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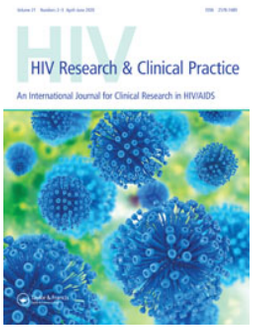

HIV Research & Clinical Practice

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/yhct21

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To cite this article: Anita C. Benoit, Ann N. Burchell, Kelly K. O'Brien, Janet Raboud, Sandra Gardner, Lucia Light, Kerrigan Beaver, Jasmine Cotnam, Tracey Conway, Colleen Price, Sean B. Rourke, Sergio Rueda, Trevor A. Hart, Mona Loutfy & on behalf of the OHTN Cohort Study Team (2020) Examining the association between stress and antiretroviral therapy adherence among women living with HIV in Toronto, Ontario, HIV Research & Clinical Practice, 21:2-3, 45-55, DOI: 10.1080/25787489.2020.1763711

To link to this article: https://doi.org/10.1080/25787489.2020.1763711

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Examining the association between stress and antiretroviral therapy adherence among women living with HIV in Toronto, Ontario

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Background: We aimed to identify the association between stress and antiretroviral therapy (ART) adherence among women in HIV care in Toronto, Ontario participating in the Ontario HIV Treatment Network Cohort Study (OCS) between 2007 and 2012.

Materials and methods: We conducted cross-sectional analyses with women on ART completing the AIDS Clinical Trial Group (ACTG) Adherence Questionnaire. Data closest to, or at the last completed interview, were collected from medical charts, through record linkage with Public Health Ontario Laboratories, and from a standardized self-reported questionnaire comprised of socio-demographic and psycho-socio-behavioral measures (Center for Epidemiologic Studies Depression Scale (CES-D), Alcohol Use Disorders Identification Test (AUDIT)), and stress measures (National Population Health Survey). Logistic regression was used to quantify associations with optimal adherence (≥95% adherence defined as missing ≤ one dose of ART in the past 4 weeks).

Results: Among 307 women, 65.5% had optimal adherence. Women with suboptimal compared to optimal adherence had higher median total stress scores (6.0 [interquartile range (IQR): 3.0–8.1] vs. 4.1 [IQR: 2.0–7.1], $p = 0.001$), CES-D scores (16 [IQR: 6–28] vs. 12 [IQR: 3–22], $p = 0.008$) and reports of hazardous and harmful alcohol use (31.1% vs. 17.9%, $p = 0.008$). In our multivariable model, we found an increased likelihood of optimal adherence with the absence of hazardous and harmful alcohol use (Adjusted Odds Ratio (AOR)=2.20, 95% confidence interval (CI): 1.12–4.32) and a decreased likelihood of optimal adherence with more self-reported stress (AOR = 0.56, 95% CI: 0.33–0.94).

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Supplemental data for this article is available online at https://doi.org/10.1080/25787489.2020.1763711

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DOI 10.1080/25787489.2020.1763711

Conclusions: Interventions supporting optimal ART adherence should address stress and include strategies to reduce or eliminate hazardous and harmful alcohol use for women living with HIV.

Keywords: Stress, depression, antiretroviral therapy, women, HIV

Introduction

High levels of antiretroviral therapy (ART) adherence are required for successful long-term virologic suppression for people living with HIV.[1–4] Optimal adherence, often characterized as having at least 95% adherence, correlates with virologic suppression and decreasing rates of virologic failure, morbidity, and mortality.[1,5,6] For women, effective ART reduces viral load in the plasma and cervicovaginal fluid, thereby reducing horizontal and vertical HIV transmission.[7–11]

