The impact of drug coverage on viral suppression among people living with HIV in Ontario, Canada

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Abstract

Objectives We investigated the effect of drug coverage on viral suppression (sVL) in Ontario, Canada, where there is no universal coverage of prescription drugs, including antiretroviral therapy (ART).

Methods Ontarians without employment coverage may be eligible for varying degrees of coverage through government-sponsored programs. Remaining individuals pay all expenses entirely out of pocket. Among participants on ART enrolled in the Ontario HIV Treatment Network Cohort Study (OCS) who were interviewed in 2008–2013 with known or imputable drug coverage, we estimated the prevalence with sVL (<200 copies/mL) as of their last viral load each year. We calculated prevalence ratios (PR) according to time-updated socio-economic and behavioural factors using multivariable generalized estimating equations with a log-link function. Multiple imputation was used to assess the sensitivity of these findings to different assumed missing data models.

Results One thousand two hundred forty-seven participants were included (3463 person-years). Compared to study participants with employer coverage, individuals covered through the Ontario Drug Benefit (ODB) were less likely to be suppressed (PR, 95% confidence interval (CI) 0.96, 0.93–0.98). After multivariable adjustment, ODB remained independently associated with less success in achieving sVL (adjusted PR, 95% CI 0.98, 0.95–0.99). These findings were robust to different assumptions about the missing data.

Conclusion Our findings suggest that drug coverage can affect viral suppression in our setting. Further research is needed to identify the mechanisms by which coverage interacts with individual patient factors to affect viral suppression. Mechanisms to improve access and coverage for ART are needed.

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Résumé

Objectifs Nous avons étudié l'effet de la couverture médicamenteuse sur la suppression virale (sVL) en Ontario, au Canada, où il n'y a pas de couverture universelle des médicaments sur ordonnance, y compris les traitements antirétroviraux (ART).

Méthodes Les Ontarien(ne)s sans couverture d'emploi peuvent être admissibles à divers degrés de couverture dans le cadre de programmes parrainés par le gouvernement. Les personnes restantes paient toutes les dépenses de leur poche. Parmi les participants sous médicaments ARV à l'étude de cohorte du Réseau ontarien de traitement du VIH (SCO) qui ont été interviewés en 2008–2013 avec une couverture médicamenteuse connue ou imputable, nous avons estimé la prévalence de sVL (<200 copies / mL) à partir de leur dernière charge virale à chaque année. Nous avons calculé les ratios de prévalence (PR) en fonction de facteurs socio-économiques et comportementaux mis à jour, en utilisant des équations d'estimation généralisées multivariées avec une fonction de liaison logarithmique. L'imputation multiple a été utilisée pour évaluer la sensibilité de ces résultats aux différents modèles de données manquantes supposées.

Résultats 1247 participants ont été inclus (3463 années-personnes). Comparativement aux participants à l'étude ayant une couverture d'employeur, les personnes couvertes par le Programme de médicaments de l'Ontario (PMO) étaient moins susceptibles d'être réprimées (Rapport de prévalence (PR), Intervalle de confiance (IC) 95%: 0,96, 0,93–0,98). Après ajustement multivariable, PMO est demeuré indépendamment associé avec moins de succès dans la réalisation de sVL (PR ajusté, IC à 95%: 0,98, 0,95–0,99). Ces résultats étaient robustes à différentes hypothèses concernant les données manquantes.

Conclusion Nos résultats suggèrent que la couverture médicamenteuse peut affecter la suppression virale dans notre cadre. Des recherches supplémentaires sont nécessaires pour identifier les mécanismes par lesquels la couverture interagit avec les facteurs individuels du patient pour affecter la suppression virale. Des mécanismes visant à améliorer l'accès et la couverture des traitements antirétroviraux sont nécessaires.

