwelling… ? 1 Owned by you or a member of this household,	S1-Q14. Which of the following best describes the residence in which you currently live? House that you own Apartment or Condominium	Housing status Owned a house or an apartment Others (rented, not rented, under-housed, homeless)

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	even if it is still being paid for 2 Rented, even if no cash rent is paid DK, RF	that you own House that you rent Floor in a house that you rent A basement apartment that you rent Apartment or Condominium that you rent Self-contained room in a house with other people Self-contained room in an apartment with other people Self-contained room with amenities Self-contained room with no amenities An HIV care group home where you have your own room but share a kitchen and bathroom and where you receive care and support related to HIV A housing facility (such as a group home) where you have your own room but share a kitchen and bathroom and where you receive care and support related to your older age, physical health, mental health, substance use, disability or rehabilitation Outdoors, on the street, parks, or in a car Couch Surfing Transition house/Halfway house/Safe House Shelter Jail Other, please specify: _____ Don't know Prefer not to answer	
Relationship (marital) status	MSNC_Q01 What is [respondent name]'s marital status? Is [he/she]: INTERVIEWER: Read categories to respondent. 1 ... married? 2 ... living common-law? 3 ... widowed? 4 ... separated? 5 ... divorced? 6 ... single, never married?	S1-Q4. What is your current legal relationship status? Legally married Common-law In a relationship, not living together Single Separated / Divorced Widowed Other, please specify: Prefer not to answer	Marital status Married/ Common-law Others type of marital status (separated, divorced, widowed) Single/never married
Education	EHG2_Q01, EDU_1	S1-Q9. What is the highest	Educational status

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	What is the highest grade of elementary or high school [respondent name] has ever completed? 1 Grade 8 or lower (Québec: Secondary II or lower) 2 Grade 9 - 10 (Québec: Secondary III or IV, Newfoundland and Labrador: 1st year secondary) 3. Grade 11 - 13 (Québec: Secondary V, Newfoundland and Labrador: 2nd to 3rd year of secondary) EHG2_Q02, EDU_2 Did [respondent name]complete a high school diploma or its equivalent? 1 Yes 2 No EHG2_Q03, EDU_3 Has [respondent name] received any other education that could be counted towards a certificate, diploma or degree from an educational institution? 1 Yes 2 No EHG2_Q04, EDU_1 What is the highest certificate, diploma or degree that [respondent name] has completed? 1 Less than high school diploma or its equivalent 2 High school diploma or a high school equivalency certificate 3. Trade certificate or diploma 4. College, CEGEP or other non-university certificate or diploma (other than trades	level of formal education you have completed? Select one. No formal education Elementary / Grade school High school / Secondary GED (General Education Diploma) Trade or Technical training CEGEP / College Undergraduate university Post-graduate education Other, please specify _____ Don't know Prefer not to answer	Secondary and below Above secondary

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
	certificates or diplomas) 5. University certificate or diploma below the bachelor's level 6. Bachelor's degree (e.g. B.A., B.Sc., LL.B.) 7. University certificate, diploma, degree above the bachelor's level EDU_Q05, SDC_8 ^ARE_C ^YOU1 currently attending a school, college, cégep or university? 1 Yes 2 No (Go to EDU_END) DK, RF (Go to EDU_END) EDU_Q06, SDC_9 ^ARE_C ^YOU1 enrolled as...? 1 A full-time student 2 A part-time student 3 Both full-time and part-time student		
Job status	Have you worked at a job or business at any time in the past 12 months? 1 Yes 2 No	S1-Q10a. People make money in a variety of ways; for instance, a regular job, and some under-the-table work. Over the last year, what were the different ways you've made money? Paid job, taxes paid Paid job, taxes unpaid / "Under-the-table work" Social assistance Pension Sex work Selling drugs / drugs paraphernalia Pan-handling/ 'squeegeeing' / recycling Worker's compensation (WCB) Employment Insurance (EI) Personal savings Loan(s) / Student Loan(s) Parent / friend / relative / partner income Honoraria (workshops, trainings) Other, please specify: ____	Categories: - Yes (paid job with or without tax) - No (others)

	CCHS 2013-2014	CHIWOS study, 2013-2015	Comparisons/categories
Household size (probably useful for income adjustments)	Hhsz	S1-Q13a. How many people are financially dependent on you, not including yourself? …..	

Selected list of variables available in CHIWOS for the first and second waves used in objectives 1 and 2

	Wave 1	Wave 2
Variables on substance use	**Variable ID, question**	**Variable ID, question**
Alcohol consumption questionnaire	**Definition:** A standard drink was considered to be contained 13.45 grams of pure alcohol or the equivalent of 0.6 ounces (oz) of 100% alcohol and was defined as 341 ml (12-oz) bottle of 5% alcohol "beer, cider or cooler", 142 ml (5-oz) glass of 12% alcohol "wine", and 43 ml (1.5-oz) serving of "liquor or spirits".	
	S6-Q1 **How often in the last year have you had a drink containing alcohol?** Never Monthly or less 2-4 times a month 2-3 times a week 4 or more times a week DK PNTA This item is also indicative of the *frequency* measure	**S7-01.** **How often in the last year have you had a drink containing alcohol?** Never Monthly or less 2-4 times a month 2-3 times a week 4 or more times a week DK PNTA
	S6-Q2 **How many drinks containing alcohol do you have on a typical day when you are drinking?** 1 or 2 3 or 4 5 or 6 7, 8 or 9 10 or more Don't know Prefer not to answer	**S7-02.** **How many drinks containing alcohol do you have on a typical day when you are drinking?** 1 or 2 3 or 4 5 or 6 7, 8 or 9 10 or more Don't know Prefer not to answer
	S6-Q3. **Considering all types of alcoholic beverages (e.g., wine, beer, etc), have you had 4 or more drinks on any one single occasion in the past month?**	**S7-03.** **How often do you have six or more drinks on one occasion?**