Optimal ART adherence levels may be disrupted by several factors with greater effects on some population sub-groups. Socio-demographic factors such as being female, not Caucasian, of younger age, having financial insecurities and low educational attainment, and less support contribute to suboptimal adherence for people living with HIV.[3,4,12–15] Treatment-specific factors (e.g., low treatment self-efficacy, complex ART regimens, adverse events),[1,3,4,12,14] patient-provider relationship and clinic setting factors (e.g., less experienced HIV clinical care teams, less reliable primary care, and lack of resources, confidentiality and receptiveness in a clinic environment),[4,16,17] and psychosocial factors (e.g., substance use, discrimination, mental health concerns, stressful life events) contribute to suboptimal adherence.[4,12,13,16,18–21] However, these studies were largely comprised of men and did not include an analysis stratified by gender.[1,4,12–14,16,19,20,22] Factors associated with suboptimal adherence in women with HIV from two American multicenter cohorts included data from at least 50% of women enrolled before 2000, the era of mono and dual therapy.[2,22–29] Socio-demographic factors (e.g., childcare burden, younger age, not being Caucasian),[2,22–25] treatment and health-related factors (e.g., frequent ART dosing, shorter duration of ART use, abdominal fat gain, low initial CD4 count),[2,24,26] and psychosocial factors (substance use, trauma)[2,24,27] are associated with suboptimal adherence among women living with HIV. While these studies provide insights into factors affecting adherence among women living with HIV, they reflect ART adherence in a U.S. context versus the Canadian publicly funded health care system.[30] It is important to note that despite free medical care in Canada, some patients may have difficulties affording ART due to the variation in cost-sharing policies across Canada's public drug programs with people living with HIV carrying financial burdens with copayments as high as 50%.[30] A recent article showed that viral suppression varied by type of drug coverage in Ontario although they did not measure ART adherence.[31] A higher proportion of individuals with employer coverage compared to those on the Ontario Drug Benefit program had viral suppression.[31] Also, unemployed individuals seeking work often paid out-of-pocket until a new coverage plan began.[31]

Achieving optimal ART adherence may be disrupted by the above factors which may be characterized as stressful life events for some people living with HIV.[1,4,12,13,16,19,20,22] Stress, is a biological acute or chronic response to life events with emotional experiences and biochemical, physiological and behavioural changes.[32,33] Individuals with stressful life events were up to three times more likely to be non-adherent to ART, have worsening HIV disease, and a greater likelihood of mortality.[34,35] The impact of stressful life events on ART adherence for women living with HIV who remain engaged in care has yet to be investigated.

We aimed to determine whether there was an association between stress and ART adherence among women living with HIV accessing specialty HIV care, services managed largely by physicians specialized in HIV or infectious diseases, in Toronto, Ontario, between 2007 and 2012.[36] Specific objectives were to: 1) assess the prevalence of optimal (≥95%) adherence among women living with HIV; and 2) identify whether there was an association between optimal ART adherence and stress for women living with HIV.

Methods

Study design and population

We conducted a cross-sectional analysis of data from the Ontario HIV Treatment Network Cohort Study (OCS), a multi-site, prospective observational cohort of people living with HIV aged 16 or over accessing specialty HIV care in Ontario, Canada.[37] Data were collected from patient medical charts via manual chart abstractions or computerized medical record systems, record linkage with Public Health Ontario Laboratories (PHOL), and from annual interviews using standardized questionnaires with socio-demographic and psycho-socio-behavioural measures. Eligible participants for inclusion in this analysis were women (cis- or trans-identified) on ART who attended one of the three clinics and completed the AIDS Clinical Trial Group (ACTG) Adherence Follow-up Questionnaire.[38] We

used questionnaire data at the last completed interview and clinical data closest to the last interview from women accessing one of three HIV clinics in Toronto from October 1, 2007 to December 31, 2012.