Keywords HIV · Viral suppression · Prescription drug coverage

Mots-clés VIH · Suppression virale · Couverture des médicaments sur ordonnance

Introduction

Advances in HIV care and the availability of antiretroviral therapy (ART) have resulted in significant decreases in HIV-related morbidity and mortality (Cohen et al. 2011). Uninterrupted access to ART is critical for improving health outcomes for people living with HIV and reducing the risk of secondary transmission of HIV (Cohen et al. 2011). Discontinuous ART can result in drug resistance, increased costs associated with care (Krentz et al. 2013; McAllister et al. 2013), hospital admissions, opportunistic infections, and death. Drug insurance that covers the cost of treatment is a necessary prerequisite for most individuals for ensuring uninterrupted access to ART. In the absence of stable coverage, the monthly costs of various drug therapies can compete with basic necessities (e.g., housing), compelling individuals to adopt strategies such as splitting tablets to extend the duration of prescriptions (McAllister et al. 2013), resulting in inadequate dosing. Evidence from the United States suggests that cost-sharing (e.g., costs shared between individual and insurer) is associated with poor adherence to ART (McAllister et al. 2013; Johnston et al. 2012). At the same time, in a study using data from a nationally representative cohort of people living with HIV in the US, availability of ART and associated health outcomes varied by the type of coverage, with greater availability and better overall survival among those with private insurance compared to those with either no insurance or coverage through a public program (Bhattacharya et al. 2003).

While Canada has universal public health insurance coverage for necessary physician services, it does not include universal coverage of prescription drugs outside the hospital setting. Canada's provinces and territories have independently established their own outpatient drug insurance programs with substantial inter- and intra-provincial variability with respect to drug formulary composition, eligibility for coverage, and costs borne by patients (Demers et al. 2008). In Ontario, drug coverage is provided through several overlapping mechanisms for those who lack private insurance. The publicly funded Ontario Drug Benefit (ODB) program provides universal coverage for low-income seniors, individuals on social assistance (Ontario Works), or those who qualify for the Ontario Disability Support Program (ODSP). Co-pays for ODB are \$2 per prescription for lower income seniors, although those with higher income are expected to pay the first \$100 in drug costs and then up to \$6.11 per prescription. Co-pays are waived for those receiving home care, on ODSP, or Ontario Works (Ontario Ministry of Health and Long-Term Care (MOHLTC) 2014). For individuals who do not meet these criteria and who do not have full coverage through private insurance through their employer, there is the Trillium Drug Program. In this program, individuals first pay an annual deductible (~4%) based on net household income and then pay up to \$2 for each prescription filled (Ontario Ministry of Health and Long-Term

Care (MOHLTC) (2014). It is worth noting that in many cases coverage through private insurance is not complete; additional co-pays and/or deductibles are needed (Binder *n.d.*). In Ontario, most antiretroviral agents are covered by ODB, including Ontario Works, ODSP, and Trillium, although there are some nuances, with some dosages covered but not others (Yoong *et al.* 2014). Similarly, most tenofovir-based drugs are not covered and some drugs like Descovy, which still needs to be reviewed, and enfuvirtide and tipranavir require special authorization (Deborah Yoong, personal communication, May 16 2018). Trillium is intended to support Ontario residents, regardless of health status, with large drug expenses (relative to their income) who have incomplete or no coverage. Note that while Trillium is available to all who choose to register, a previous study in our setting has demonstrated that there are many obstacles, including high deductibles, associated with Trillium that may lead to gaps in coverage in Ontario (Yoong *et al.* 2015).

Although there are no published data examining the impact of incomplete drug coverage for people living with HIV in Canada, previous evidence from our setting suggests that challenges accessing and affording ART are prevalent (Yoong *et al.* 2015). Given the critical need to ensure that people living with HIV have continuous access to ART, our objective was to investigate the effect of drug coverage on viral suppression among people living with HIV in a clinical cohort in Ontario, Canada.

Methods

Data sources and study design

The Ontario HIV Treatment Network Cohort Study (OCS) is a multi-site clinical cohort of people receiving HIV care in Ontario, Canada (population 13.6 million). The cohort has been described elsewhere (Rourke *et al.* 2013). In brief, its source population consists of people living with HIV, aged 16 years and older, and who receive medical care at specialty clinics within a system of publicly funded access to medically necessary physician and hospital services. Participants are recruited from nine participating sites which include both outpatient clinics based at hospitals as well as community-based practices which provide care to over 75% of patients who receive viral load testing in the province. Clinical data captured during routine follow-up visits are abstracted from clinic records. Participants complete a baseline questionnaire upon enrolment and an annual follow-up interview that elicits information on demographics, employment, income, mental health, and substance use. Record linkage is conducted with the HIV viral load database at the Public Health Ontario Laboratories (PHOL), the sole provider of viral load testing in the province. Participants are linked to PHOL using a

unique encrypted identifier that cannot be decoded to determine the original identifiers. Currently, active ascertainment of death does not occur in our cohort and there is no information on hospitalizations.