	And **S6-Q4.** **How many times in the past month have you had 4 or more drinks on any one single occasion?**	
Stimulant use	**S6-Q10b.** **[3 months before HIV diagnose] Within three months before your HIV diagnosis, did you use any of the following drugs?** - Cocaine - Crack [crack cocaine] - Methamphetamine, - Speed [amphetamine/MDA]	---
	S6-Q11b. **[3 months after HIV diagnose] Within three months after your HIV diagnosis, did you use any of the following drugs?** - Cocaine - Crack [crack cocaine] - Methamphetamine, - Speed [amphetamine/MDA]	---
	S6-Q12b. **[Last three months] Over the last *three* months (current), did you use any of the following drugs?** - Cocaine - Crack [crack cocaine] - Methamphetamine, - Speed [amphetamine/MDA]	**S7-11. <u>And</u> S7-14** **Within *six* months before your HIV diagnosis, did you use any of the following drugs?** - Cocaine - Crack [crack cocaine] - Methamphetamine, - Speed [amphetamine/MDA] - Goofballs (heroin + crystal meth) (only in w2; then, removed)
Opiate/Opioids	**S6-Q10b.** **[3 months before HIV diagnose] Within three months before your HIV diagnosis, did you use any of the following drugs?** - Heroin - Speedball - Morphine - Methadone - OxyContin/Oxycodone - Codeine (t3 & T4) - Fentanyl - Dilaudid (hydromorphone) - Talwin & Ritalin (T & R))	---
	S6-Q11b. **[3 months after HIV diagnose] Within three months after your HIV diagnosis, did you use any of the following drugs?** - Heroin - Speedball	---

	- Morphine - Methadone - OxyContin/Oxycodone - Codeine (t3 & T4) - Fentanyl - Dilaudid (hydromorphone) - Talwin & Ritalin (T & R))	
	S6-Q12b. **[Last three months] Over the last *three* months (current), did you use any of the following drugs?** - Heroin - Speedball - Morphine - Methadone - OxyContin/Oxycodone - Codeine (t3 & T4) - Fentanyl - Dilaudid (hydromorphone) - Talwin & Ritalin (T & R))	**S7-11. <u>And</u> S7-14** **Over the last *six* months (current), did you use any of the following drugs?** - Heroin - Speedball - Morphine - Methadone - OxyContin/Oxycodone - Codeine (t3 & T4) - Fentanyl - Dilaudid (hydromorphone) - Talwin & Ritalin (T & R))
Clinical outcomes		
Current ART use	**S2-Q8.** **Are you currently taking ARVs?**	**S2-02d.** **Are you currently taking ARVs for your own health?**
Treatment adherence Last month	**S2-Q9b.** **We understand that many people on HIV medications find it difficult to take….** **Optimal adherence**: Yes if ≥95% No if <95%	**S2-06.** **We understand that many people on HIV medications find it difficult to take….**
Viral load suppression status	**S2-Q12b.** **What was your most recent viral load, undetectable or detectable?** Undetectable (i.e. below 40 copies/mL) Detectable (i.e. over 40 copies/mL) DK PNTA **S2-Q12c.** **Do you remember the exact result?** Indicate result: _____ copies/mL	**S2-11a.** **What was your most recent viral load, undetectable or detectable?** **S2-11a.** **Do you remember the exact result?** Indicate result: _____ copies/mL
Other variables (social determinants and exploratory variables)		
Age at interview	**Participant's Date of Birth**	---

Biological sex at birth	**S1-Q1.** **What was your biological sex at birth?** Male Female Intersex Undetermined Other, please specify: Don't know Prefer not to answer	---
Current gender identity	**S1-Q2a.** **With respect to your gender, how do you <u>currently</u> identify?** Woman Trans Man (Female to Male) (excluded) Trans Woman (Male to Female) Two-spirited Intersex Gender Queer Other, Man (excluded)	**S1-01** **With respect to your gender, how do you currently identify?** Woman Trans Man (Female to Male) (excluded) Trans Woman (Male to Female) Two-spirited Intersex Gender Queer Other, Man (excluded)
Sexual orientation	**S1-Q3.** **With respect to your sexual orientation, how do you <u>currently</u> identify?** Heterosexual / Straight Lesbian Gay Queer Bisexual Two-spirited Questioning Others DK PNTA	**S1-04.** **With respect to your sexual orientation*, how do you currently identify?**
Marital status	**S1-Q4.** **What is your <u>current</u> legal relationship status?** Legally married Common-law In a relationship, not living together Single Separated / Divorced Widowed Other, please specify: Prefer not to answer	**S1-05.** **What is your current legal relationship status?**
Legal status	**S1-Q6.** **What is your <u>current</u> legal status in Canada?** Canadian citizen Landed Immigrant/Permanent Resident	**S1-06.** **What is your current legal status in Canada?** Canadian citizen Landed Immigrant/Permanent Resident Refugee/Protected Person