Measurements

Measurement of outcome: Antiretroviral therapy adherence

We used the ACTG Adherence Follow-up Questionnaire[38] which was part of the standardized OCS questionnaire to determine: i) whether ART doses were missed in the past 4 days, ii) the number of days over the past 4 days on which all doses were missed, iii) whether ART was missed the previous weekend, iv) and the last time a dose was missed with responses ranging from within the past week, 1–2, 2–4 or more than 4 weeks ago. Adherence was defined as a dichotomous variable based on responses to the ACTG questions[38] and this dichotomy was determined in consultation with HIV Specialists from a specialty HIV care site (personal communication). Optimal adherence was defined as ≥95% adherence, meaning an individual missed at most one dose in 4 weeks captured by any of the ACTG questions. Suboptimal adherence was defined as two or more missed doses in 4 weeks also captured by any of the ACTG questions.

Measurement of exposure: Stressful life events

Stress was measured using a published, standardized questionnaire from the National Population Health Survey (NPHS) included in the OCS questionnaire. The NPHS which is part of a Canada-wide survey possesses distinct items for recent life events, ongoing problems, and early childhood adversities (Supplemental Table 1).[39] To our knowledge, the psychometric properties of the NPHS, such as its validity and reliability, have not been assessed among people living with HIV. Recent life events (10 items) describes stressful events within the 12 months prior to completing the survey. Ongoing problems (17 items) describes the chronicity of stressful situations as indices or specific (16 items) and general chronic stress (11 items). Early childhood adversities (7 items) are adverse events during childhood or adolescence. We computed a "total stress" score ranging between "0 and 21" by summing recent life events and general chronic stress scores, both presently amenable to change by interventions. Specific chronic stress was not used to compute "total stress" because of low response rates to items focused on whether a participant had a partner or child. Early childhood adversity items were also not used to compute "total stress" because it is unclear whether these past adversities impacted the present stress for the women as this was not asked in the OCS questionnaire. Both specific chronic stress and early childhood adversity scores are reported separately. Higher "total stress" scores correlated with greater frequency and diversity of stressors.

Potential correlates: socio-demographic, psychosocial and clinical factors

From the standardized questionnaire responses, we examined data on socio-demographic factors, HIV risk factors, age, sexual orientation, race/ethnicity, immigration status, housing, education, employment, income, relationship and parental status. Psychosocial factors were stress as detailed above, depression, drug and alcohol use. We used the 20-item Center for Epidemiologic Studies Depression (CES-D) scale to screen for the prevalence of depressive symptoms during the week prior to completing the questionnaire.[40,41] Scores <16 were suggestive of low to no depressive symptoms and ≥16 of depressive symptoms and a need for follow-up care.[40] We evaluated depression as both a dichotomous (≥16 or <16) and a continuous variable. We measured alcohol use with the 10-item Alcohol Use Disorders Identification Test (AUDIT) where scores ≥8 indicate hazardous and harmful alcohol use.[42] Clinical variables from participants' charts included CD4 count, hepatitis C and B serostatus, time since HIV diagnosis, AIDS-defining illness,[43] number of daily antiretroviral pills, antiretroviral class and ART adherence. Viral loads were obtained from charts or PHOL linkage.

Sample size

As of December 31, 2012, 1,664 individuals completed the OCS questionnaire at one of the three clinic sites in Toronto that administered the ACTG questions. Among the 1,516 respondents who were on ART, 308 self-identified as women (n < 6 trans women). One woman did not answer the ACTG questions and was excluded, resulting in 307 women for the analysis. The sample size resulted in 80% power to detect a difference of 1 or greater in total stress scores between women with suboptimal (n=∼100) and optimal (n=∼200) ART adherence, assuming a standard deviation of 3 and a type 1 error probability of 0.05 (PS: Power and Sample Size Calculation version 3.1.2, 2014 by W.D. Dupont & W.D. Plummer Jr).