Between January 1995 and December 2014, 6671 participants were enrolled in the OCS. All participants provide written informed consent upon recruitment to participate in the cohort study. The cohort design and consent forms were approved by the University of Toronto Research Ethics Boards (REB) and REBs at the individual study sites.

Study population

We used cohort data available as of December 31, 2014, to define our study population. Entry into the study population occurred on January 1, 2001, or entry to HIV care, whichever was later. Participants were eligible for this analysis if they were still under follow-up and had completed at least one questionnaire between 2008 and 2013, had been on ART for at least 1 year with no evidence of having stopped in the given year (as evidenced by a medication stop date provided in that year), and had known drug coverage or drug coverage that could be imputed from the data available in the clinical records from 2007 to 2013. While drug coverage information was available from 1996 onwards, questionnaire indicators were only available from 2008 onwards. Therefore, we restricted our analysis to 2008–2013. In order to create a cleaner dataset, we restricted our analysis to participants under the age of 65 years as those who are 65 years of age or older are all eligible for coverage through ODB (Fig. 1).

Measures/outcomes

Our outcome was suppressed viral load (yes/no), defined as < 200 copies/mL at the last measurement in each year. Our primary predictor of suppressed viral load (sVL), drug coverage, was obtained from chart review and is all self-reported. It consisted of five mutually exclusive categories: Employer (reference), Ontario Drug Benefit (ODB), paying entirely Out of pocket, Trillium, and the derived category Co-pay, which consisted of reporting multiple sources of coverage and paying out of pocket. For years when drug coverage for a given study participant was unknown or missing, the initial imputation method was to carry forward the last known category. Any years preceding the first year with known drug coverage were excluded (Fig. 1). We combined gender, sexual orientation, and reported sex behaviours (e.g., sex with other men) to derive a single variable called sex that had three categories: female; male who reports sex with men (MSM); male who does not report sex with men/unknown. Additional factors of interest included age, ethnicity, citizenship and immigration status, marital status, living alone, education level, gross annual personal income, employment status, years

Fig. 1 Study flow of included participants

living with HIV, and years on ART. A participant was defined as having mental health concerns (yes/no) if they scored ≥ 22 on the 10-item Kessler Psychological Distress Scale or ≥ 23 on the Center for Epidemiologic Studies Depression Scale (CES_D scale). Substance use behaviours included cigarette smoking in the past 30 days, hazardous drinking in the past year (yes/no) measured by the 3-item Alcohol Use Disorders Identification Test, and reported recreational drug use (including injection) in the past 6 months.

Data analysis

We used descriptive statistics, including proportions for categorical variables and median and the interquartile range (IQR) for continuous variables. Chi-square or Fisher's exact tests with tests for trend as appropriate were used to examine potential relationships between categorical variables and the outcome at baseline. We estimated the annual prevalence of participants with sVL. We calculated prevalence ratios adjusted for various predictors, using multivariable generalized estimating equations with a log-link function, an exchangeable correlation structure, and robust error variances. Prevalence ratios are useful when the prevalence of the outcome is high (Barros and Hirakata 2003). Variable selection was primarily

based on a priori knowledge of associations with suppression, collinearity between variables, and potential confounding. We explored the effect of interview year, and multivariable models were also adjusted for clinic site as a fixed effect to account for unmeasured differences in case mix of participants at included clinics.

We performed a variety of sensitivity analyses where multiple imputation (Rubin 1987) for drug coverage and other covariates was used to accommodate a number of different missing data models. These sensitivity analyses included imputations under a Missing At Random model (Little and Rubin 2002) and a variety of Missing Not At Random models captured through pattern-mixture modelling (Rubin 1987; Buuren and Groothuis-Oudshoorn 2011) to allow for plausible deviations from the missing at random assumption in terms of a range of multiplicative increases to the relative probability of imputing each of the drug coverage categories. Patterns of missingness varied across sites, so a sensitivity analysis excluding sites with large numbers of participants with unknown drug coverage was also conducted. Both single-level and multi-level multiple imputation were employed using the MICE package in R (Buuren and Groothuis-Oudshoorn 2011). We conducted all other analyses using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina).