	Refugee/Protected Person Refugee claimant/Person in need of protection Here with Temporary Work Papers Here with Humanitarian and Compassionate approval Here as a visitor Here on a Student Visa Undocumented/Illegal Immigrant Other, please specify: Don't know Prefer not to answer	Refugee claimant/Person in need of protection Here with Temporary Work Papers Here with Humanitarian and Compassionate approval Here as a visitor Here on a Student Visa Undocumented/Illegal Immigrant Other, please specify: Don't know Prefer not to answer
Ethno-racial	**S1-Q7.** **What do you consider to be your racial and/or ethnic background?** Many groups …	---
Educational attainment	**S1-Q9.** **What is the highest level of formal education you have completed?** Many groups …	**S1-23.** **What is the highest level of formal education you have completed*?**
Employment status	**S1-Q10a.** **People make money in a variety of ways; for instance, a regular job, and some under-the-table work. Over the last year, what were the different ways you've made money?** Many groups …	**S1-24.** **Are you currently employed?**
Household income	**S1-Q11a.** **How much does your household make in a year, before taxes *(i.e., household gross yearly income)*?** Less than 10,000 10,000 to 19,999 20,000 to 29,999 30,000 to 39,999 40,000 to 49,999 ….	**S1-27.** **Considering all income sources, how much does your household make in a year, before taxes (i.e., household gross yearly income*)?**
Household income	**S1-Q11b.** **If unable to answer gross yearly household income, prompt for gross monthly income:** Indicate gross monthly income in dollars: …….	---

Personal income	**S1-Q12a.** **How much do you make in a <u>year</u>, before taxes *(i.e., personal gross yearly income)*?** Less than 10,000 10,000 to 19,999 20,000 to 29,999 30,000 to 39,999 40,000 to 49,999 ….	**S1-28.** **Considering all income sources, how much do you make in a year, before taxes (i.e., personal gross yearly income*)?**
Personal income	**S1-Q12b.** **If unable to answer gross <u>yearly</u> personal income, prompt for gross monthly income:** Indicate gross monthly income in dollars: …….	---
Difficulty in meeting monthly housing costs	**S1-Q18.** **Given your total household income, how difficult is it to meet your monthly housing costs including rent/mortgage, property taxes, and utilities (e.g., heat, electricity, water and gas)? Would you say that it is**	**S1-36.** **Given your total household income, how difficult is it to meet your monthly housing costs**
Number of dependents	**S1-Q13a.** **How many people are financially dependent on you, not including yourself?** Indicate the number of people: ……	---
Housing status	**S1-Q14.** **Which of the following best describes the residence in which you <u>currently</u> live?** Many groups …	**S1-29.** **Since your last visit, have you been homeless*?** **S1-30.** **Do you have a regular place to stay right now?** **S1-33.** **What type of place are you currently living in?** **S1-37.** **My current housing situation is stable**

Geographic location	**S1-Q19.** **What are the first three digits of the postal code at which you are <u>currently</u> living?** *Only record first three digits* Postal Code: ……	**S1-31.** **What is the postal code for the place where you are currently living or regularly sleep?**
Food insecurity **In past 12 months**	**S1-Q23.** **Item 1** **Item 2** **Item 3**	---
Specific addiction treatment enrollment <u>Ever status</u> which makes it difficult to use, but since occur before baseline time point, we can use it.	**S6-Q17.** **Now I am going to ask you some questions about your use of substance related services, as they relate to your use of drugs or alcohol (not tobacco).** **Have you <u>ever</u> used any of the following substance-related services?**	**S7-17.** **Since your last CHIWOS interview, have you used any of the following substance-related services?**
Addiction treatment enrollment (overall)	**S6-Q17.** **Now I am going to ask you some questions about your use of substance related services, as they relate to your use of drugs or alcohol (not tobacco).** **Have you <u>ever</u> used any of the following substance-related services?**	**S7-17.** **Since your last CHIWOS interview, have you used any of the following substance-related services?**
Time since HIV diagnosis (HIV duration)	**S2-Q4a.** **When were you diagnosed with HIV?**	---
Age at HIV diagnose	**S2-Q4a.** **When were you diagnosed with HIV?**	---
Time since ART initiation (duration of ART uptake)	**S2-Q7.** **When was the first time you ever took ARVs?**	---
Time for last CD4 count Current status	**S2-Q10a.** **When did you last receive your CD4 count results?**	**S2-07.** **When did you last receive your CD4 count results?**
CD4 count measure Current status!	**S2-Q10b.** **What was your <u>most recent</u> CD4 count?** **S2-Q10c.** **Are you able to estimate your most recent CD4 count?**	**S2-08a.** **What was your most recent CD4 count?** **S2-08b.** **Are you able to estimate your most recent CD4 count?**
Time since nadir CD4	**S2-Q11a.**	---