Statistical analysis

Descriptive statistics

Participant characteristics were presented as frequencies and proportions for categorical variables and medians and interquartile ranges (IQR) for continuous variables. Characteristics between women with

Table 1 Comparison of characteristics between women with suboptimal and optimal ART adherence

	Suboptimal Adherence (n = 106)	Optimal adherence (n = 201)	p
Socio-demographic characteristics			
Age at interview (years) [IQR]	44 [35–51]	43 [36–50]	0.82
Ethnicity			
African, Caribbean, or Black	58 (56.3%)	123 (63.1%)	0.50
White	30 (29.1%)	50 (25.6%)	
Other (e.g. Indigenous)	15 (14.6%)	22 (11.3%)	
Immigration status			
Canadian born	29 (30.5%)	53 (27.5%)	0.93
Canadian citizen	37 (39.0%)	77 (39.9%)	
Landed, permanent resident	16 (16.8%)	32 (16.6%)	
Other	13 (13.7%)	31 (16.1%)	
Partnership status			
Married, common law, committed relationship	35 (33.0%)	61 (30.3%)	0.89
Separated, divorced, widowed	22 (20.8%)	44 (21.9%)	
Single	49 (46.2%)	96 (47.8%)	
Have child/children (Yes)	74 (69.8%)	142 (70.6%)	0.88
Education			
Completed college, university, trade school	49 (46.2%)	100 (49.8%)	0.93
Some college, university, trade school	13 (12.3%)	25 (12.4%)	
Completed high school	22 (20.8%)	38 (18.9%)	
Less than grade 12/13	22 (20.8%)	38 (18.9%)	
Employment status			
Disability (e.g., financial assistance, benefits)	54 (50.9%)	96 (47.8%)	0.86
Retired, student, volunteer, unemployed	19 (17.9%)	35 (17.4%)	
Employed full-time/part-time	33 (31.1%)	70 (34.8%)	
Personal gross yearly income (CAD)			
>$50,001	12 (11.4%)	25 (12.8%)	0.90
$20,000-$50,000	33 (31.4%)	64 (32.6%)	
<$20,000	60 (57.1%)	107 (54.6%)	
Live alone (Yes)	24 (22.6%)	58 (28.9%)	0.24
HIV risk factors			
Country of high HIV prevalence	56 (54.4%)	118 (60.5%)	0.52
Heterosexual transmission	31 (30.1%)	54 (27.7%)	
Other	16 (15.5%)	23 (11.8%)	
Psychosocial characteristics			
Hazardous and harmful alcohol use	33 (31.1%)	36 (17.9%)	0.008*
Injection drug use (last 6 months)	(2.8%)	(0.5%)	0.09
Recent life events score	1 [0–2.2]	0 [0–1.3]	0.07
General chronic stress score	5 [3–7]	4 [2–5.5]	0.0009*
Specific chronic stress score	13.9 [9.6–16]	12.8 [9.6–14.9]	0.12
Early childhood adversities score	2 [1–3]	1 [0–2]	0.003*
Total stress (Recent life events-General chronic stress) score	6.0 [3.0–8.1]	4.1 [2.0–7.1]	0.001*
Total CES-D score	16 [6–28]	12 [3–22]	0.008*
CES-D level (score <16)	162 (54.7%)	52 (49.1%)	0.14
Clinical characteristics			
Years since HIV diagnosis [IQR]	11 [8–18]	11 [6–17]	0.15
CD4 count >200 cells/mm^3	90 (90.9%)	168 (92.3%)	0.68
Viral load <$\overline{50}$ copies/mL	84 (85.7%)	162 (88.5%)	0.50
AIDS-defining illness	40 (37.7%)	75 (37.3%)	0.94
Antiretroviral use (not mutually exclusive)			
Protease inhibitor	89 (34.9%)	166 (65.1%)	0.44
Non-nucleoside reverse transcriptase inhibitor	38 (33.0%)	77 (67.0%)	
Integrase inhibitor / Entry inhibitor	7 (23.3%)	23 (76.7%)	
Number of daily pills			
One pill	40 (41.7%)	68 (37.0%)	0.44
≥ two pills	56 (58.3%)	116 (63.0%)	
Hepatitis C (Yes)	10 (9.4%)	21 (10.4%)	0.78

Continuous variables are presented as medians with interquartile range [IQR]; categorical variables presented as n (%). Not *living alone* includes living with children, partner, spouse, extended family, parents, siblings, and unrelated people; categories which are not mutually exclusive.