Results

In total, the study population consisted of 1247 participants representing 3463 person-years. The overall proportions with sVL over time were as follows: 94.7% in 2008; 91.5% in 2009; 92.0% in 2010; 94.1% in 2011; 92.7% in 2012; and 92.0% in 2013. There were no significant differences in the proportion with sVL across year ($p = 0.6284$). Suppression varied by drug coverage type at baseline ($p = 0.0348$). The lowest proportions of participants with sVL were among those who were on ODB (90.8%) and the highest was among participants with coverage through an employer (96.1%). This tendency was consistent over time (2008–2013) ($p = 0.004$) (median visits 2, IQR 1–3, range 1–6 visits). Median age was 46 (IQR 19–64). A total of 284 participants with an interview in 2008–2013 had evidence of stopping ART during the year over the study period. There were significant differences in term of drug coverage with a higher proportion of those who have stopped ART paying out of pocket compared to those who did not stop ART (15.3% vs. 4.6%, $p < 0.001$) (data not shown). Table 1 describes the participant population at baseline.

Suppression also varied across other predictors, with statistically significant differences occurring in different categories of age, education level, income, mental health concerns, smoking, and drug use (Table 1). The distribution of drug coverage also varied significantly across the different participant characteristics (Supplementary Table 1). Drug coverage through an employer was highest for participants who were classified as men who had sex with men (25.5%), White (25.5%), born in Canada (24.4%), those on ART for 10 years or more (23.4%), had a university degree (34.6%), employed FT/PT (37.1%) and had an income of $\geq \$60,000/\text{year}$ (52.7%), and those with no mental health concerns (24.3%). ODB was most common for other men who do not have sex with men (60.5%), women (62.5%), those with an income of $< \$20,000$ (76.2%) or who completed some high school or less (72.3%), individuals on disability (58.5%), current smokers (62.4%), and individuals reporting injection drug use (80.3%) or mental health concerns (65.9%). Individuals who were unemployed and seeking work reported the highest proportion of individuals paying out of pocket (11.8%).

In unadjusted analyses, compared to coverage via an employer, individuals paying out of pocket (not significant) or covered through ODB were less likely to be suppressed (prevalence ratio (PR), 95% confidence intervals (CI) 0.96, 0.93–0.98). After multivariable adjustment (Table 2), being on ODB remained negatively associated with sVL (adjusted PR 0.98, 0.95–0.99). Other factors negatively associated with viral suppression included ≤ 35 years of age (vs. > 35 : 0.95, 0.91–0.99), mental health concerns (vs. no mental health concerns 0.97, 0.95–0.99), smoking (vs. never smoking 0.97, 0.95–0.99) and injection drug use (vs. no drug use 0.90, 0.83–0.97).

Unknown drug coverage ranged from 44.8% in 2013 to 51.4% in 2008 and varied across sites. The proportion with unknown drug coverage decreased over time. Drug coverage was imputed for 88 unknown observations between 2007 and 2008, another 836 values were imputed for unknown observations between 2008 and 2013. After exploring the relationship between drug coverage and viral suppression under a variety of plausible missing data mechanisms, we did not observe any substantial differences in estimated prevalence ratios for drug coverage types.

Discussion

Among participants living with HIV in a clinical cohort in Ontario, Canada, we found that viral suppression varied by type of drug coverage. A higher proportion of participants with employer coverage were virally suppressed compared to those who had coverage through ODB. We did find that a high proportion of individuals who were unemployed but seeking work reported paying out of pocket, which may in part be due to delays related to the application process for coverage or the transition between different types of coverage (e.g., applying to public program after losing work benefits). We identified other factors, including current smoking and injection drug use, that were negatively associated with viral suppression. Our findings suggest that even when individuals have access to a provincial drug plan, challenges with adherence and/or accessing ART remain.