count	**When did you receive your lowest (nadir) CD4 count results?**	
Results of nadir CD4 count	**S2-Q11b.** **What was your lowest (nadir) CD4 count?** **S2-Q11c.** **Are you able to estimate your lowest (nadir) CD4 count?**	---
CD4 count first time diagnosed with HIV	---	**S2-09b.** **Are you able to estimate your CD4 count when you were first diagnosed with HIV?**
CD4 count at time ART initiated	---	**S2-09c.** **Are you able to estimate your CD4 count when you first started taking ARVs (i.e., for the first time ever)?**
Change ART since last CHIWOS wave	---	**S2-03.** **Since your last CHIWOS interview, have there been any changes in your HIV antiretroviral therapy medications (i.e. ARVs*)?**
Viral load last result (time)	**S2-Q12a.** **When did you last receive your HIV viral load results?** Indicate Year: ….. Indicate Month: …. Never received viral load results DK PNTA	**S2-10.** **When did you receive your most recent HIV viral load* results?** Indicate Year: ….. Indicate Month: …. Never received viral load results DK PNTA
Time takes to travel to HIV clinic [where primarily receive HIV medical care]	**S3-Q19.** **How much time does it take to travel one-way from your residence to this clinic?** Between 0 and <30 min Between 30 and <60 min Between 1 and <3 hours Between 3 and <5 hours Five hours or more Don't know Prefer not to answer	---
HIV medical care satisfaction	**S3-Q30** **All 6 items**	S3-30 All 6 items
HCV infection and medication	**S2-Q15a.** **Have you <u>ever</u> been told by a doctor or nurse that you have or had hepatitis C (Hep C)?**	**S2-15.** **Have you ever been told by a doctor or nurse that you have hepatitis C (Hep C)?**

	S2-Q15b. **Have you ever taken medication for hepatitis C?**	**S2-16** **Have you ever taken medication for hepatitis C?**
HBV	**S2-Q16.** **Have you <u>ever</u> been told by a doctor or nurse that you have hepatitis B (Hep B)?**	**S2-17** **Since your last CHIWOS interview, have you been told by a doctor or nurse that you have hepatitis B (Hep B)?**
Quality of life **<u>Last 4 weeks</u>**	**Using SF-12** **S9-Q5. (both items)** **S9-Q6. (both items)** **S9-Q7. (both items)** **S9-Q8.** **S9-Q9. (all three items)** **S9-Q10.** **S9-Q11.**	**Using SF-12** **S4-04 (both items)** **S4-05 (both items)** **S4-06 (both items)** **S4-07** **S4-08 (all three items)** **S4-09** **S4-10**
Social support **MOS-SS scale**	**S9-Q4** **Item 1** **Item 2** **Item 3** **Item 4**	---
Resilience **Connor-Davidson resilience scale (CDRS)** **<u>Without time limit!</u>**	**S9-Q12** **All items in this scale**	---
HIV stigma **Berger HIV stigma scale** **<u>Without time limit!</u>**	**S5-Q1** **All items under this scale**	**S6-01** **All items under this scale**
Experience of Racial discrimination (time: day-to-day) **Detroit Area study (EDS) scale**	**S5-Q2** **All items under this scale**	
Experience of sexism (time: day-to-day)	**S5-Q3** **All items under this scale**	
Willingness to HIV status disclosure	**S5-Q5** **All items under this scale**	S6-02 **All items under this scale**
Depressive symptoms **CES-D 10 scale – <u>past week</u>**	**S9-Q2** **All items under this scale**	**S4-02** **All items under this scale**
Distress **Kessler Psychological Distress scale (K6) – <u>during past 30 days</u>**	---	**S4-03** **All items under this scale**

PTSD **PTSD checklist (PCL-C)**	**S9-Q3** **All items under this scale**	---
Mental health conditions (overall) **Ever**	**S9-Q1a.** **Have you ever been diagnosed with a mental health condition by a care provider?**	**S4-01** **Which, if any, of the following mental health conditions are you currently living with? Please only include conditions that have been diagnosed by a healthcare provider**
Specific mental health conditions	**S9-Q1b.** **Which ones [mental health conditions]?**	**S4-01** **Which, if any, of the following mental health conditions are you currently living with? Please only include conditions that have been diagnosed by a healthcare provider**
Recent incarceration	**S1-Q29.** **In the last year, have you been incarcerated, or held in custody overnight or longer, in Canada?**	**S1-38.** **Since your last CHIWOS interview, have you been incarcerated*, or held in custody overnight or longer, in Canada?**
Any experience of *violence* in the past 3 months (adulthood violence, ≥ 16 years)	**S7-Q2c.** **Has this [physical violence] happened in the last 3 months?** **S7-Q3c.** **Has this [insulted, threatened, screamed, or cursed] happened in the last 3 months?** **S7-Q4c.** **Has this [restricted your actions by controlling] happened in the last 3 months?** **S7-Q5c.** **Has this [sexually forced] happened in the last 3 months?**	**S8-02** **In the last 3 months, has someone ever physically hurt you?** **S8-08.** **In the last 3 months, has someone insulted, threatened, screamed, or cursed at you?** **S8-12.** **In the last three months, has someone restricted your actions by controlling where you can go and what you can do?** **S8-16** **In the last three months, has someone sexually forced themselves on you, or forced you to have sex?**
Adverse childhood experiences	**i) Any experience of *violence* in childhood (< 16 years)** S7-Q6a. This second series of questions are about experiences you had as a child. For our purposes, child is defined as less than 16 years of age. During your childhood, did an adult ever physically hurt you? S7-Q8a. During your childhood, did someone ever sexually force themselves on you, or forced you to	