Center for Epidemiologic Studies Depression Scale is abbreviated as CES-D.

*Statistically significant.

suboptimal and optimal adherence were compared using t-tests and Wilcoxon rank-sum tests for continuous variables and Pearson's $\chi 2$ tests for categorical variables. Statistical analyses were performed using SAS Statistical Software Version 9.4 (SAS Institute Inc., Cary, NC, USA). Calculated total scores for scales and subscales were adjusted for missing values using mean imputation. Substitution for missing values was done using the mean score of the observed values for that variable. Missing values were imputed for scores

for which individual questions were not completed if at least 50% of the items on the scale had valid responses. Data were not imputed for questions which were not applicable; in these cases, the upper score value was adjusted. Descriptive summaries were suppressed for cell sizes less than 6 to ensure confidentiality.

Logistic regression analysis

We used logistic regression models to determine the unadjusted and adjusted odds ratio (AOR) of optimal adherence associated with *a priori* variables selected based on previous studies:[2,13,22,24] age, ethnicity, employment, living alone and the number of daily antiretroviral pills. All variables were evaluated in univariate analyses and those with $p < 0.10$ were included in the multivariate model. Age and ethnicity were chosen to be forced in the model *a priori*.

Results

Participant characteristics

The median age of the 307 women was 44 years [IQR: 33–51], the majority of whom identified as African, Caribbean, or Black [n = 58, 56.3% with suboptimal adherence; n = 123, 63.1% with optimal adherence]. Among the 307 participants, 201 (65.5%) reported optimal adherence defined as ≥95% ART adherence (Table 1). There were no clinically important or statistically significant differences between women with suboptimal versus optimal adherence with regard to the percentages with undetectable viral loads (n = 84, 85.7% vs. n = 162, 88.5%, p = 0.50) and CD4 T cell count ≥200 cells/mm^3 (n = 90, 90.9% vs. n = 168, 92.3%, p = 0.68). However, women with suboptimal adherence self-reported hazardous and harmful alcohol use (n = 33, 31.1% vs. n = 36, 17.9%, p = 0.008) more often than women with optimal adherence and the difference was significant. Further details on participant demographic characteristics are described in Table 1.

Differences between women with suboptimal versus optimal adherence in the severity of stress and depression

Women with suboptimal adherence had higher total stress scores (6.0 [IQR: 3.0–8.1] vs. 4.1 [IQR: 2.0–7.1], p = 0.001) and higher median CES-D scores (16 [IQR: 6–28] vs. 12 [IQR: 3–22], p = 0.008) compared women with optimal adherence (Table 1). These differences were statistically significant.

Among the stress measures, women with suboptimal adherence had statistically more early childhood adversities than women with optimal adherence (2 [IQR: 1–3] vs. 1 [IQR: 0–2], p = 0.003). The two most frequently reported early childhood adversities for women with suboptimal adherence compared to optimal adherence was "Something happened that scared you so much you thought about it for years after" [59.6% (n = 62/104/) vs. 43.8% (n = 85/194), p = 0.009] and "You were physically abused by someone close to you" [46.7% (n = 49/105) vs. 25.5% (n = 50/196), p = 0.0002]. More general chronic stress (5 [IQR: 3–7] vs. 4 [IQR: 2–5.5], p = 0.0009) were observed for women with suboptimal versus optimal adherence. The ongoing problems items most frequently reported between women with suboptimal versus optimal adherence were from the personal stress index (2 out of 5 items): "Your work around the home is not appreciated" [34.0% (n = 36/106) vs. 17.9% (n = 36/201), p = 0.007] and "People are too critical of what you do" [37.1% (n = 39/105) vs. 20.3% (n = 39/192), p = 0.002]. Two out of three items of the environment stress index were also different between women with suboptimal versus optimal adherence: "You would like to move, but you cannot" [48.6% (n = 51/105) vs. 36.5% (n = 73/200), p = 0.04] and "Your neighborhood or community is too noisy or too polluted" [31.1% (n = 33/106) vs. 19.0% (n = 38/200), p = 0.04] (data not shown).