Cost-related challenges have been identified as a major barrier for ART access and adherence (McAllister et al. 2013; Johnston et al. 2012; Zamani-Hank 2016). Studies from the US have demonstrated that no insurance and/or financial stress can lead to ART interruptions (Johnston et al. 2012; Zamani-Hank 2016) and a lower likelihood of being virally suppressed (Zamani-Hank 2016; Yehia et al. 2016). In Australia, medication is covered by the Australian Government Pharmaceutical Benefits Scheme, although ART still incurs a co-payment ranging between \$5.60 and \$34.20 per month. A 2012 Australian study noted that co-payments and other competing needs can affect HIV outcomes (McAllister et al. 2013). Similar findings were demonstrated in the current study. In Canada, a higher proportion of HIV-positive residents are on ART in British Columbia, where ART is provided free of charge to all residents living with HIV, in contrast to Ontario, where it is not (Hogg et al. 2012). A national pharmacare plan would not only reduce total spending on prescription drugs, but could address gaps in coverage and disparities within Canada (Yoong et al. 2015; Morgan et al. 2013).

In Ontario, the costs of currently recommended ART regimens are prohibitive (~\$1400/month) (Ontario Ministry of Health and Long-Term Care (MOHLTC) 2014). In their study exploring their compassionate access program, Yoong et al.

Table 1 Characteristics of included participants at baseline and the proportion with suppressed viral load (sVL) in the OCS, 2008–2013 ($n = 1247$)

Variable	Frequency (% of total)	Proportion with sVL	<i>p</i> value
Drug coverage			
Employer	253 (20.3)	243 (96.1)	0.0348+
Co-pay	104 (8.3)	97 (93.3)	
Ontario Drug Benefit	588 (47.2)	534 (90.8)	
Out of pocket	60 (4.8)	55 (91.7)	
Trillium	242 (19.4)	231 (95.5)	
Age			
≤ 35	198 (15.9)	176 (88.9)	0.0128
> 35	1049 (84.1)	984 (93.8)	
Sex/orientation			
Male: MSM	730 (58.5)	687 (94.1)	0.2016
Male: non-MSM/unknown	248 (19.9)	227 (91.5)	
Female	269 (21.6)	246 (91.5)	
Ethnicity/race			
White	775 (62.2)	716 (92.4)	0.3083
ACB	195 (15.6)	183 (93.9)	
Indigenous	171 (13.7)	158 (92.4)	
Other	106 (8.5)	—	
Citizenship and immigration			
Born in Canada	908 (72.8)	839 (92.4)	0.3634
Immigrated ≤ 10 years	143 (11.5)	135 (94.4)	
Immigrated > 10 years	196 (15.7)	186 (94.9)	
Years since HIV diagnosis			
1–< 5	317 (25.4)	296 (93.4)	0.7791
5–< 10	264 (21.2)	243 (92.1)	
≥ 10	666 (53.4)	621 (93.2)	
Years on ART			
1–< 5	449 (36.0)	415 (92.4)	0.8128
5–< 10	277 (21.2)	258 (93.1)	
≥ 10	521 (40.8)	487 (93.5)	
Gross personal income (CAD/year)			
< \$20,000	411 (35.9)	374 (91.0)	0.0289
\$20,000–< \$40,000	264 (23.1)	243 (92.1)	
\$40,000–< \$60,000	155 (13.5)	145 (93.6)	
≥ \$60,000	315 (27.5)	304 (96.5)	
Education			
Some high school or less	253 (20.3)	227 (89.7)	0.0058
Completed high school	235 (18.9)	220 (93.6)	
Trade/some college	194 (15.6)	173 (89.2)	
College/some university	331 (26.5)	317 (95.8)	
University degree(s)	234 (18.8)	223 (95.3)	
Employment status			
Employed full time/part time	512 (41.1)	483 (94.3)	0.3143
Unemployed and seeking	93 (7.5)	84 (90.3)	
Not in the labour force	192 (15.2)	178 (93.7)	
Disability	452 (36.3)	415 (91.8)	
Marital status			
Single	570 (45.7)	529 (92.8)	0.6126
Married/living common-law/committed relationship	516 (41.4)	481 (93.2)	
Separated/divorced	119 (9.5)	109 (91.6)	
Widowed	42 (3.3)	—	
Mental health concerns*			
No	895 (71.8)	845 (94.4)	0.0021
Yes	352 (28.2)	315 (89.5)	
Cigarette smoking (past 30 days)			
Current/occasional smoker	604 (48.4)	544 (90.1)	0.0002
Former smoker	262 (21.0)	255 (97.3)	
Never smoked	381 (30.6)	376 (94.8)	
Hazardous drinking (past year)			
No	846 (67.8)	785 (92.8)	0.6380
Yes	401 (32.2)	375 (93.5)	