	have sex? **ii) S1-Q25. Have you ever been under the care of *Child Protection Services*? Select one.** Yes No Don't know Prefer not to answer **iii) S1-Q26. Have you ever been in *foster care*? Select one.** Yes No Don't know Prefer not to answer	
Barriers to care scale	**S3-42. Please indicate to what extent each of the following circumstances have made it difficult for you to receive the care, services, or opportunities you wish to obtain over the past year** 1. Long distances to medical facilities and personnel 2. Medical personnel (e.g. physicians, nurses), who decline to provide direct care to persons with HIV/AIDS 3. The lack of health care professionals who are adequately trained and competent in HIV/ care 4. The lack of transportation to access the services you need 5. The shortages of psychologists, social workers and mental health counselors who can help address mental health issues 6. The lack of psychological support groups for persons with HIV/AIDS 7. The level of knowledge about HIV/AIDS among residents in the community 8. Community residents' stigma against persons living with HIV/AIDS 9. The lack of employment opportunities for people living with HIV/AIDS 10. The lack of supportive and understanding work environments for people living with HIV/AIDS 11. Your personal financial resources 12. Lack of adequate and affordable	**Please indicate to what extent each of the following circumstances have made it difficult for you to receive the care, services, or opportunities you wish to obtain over the past year** 1. Long distances to medical facilities and personnel 2. Medical personnel (e.g. physicians, nurses), who decline to provide direct care to persons with HIV/AIDS 3. The lack of health care professionals who are adequately trained and competent in HIV/AIDS care 4. The lack of transportation to access the services you need 5. The shortages of psychologists, social workers and mental health counselors who can help address mental health issues 6. The lack of psychological support groups for persons with HIV/AIDS 7. The level of knowledge about HIV/AIDS among residents in the community 8. Community residents' stigma against persons living with HIV/AIDS 9. The lack of employment opportunities for people living with HIV/AIDS 10. The lack of supportive and understanding work environments for people living with HIV/AIDS 11. Your personal financial resources 12. Lack of adequate and affordable housing

	housing	
Access to medical care	**S2-Q4b. After receiving your HIV diagnosis, when did you first access HIV medical care?** Indicate Year: …… Indicate Month: …… I have never accessed HIV medical care Don't know Prefer not to answer	
Access to medical care	**S3-Q41a. Have you ever tried to access HIV support services and been unable to?** Select one. Yes No Don't know Prefer not to answer	

Appendix F: Curriculum Vitae (CV)

[Mostafa Shokoohi's CV updated on April 2019]

1. BIOGRAPHICAL INFORMATION

Primary office	Epidemiology and Biostatistics Kresge Building, Room K201 London, Ontario, Canada, N6A 5C1

2. DEGRESS

Sep 2015 – Jun 2019	*Degree and program*: PhD in Epidemiology and Biostatistics, The University of Western Ontario, London, Ontario, Canada *Supervisor*: Dr. Greta R. Bauer
Sep 2006 – July 2009	*Degree and program*: Master of Sciences in Epidemiology, Tehran University of Medical Sciences, Tehran, Iran *Supervisor*: Dr. Reza Majdzadeh
Sep 2002 – Jun 2006	*Degree and program*: Bachelor of Sciences in Clinical Nursing, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3. HONOURS AND AWARDS (from Sep 2015 when my PhD program started)

Sep 2015 – Sep 2019	Ontario Trillium Scholarship (OTS) – an educational award for a course of four years from 2015 to 2019; Total amount: $40,000 per year
Sep 2015	Ontario Graduate Scholarship (OGS) ($30,000; declined)
June 2018	Graduate Student Teaching (TA) Award ($500)
July 2017	WHO, Bio-behavioural Survey Guidelines (BBSG) Questionnaire Workshop; Total amount: hotel costs, flight costs, living expenses
July 2016	Scholarship for oral scholarship and poster presentation; AIDS 2016 Conference International Scholarship, 21st International AIDS Conference, Durban, South Africa | July 18-22, 2016; Total amount: Hotel costs, flight costs, living expense

4. PEER-REVIEWED ACTIVITIES

Manuscript Reviews for various journals (Selected)

Sep 2015 – Jun 2019 - AIDS and Behavior (2018)

- International Journal of STD & AIDS (2018)
- American Journal of Public Health (2018)
- BMC Health Services Research (2018-19)
- Sexual and Relationship Therapy (2018)
- The American Journal of Drug and Alcohol Abuse (2018)
- Osong Public Health and Research Perspectives (2018)
- Drug and Alcohol Dependence (2017)
- The Lancet HIV (2017)
- International Journal of Health Policy and Management (2015-2018)
- Journal of Health, Population and Nutrition (2016-2019)

5. PUBLICATIONS (from Sep 2015 when my PhD program started)

5A. Peer-reviewed publications

1. **Shokoohi M**, Noroozi A, Rahimi-Movaghar A, Karamouzian M. A public health approach to alcohol use and its related harms in Iran. *The Lancet Public Health* **2019** Apr;4(4):e175-e176.
2. **Shokoohi M,** Bauer GR, Kaida A, et al. A Latent Class Analysis of the Social Determinants of Health Impacting Heavy Alcohol Consumption Among Women Living with HIV in Canada: The Canadian HIV Women's Sexual and Reproductive Health Cohort Study. *AIDS and Behavior* **2019**
3. **Shokoohi M**, Bauer GR, Kaida A, et al. Patterns of social determinants of health associated with drug use among women living with HIV in Canada: a latent class analysis. *Addiction*. **2019**
4. **Shokoohi M**, Bauer GR, Kaida A, et al. Social Determinants of Health and Self-Rated Health Status: A Comparison between Women with HIV and Women without HIV from the General Population in Canada. *PLoS One* **2019**;14(3):e0213901.
5. **Shokoohi M**, Karamouzian M, Sharifi H, et al. Substance Use Typologies among Female Sex Workers in Iran: A Latent Class Analysis. Submitted to *Journal of Urban Health* **2019** (under review)
6. **Shokoohi M**, Karamouzian M, Sharifi H, et al. Social and structural determinants of health associated with drug use patterns among female sex workers in Iran: A latent class analysis. *International Journal of Drug Policy* **2019** (under review)
7. Karamouzian M, **Shokoohi M**, Kaplan RL, Noroozi A, Sharifi H, Baral SD, et al. Characterizing the relationship between incarceration and structural risks among female sex workers in Iran: Findings of a nation-wide bio-behavioural surveillance survey. *Annals of Epidemiology* **2019**
8. Mirzazadeh A, **Shokoohi M**, KhajehKazemi R, et al. HIV trend and other sexually transmitted infections among female sex workers in Iran; a reduction that may be attributed to fewer drug injection. *Sexually Transmitted Infections* **2019** (revision requested)