Socio-demographic, psychosocial and clinical correlates of optimal ART adherence

In the univariate and multivariate model, *a priori* variables were not correlated with optimal adherence (Table 2).

In the multivariate model, the absence of hazardous and harmful alcohol use was associated with higher odds of optimal adherence (AOR: 2.20, 95% CI: 1.12–4.32) and a greater number of stress with lower odds of optimal adherence (AOR: 0.56, 95% CI: 0.33–0.94).

Discussion

In our sample of 307 women living with HIV accessing HIV care in Toronto, Ontario, approximately one third had suboptimal ART adherence. Increased likelihood of suboptimal adherence was associated with the presence of hazardous alcohol use and higher self-reported stress scores.

We reported more stress from recent life events, and statistically more ongoing problems and early childhood adversities for women with suboptimal adherence. Socio-demographic factors (e.g. younger age, non-white race/ethnicity, lower income, lower literacy, and unstable housing) that contribute to stress or expose individuals to greater stressors have previously been shown to impact ART adherence for people

Table 2 Unadjusted and adjusted correlates of optimal ART adherence of women in HIV care in Ontario, Canada

n = 307	Unadjusted Odds Ratio [95% Confidence Interval]	Adjusted Odds Ratio [95% Confidence Interval]
Socio-demographic Characteristics		
Age at interview (years)		
≥ 45	1	1
36–44	1.38 [0.78–2.45]	1.40 [0.72–2.73]
≤ 35	0.96 [0.54–1.71]	1.46 [0.71–3.00]
Ethnicity		
White	1	1
African, Caribbean, Black	1.27 [0.73–2.20]	1.18 [0.59–2.35]
Other (e.g. Aboriginal)	0.88 [0.40–1.95]	0.67 [0.27–1.68]
Employment status		
Retired, student, volunteer, unemployed	1	1
Disability	0.96 [0.50–1.85]	1.36 [0.64–2.91]
Employed full-time/part-time	1.12 [0.55–2.28]	1.19 [0.53–2.66]
Live alone		
Yes	1	1
No	0.72 [0.42–1.25]	0.66 [0.36–1.23]
Psychosocial characteristics		
Hazardous and harmful alcohol use		
Yes	1	1
No	2.07 [1.20–3.58]	2.20 [1.12–4.32]
Total Stress (Recent life events – general chronic stress) score	0.54 [0.38–0.79]	0.56 [0.33–0.94]
Total CES-D score	0.79 [0.66–0.94]	1.14 [0.89–1.46]
Clinical characteristics		
Number of daily pills		
One pill	1	1
≥ two pills	1.22 [0.74–2.02]	1.44 [0.83–2.52]

Not *living alone* reflects living with children, partner, spouse, extended family, parents, siblings, and unrelated people, categories which are not mutually exclusive.
Center for Epidemiologic Studies Depression Scale is abbreviated as CES-D.

living with HIV.[3,4,18,38,44] The factors we investigated (i.e., younger age, non-white race/ethnicity, lower-income and employment status) were not correlates of ART adherence. Evidence associating poor ART adherence and socio-demographic factors is conflicting, but when an association is found, the directionality is consistent. More consistently associated with non--adherence or suboptimal ART adherence are depression, other psychiatric morbidities, active drug or alcohol use, stressful life events and lack of social support.[17,20,45–51] Therefore, it is important to determine how health outcomes and behaviors can be affected by stress. Studies have shown that childhood adversities have been linked to long-term negative consequences on health.[52] Also, duration of stress may be more clinically meaningful since chronic stress is detrimental to women's health and adherence.[32–34] Moreover, stressful life events and a personal and familial history of depression have been implicated in increasing the susceptibility to depression.[53]

In our study, we found that the proportions of women with depressive symptoms were higher than reported in the general Canadian population and levels previously reported in women with HIV.[37,54,55] Given the consistently high levels of depressive symptoms in the present study and other studies of women with HIV,[37,54,55] attempts to diagnose and treat depression are warranted. Importantly, women in our study were accessing care so health-related concerns such as depression may have been addressed quickly. The prevalence and severity of depression for women may be higher for those not accessing care given the adverse effects depression may have on service use.[34,56] In addition, individuals with depression and suboptimal adherence have almost six times greater likelihood of mortality than those without depressive symptoms.[56] We found significantly more depressive symptoms in women with suboptimal adherence; however, we did not observe an association between depression as measured with the CES-D and adherence in our logistic regression model. The literature does suggest that acute rather than baseline depression impacts medication adherence and the CES-D does not characterize depression as acute or chronic.[57,58]

Many studies show that alcohol use has been associated with an increased likelihood of suboptimal adherence.[2,12,17,38,59] Our findings are consistent with the literature and worrisome considering alcohol consumption is under-reported by women and men.[60] For women in the general population, depression has been

associated with excessive alcohol use.[61] Alcohol use has been reported as a coping strategy for stress, depression and other mental health issues in women.[62] In fact, a longitudinal study of women with HIV showed alcohol use predicted depression and depression worsening HIV health outcomes.[63] For women, alcohol use has been stigmatized and used to manage stress and psychiatric conditions.[62] Despite few studies, excessive alcohol use by women has implications on health (e.g., increased likelihood of unprotected sex and sexually transmitted infections, cognition deficits, cancer, liver and cardiovascular diseases).[64–68] This is concerning given the already high rates of comorbidities (e.g., cardiovascular diseases, neurologic and metabolic disorders, mental health issues and cancers) in persons living HIV with a higher prevalence reported by women.[69,70] A review has reported an association between substance use and high comorbid rates of mental disorders specifically alcohol and depression.[71] As such, alcohol use to cope with mental health issues could potentially affect medication adherence against HIV and comorbidities for women in our study if their engagement to care is disrupted, stressful life events persists, and depression goes unmanaged.

Our findings must be interpreted with caution. Selection bias arises since women are accessing specialty HIV care in an urban setting and willing to complete the interview-administered OCS questionnaire; relationships may differ from women not accessing HIV care or in less urban environments. Using data from a clinical cohort reflective of Ontarians diagnosed with HIV was a strength of this study. Another strength was our use of information from clinical charts and interviews enabling us to study the associations between stress and adherence from a socio-demographically diverse sample of women.[37,72] However, we may have been inadequately powered to detect some associations. Thus, our findings must be interpreted cautiously given our small sample size and sample variation. Larger sample size with a more homogenous population may have provided more narrow and precise confidence intervals particularly with regards to our findings showing associations between adherence with alcohol use and with self-reported stress. Our definition of adherence may not have been sensitive enough to classify women with clinically relevant non-adherence. Since in our study, women with suboptimal and optimal adherence had similarly high rates of undetectable viral loads and CD4 T cell counts $\geq$200 cells/mm^3. Also, the lowest rate of adherence that we could calculate with the ACTG questions was 87%. Unsurprisingly a systematic review of 43 studies across 26 countries demonstrated that different optimal adherence levels (greater than or equal to 98–100%, 95%, and 80–90%) were adequate for achieving virologic suppression with newer ART drugs (2000–2015) as compared to obsolete ART drugs.[73] Our data reflects adherence levels measured in a cohort of women accessing care between 2007 and 2012 so newer ARTs may similarly influence desired adherence levels. Furthermore, the timing and sequence of events were not known in our cross-sectional analysis, limiting our ability to draw causal inferences. Adherence over 4 weeks may not reflect adherence over a longer period thus longitudinal analyses are required. Further, women in our study are young (44 years IQR[35–51] suboptimal adherence and 43 years IQR[36–50] optimal adherence) and with increasing life expectancy more comorbidities along with comedications are expected and this has been shown to increase the risk of ART non-adherence.[74] The NPHS has not been validated and affirmative/negative response options may have resulted in misclassification as it does not capture perceived stress which may differ between individuals. Also, the NPHS may not be appropriate for measuring stress in an ethnically or racially diverse population with distinct life experiences, such as racism in Canada, despite being part of a national survey administered by Statistics Canada. Moreover, the NPHS does not capture experiences of sexism, HIV-related stigma or precarious immigration status which may be important given the high proportion of African, Caribbean, or Black women in our study. The AUDIT's performance has been shown to have a gender bias possibly underestimating alcohol use.[75–78] Age and ethnicity were not confounders in our multivariable model; nevertheless, there may have been other unmeasured confounders missed in our analysis.