9. Moazen B, et al. National and Sub-National HIV/AIDS-Related Mortality in Iran; 1990 to 2015: A Population-Based Modelling Study. *International Journal of STD & AIDS* **2019** (Accepted)
10. Chegani M, Kamel Khodabandeh A, Karamouzian M, **Shokoohi M**, Abedi L, Khalili M, et al. Alcohol consumption in Iran: a systematic review and meta-analysis. *Drug and Alcohol Dependence* **2019** (revision requested)
11. Vingilis E, Noori A, **Shokoohi M**. Toward the Development of a "Know-how" Knowledge-to-Action Model. *Systemic Practice and Action Research* **2019** (Submitted)
12. Lacombe-Duncan A, Newman P, Bauer G, Logie C, Persad Y, **Shokoohi M**, et al. Gender-affirming Healthcare Experiences and Medical Transition among Transgender Women Living with HIV: A Mixed-Methods Study. *Sexual Health* **2019**
13. Lacombe-Duncan A, Bauer GR, Logie CH, Newman PA, **Shokoohi M**, Kay ES, et al. The HIV Care Cascade among Transgender Women with HIV in Canada: A Mixed-Methods Study. *AIDS Patient Care and STDs* **2019**
14. Mirzazadeh A, et al. One-stop shop community-based hepatitis C screening, diagnosis and treatment model for people who inject drugs in Iran: The Rostam Study. *International Journal of Drug Policy* **2019** (under review)
15. **Shokoohi M**, Karamouzian M, Bauer GR, et al. Drug Use Patterns and Associated Factors among Female Sex Workers in Iran. *Addict Behav.* **2019** Mar;90:40-47
16. Hosseini-Moghaddam SM, **Shokoohi M**, Singh G, Dufresne SF, Boucher A, Jevnikar A, Prasad GVR, Shoker A, Kabbani D, Hebert M, Cardinal H, Houde I, Humar A, Kumar D. A Multi-Center Case-Control Study of the Effect of Acute Rejection and Cytomegalovirus Infection on Pneumocystis Pneumonia (PCP) in Solid Organ Transplant Recipients. *Clin Infect Dis.* **2018** Aug 13.
17. Hosseini Hooshyar S, Karamouzian M, Mirzazadeh A, Haghdoost AA, Sharifi H, **Shokoohi M**. Condom Use and its Associated Factors Among Iranian Youth: Results From a Population-Based Study. *Int J Health Policy Manag*. **2018** Aug 4;7(11):1007-1014.
18. Sharifi H, Mirzazadeh A, **Shokoohi M**, Karamouzian M, Khajehkazemi R, Navadeh S, Fahimfar N, Danesh A, Osooli M, McFarland W, Gouya MM, Haghdoost AA. Estimation of HIV incidence and its trend in three key populations in Iran. *PLoS One*. 2018 Nov 29;13(11):e0207681
19. Esmaeili A, **Shokoohi M**, Danesh A, Sharifi H, Karamouzian M, Haghdoost A, Shahesmaeili A, Akbarpour S, Morris MD, Mirzazadeh A. Dual Unsafe Injection and Sexual Behaviors for HIV Infection Among People Who Inject Drugs in Iran. *AIDS Behav.* 2018 Nov 20.
20. Abdollahpour I, Nedjat S, Salimi Y, Moradzadeh R, Mansournia MA, Sahraian MA, **Shokoohi M**. No association between socioeconomic status and risk of multiple sclerosis: A population-based incident case-control study in a developing country. *Mult Scler Relat Disord*. **2018** Oct;25:292-296.