In summary, the absence of hazardous and harmful alcohol use and lower stress scores were associated with optimal ART adherence for women living with HIV accessing care in Toronto, Ontario, between 2007 and 2012. The ART regimens in the current treatment era of our study may have been more forgiving to suboptimal adherence. It may be important to assess other adherence levels using different measures of adherence. A comprehensive collaborative care plan and interventions aimed at reducing stress and excessive alcohol use may promote ART adherence among women living with HIV. Stress-reduction interventions may also include strategies to facilitate ART adherence for women living with HIV.

Acknowledgements

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We gratefully acknowledge all of the people living with HIV who volunteered to participate in the OHTN Cohort Study and the work and support of the past and present members of the OCS Governance Committee: Adrian Betts, Anita C. Benoit, Breklyn Bertozzi, Les Bowman, Lisungu Chieza, Tracey Conway, Patrick Cupido, Tony Di Pede, Brian Finch, Esther Guzha, Muluba Habanyama, Michael J. Hamilton, Brian Huskins, Rick Kennedy, Ken King, Nathan Lachowsky, Joanne Lindsay, Shari Margolese, John MacTavish, Mark McCallum, Martin McIntosh, Colleen Price, Rodney Rousseau, Lori Stoltz, Darien Taylor, Rosie Thein, and Drs. Ahmed Bayoumi, Evan Collins, Curtis Cooper, Clemon George, Troy Grennan, Claire Kendall, and Greg Robinson. We acknowledge the current members of the Scientific Steering Committee: Dr. Barry Adam, Dr. Anita Benoit, Adrian Betts, Dr. David Brennan, Dr. Ann Burchell, Tracey Conway, Dr. Curtis Cooper, Pierre Giguere, Dr. Trevor Hart, Dr. Winston Husbands, Dr. Abigail Kroch, Lucia Light, Dr. Mona Loufty, Dr. Lawrence Mbuagbaw, Wesley Oakes, Dr. Kelly O'Brien, and Dr. Sergio Rueda. We thank all the interviewers, data collectors, research associates and coordinators, nurses and physicians who provide support for data collection and extraction. The authors wish to thank the OCS staff for data management, IT support, and study coordination: Eliot Winkler, Wesley Oakes, Robert Hudder, Lucia Light, Veronika Moravan, Nahid Qureshi, Tsegaye Bekele, Sean Colyer, Kumaran Sivagnanam, and Dr. Maya Kesler. We also acknowledge the Public Health Laboratories, Public Health Ontario, for supporting record linkage with the HIV viral load database.

Disclosure statement

The opinions, results and conclusions are those of the authors and no endorsement by the Ontario HIV Treatment Network or Public Health Ontario is intended or should be inferred.

Funding

The OHTN Cohort Study is supported by the Ontario Ministry of Health and Long-Term Care. Other supports include Canadian Institutes of Health Research (CIHR) New Investigator awards to SR and AB, and an OHTN Chair to JR and TH and support from the Toronto and Western Hospital Foundation Skate the Dream Fund for JR.

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