21. **Shokoohi M**, Bauer GR, Kaida A, et al. Substance use patterns among women living with HIV compared with the general female population of Canada. *Drug Alcohol Depend*. **2018** Oct 1;191:70-77.
22. Shahesmaeili A, Karamouzian M, **Shokoohi M**, et al. Symptom-Based Versus Laboratory-Based Diagnosis of Five Sexually Transmitted Infections in Female Sex Workers in Iran. *AIDS Behav*. **2018** May.
23. **Shokoohi M**, Karamouzian M, Sharifi H, Rahimi-Movaghar A, Carrico AW, Hosseini Hooshyar S, Mirzazadeh A. Crystal methamphetamine use and its correlates in women engaged in sex work in a developing country setting. *Drug Alcohol Depend*. **2018** Feb 14;185:260-265.
24. Mirzazadeh A, **Shokoohi M**, Navadeh S, Danesh A, Jain JP, Sedaghat A, Farnia M, Haghdoost AA. Underreporting in HIV-Related High-Risk Behaviors: Comparing the Results of Multiple Data Collection Methods in a Behavioral Survey of Prisoners in Iran. *The Prison Journal* **2018**; 1–16
25. Sharifi H, Karamouzian M, Baneshi MR, **Shokoohi M**, Haghdoost AA, McFarland W, Mirzazadeh A. Population size estimation of female sex workers in Iran: Synthesis of methods and results. *PLoS One* **2017**; 12(8): e0182755.
26. **Shokoohi M**, Noori A, Karamouzian M, Sharifi H, Khajehkazemi R, Fahimfar N, Hosseini-Hooshyar S, Kazerooni PA, Mirzazadeh A. Remaining Gap in HIV Testing Uptake Among Female Sex Workers in Iran. *AIDS Behav*. **2017** Aug; 21(8): 2401-2411.
27. Sharifi H, **Shokoohi M**, Ahmad RafieiRad A, Sargolzaie Moghadam M, Haghdoost AA, Mirzazadeh A, Karamouzian M. Methamphetamine Use among Iranian Youth: A Population-based Knowledge, Attitude, and Practice study. *Subst Use Misuse* **2017** Jul; 52(9): 1232-1239.
28. Karamouzian M, Mirzazadeh A, Rawat A, **Shokoohi M**, Haghdoost AA, Sedaghat A, Shahesmaeili A, Sharifi H. Injection drug use among female sex workers in Iran: Findings from a nationwide bio-behavioural survey. *Int J Drug Policy* **2017**; 44: 86–91
29. Scheim AI, Bauer GR, **Shokoohi M**. Drug use among transgender people in Ontario, Canada: Disparities and associations with social exclusion. *Addict Behav*. **2017** Mar 31;72:151-158.
30. Karamouzian M, Mirzazadeh A, **Shokoohi M**, Khajehkazemi R, Sedaghat A, Haghdoost AA, Sharifi H. Lifetime Abortion of Female Sex Workers in Iran: Findings of a National Bio-Behavioural Survey in 2010. *PLoS One* **2016** Nov; 11(11): e0166042
31. Nasreen S, **Shokoohi M**, Malvankar-Mehta MS. Prevalence of Latent Tuberculosis among Health Care Workers in High Burden Countries: A Systematic Review and Meta-Analysis. *PLoS One* **2016**; 11(10): e0164034.
32. Scheim AI, Bauer GR, **Shokoohi M**. Heavy episodic drinking among transgender persons: Disparities and predictors. *Drug Alcohol Depend* **2016** Oct; 167: 156-62.

33. **Shokoohi M**, Karamouzian M, Mirzazadeh A, et al. HIV Knowledge, Attitudes, and Practices of Young People in Iran: Findings of a National Population-Based Survey in 2013. Keyhani S, ed. *PLoS One* **2016**; 11(9): e0161849.
34. **Shokoohi M**, Karamouzian M, Osooli M, Sharifi H, Fahimfar N, Haghdoost AA, Zamani O, Mirzazadeh A. Low HIV testing rate and its correlates among men who inject drugs in Iran. *Int J Drug Policy* **2016** Jun; 32: 64-9.
35. Shahbazi M, Moazen B, Rezaei F, **Shokoohi M**, Farnia M; Moradi G, Dolan K. Views of Prison Staff towards Needle Exchange Program in Prisons: A Qualitative Study in Iran. *Drugs: Education, Prevention and Policy* **2016**; 23(2): 113-19.
36. Nikfarjam A, **Shokoohi M**, Shahesmaeili A, Haghdoost AA, Baneshi MR, Haji-Maghsoudi S, et al. National Population Size Estimation of Illicit Drug users through the Network Scale-up Method in 2013 in Iran. *Int J Drug Policy* **2016** May; 31:147-52.
37. **Shokoohi M**, Karamouzian M, Khajekazemi R, Osooli M, Sharifi H, Haghdoost AA, et al. Correlates of HIV Testing among Female Sex Workers in Iran: Findings of a National Bio-Behavioural Surveillance Survey. *PLoS One* **2016**; 11(1): e0147587.

5B. Presentations and Abstracts (from Sep 2015 when my PhD program started)

1. Parhizgari N, Karamouzian M, **Shokoohi M**, Tavakoli F, Haghdoost AA, Ghasemzadeh I, et al. Low rate of HIV Testing among Iranian Prison inmates: Findings from nationwide repeated behavioral surveys. Poster presentation at the STI & HIV 2019 World Congress; Vancouver, Canada | July 14 - 17, 2019 (Accepted)
2. Karamouzian M, Rahmani A, **Shokoohi M**, Sharifi H, Mirzazadeh A. Heterosexual Anal Sex among Female Sex Workers in Iran; Findings from a Nation-wide Bio-behavioural Surveillance Survey. Poster presentation at the STI & HIV 2019 World Congress; Vancouver, Canada | July 14 - 17, 2019 (Accepted)
3. **Shokoohi M**, Bauer GR, Kaida A, Lacombe-Duncan A, Kazemi M, Gagnier B, de Pokomandy A, Loutfy M. Social Determinants of Health and Self-Rated Health Status: A Comparison between Women with HIV and Women without HIV from the General Population in Canada. Poster presentation at the 22nd International AIDS Conference (AIDS 2018) Amsterdam, Netherlands | Will be on 23-27 July 2018 RAI Amsterdam Convention Centre
4. Lacombe-Duncan A, Bauer GR, Logie CH, Newman PA, **Shokoohi M**, Kay ES, Persad Y, O'Brien N, Kaida A, de Pokomandy A, Loutfy M. (2019, May). A mixed-methods investigation of the HIV care cascade among transgender women with HIV in Canada. 28th Annual Canadian Conference on HIV/AIDS Research, Saskatoon, SK, Canada.
5. **Shokoohi M**, Karamouzian M, Sharifi H, Rahimi-Movaghar A, Carrico AW, Hosseini-Hooshyar S, Mirzazadeh A. Crystal Methamphetamine Use and its Associated Factors in Female Sex Worker in Iran, 2015. Poster presentation at the 22nd International AIDS Conference (AIDS 2018) Amsterdam, Netherlands | Will be on 23-27 July 2018 RAI Amsterdam Convention Centre

6. Moazen B., Saeedi Moghaddam S., **Shokoohi M**., et al. National and Subnational HIV/AIDS Related Mortality in Iran From 1990 To 2015: An Innovative Approach To Estimation. Poster presentation at the 22nd International AIDS Conference (AIDS 2018) Amsterdam, Netherlands | Will be on 23-27 July 2018 RAI Amsterdam Convention Centre
7. Lacombe-Duncan A, Bauer GR, Newman PA, Logie CH, Persad Y, **Shokoohi M**, Kaida A, de Pokomandy A, Butler-Burke N, O'Brien N, Loutfy M. The HIV Care Cascade Among Trans Women in Canada: Barriers and Facilitators. Poster presentation at the 22nd International AIDS Conference (AIDS 2018) Amsterdam, Netherlands | Will be on 23-27 July 2018 RAI Amsterdam Convention Centre
8. **Shokoohi M**, Singh G, Dufresne SF, Jevnikar A, Prasad R, Shoker A, Kabbani D, Hebert M, Cardinal H, Houde I, Humar A, Kumar D, Hosseini-Moghaddam SM. The Association of Acute Rejection and Cytomegalovirus Infection after Transplantation on the Development of Pneumocystis Pneumonia (PCP) in Solid Organ Transplant Recipients: A Multi-Center Case-Control Study. Poster presentation at the Department of Medicine Resident Research Day; May 11, 2018: London, ON
9. **Shokoohi M**, Bauer GR, Angela Kaida, Lacombe-Duncan A, Kazemi M, Gagnier B, de Pokomandy A, Loutfy M. Social Determinants of Health and Self-Rated Health Status: A Comparison between Women with HIV and Women without HIV from the General Population in Canada. Poster presentation at the Canadian Conference on HIV/AIDS Research (CAHR) 2018
10. Moazen B., Saeedi Moghaddam S., **Shokoohi M**., et al. National and Subnational HIV/AIDS Related Mortality in Iran From 1990 To 2015: An Innovative Approach To Estimation. 2017 Australian HIV&AIDS Conference 2017. 6-9 November 2017, Canberra, Australia. Paper No.: 445
11. Bauer GR, **Shokoohi M**, Hammond R, Scheim AI. (2016). Factors affecting HIV testing among transgender people in Ontario, Canada: results from a respondent-driven sampling survey. *Journal of the International AIDS Society*, 19(Suppl 5): 46.
12. Hosseini Hooshyar S. **Shokoohi M**., Karamouzian M., et al. Female Condom Use among Female Sex Workers in Iran in 2015. MENAHRA 3rd Regional Conference on Harm Reduction, 23-25 November 2016, Beirut, Lebanon.
13. Scheim AI, Bauer GR, **Shokoohi M**. Impacts of social exclusion on problematic substance use among transgender people: A respondent-driven sampling survey in Canada's most populous province. Oral presentation at the Annual Meeting of the American Public Health Association. Denver, USA. October 31, 2016
14. Fahimfar N., **Shokoohi M**., Valipour A., et al. Condom use and decision-making in the context of HIV prevention among female sex workers in Iran. The 21st International AIDS Conference (AIDS 2016), 18-22 July 2016, Durban, South Africa.
15. Bauer GR, **Shokoohi M** (Presenting author), Hammond R, Scheim AI. Factors affecting HIV testing among transgender people in Ontario, Canada: results from a respondent-

driven sampling survey. Oral presentation at the 21st International AIDS Conference, Durban, South Africa. July 20, 2016.

16. Mirzazadeh A., **Shokoohi M.**, Khajehkazemi R., et al. HIV and sexually transmitted infections among female sex workers in Iran: findings from the 2010 and 2015 national surveillance surveys. The 21st International AIDS Conference (AIDS 2016), 18-22 July 2016, Durban, South Africa
17. Noori A., **Shokoohi M**., Karamouzian M., et al. HIV testing triples over five years surveillance among HIV-negative female sex workers in Iran: the findings of a bio-behavioral survey in 2015. The 21st International AIDS Conference (AIDS 2016), 18-22 July 2016, Durban, South Africa
18. Scheim AI, Bauer GR, Hammond R, **Shokoohi M**. Substance use among transgender people in Canada's most populous province: A respondent-driven sampling survey. Oral presentation at the World Professional Association for Transgender Health Symposium, Amsterdam, the Netherlands. June 20, 2016.
19. Bauer GR, **Shokoohi M**, Scheim AI, Hammond R. HIV testing among trans people in Ontario, Canada. Oral presentation at the World Professional Association for Transgender Health Symposium, Amsterdam, the Netherlands. June 19, 2016.
20. Shahesmaeili A. Mirzazadeh A., Karamouzian M., **Shokoohi M**., et al. Syndromic versus laboratory based diagnosis of five sexually transmitted infections in female sex workers in Iran. The 17th IUSTI World Congress, 9-12 May 2016, Marrakech, Morocco