Table 1 (continued)

Variable	Frequency (% of total)	Proportion with sVL	<i>p</i> value
Drug use (past 6 months)			
No drug use	1053 (84.4)	981 (93.2)	<i>0.0308</i>
Yes: no injection	133 (10.7)	127 (95.5)	
Yes: injection	61 (4.9)	52 (85.3)	
Interview year			
2008	361 (29.0)	342 (94.7)	<i>0.6284</i>
2009	246 (19.7)	225 (91.5)	
2010	250 (20.1)	230 (92.0)	
2011	169 (13.6)	159 (94.1)	
2012	109 (8.7)	101 (92.7)	
2013	112 (9.0)	103 (92.0)	

ACB African, Caribbean, and Black; *MSM* men who have sex with other men

*A participant was defined as having mental health concerns if they scored ≥ 22 on the 10-item Kessler Psychological Distress Scale or ≥ 23 on the Center for Epidemiologic Studies Depression Scale (CES_D scale)

+*p* = 0.0041 in GEE model adjusting for correlation within participants over time

p-value < 0.05 italicized

(2015) demonstrated that almost 8 years' worth of ART (~\$134,860 CAD) was provided to 42 patients over a 1-year period in order to prevent treatment delays and interruptions (Yoong et al. 2015). Approximately 13% of OCS participants report difficulty paying for ART, reporting that they have had to decide between paying for food, debt, and other medications or their ART at least once in the past year (preliminary analysis findings, April 5, 2018). This trend has also been reported by providers in our setting (Yoong et al. 2015). In this study, patients reporting paying out of pocket for their ART had the lowest levels of suppression, although this was not significantly different from the employer group in our analyses. This may partly be explained by the low number of people reporting that they had to pay out of pocket in our cohort. The OCS, an in-care cohort, likely represents the best case scenario for people living with HIV in Ontario. However, it is worth noting that just over 10% of those who were unemployed but seeking work reported that they had to pay out of pocket. Such individuals may have had employer coverage at one point and are shifting to a public program either with ODB or Trillium or are in the process of looking for a job with coverage. Trillium approval can take approximately 2–3 weeks, if all application pieces are done correctly the first time (much longer if signatures or other information is missing), and for those who have been approved for ODSP, the application can take up to 12 weeks (Personal communication: Deborah Yoong, St. Michael's Hospital, September 5, 2017). Problems with the application process related to Trillium were reported in our setting (Yoong et al. 2015). However, our findings suggest that once an individual is able to get on Trillium, they are able to achieve viral suppression. This suggests that ensuring timely access to and receipt of coverage through the provincial programs can lead to improved HIV-related outcomes.

Our finding that participants on ODB were significantly less likely to be suppressed than those with employer drug

coverage has important implications given that, in this study, almost half of participants had ODB coverage. While we noted a modest effect of ODB coverage, it may be that our ability to see the effects on suppression is limited given that we only looked at the last viral load in each year as recommended by other studies (Gourlay et al. 2017; Medland et al. 2015). While the ODB program covers the majority of drug costs (with the exception of a co-payment), eligibility is restrictive and co-pays can still act as a financial barrier (McAllister et al. 2013). As well, certain doses may not be covered, which can affect pill burden as individuals may have to take multiple pills that are covered to reach the total dosage that is not. ODSP is the most common mechanism for obtaining ODB coverage among OCS participants (preliminary analysis findings, April 5, 2018), and in the current study, 76.1% of participants on disability were on ODB at baseline. While individuals living with HIV who are on disability likely face multiple barriers to achieving viral suppression, including comorbid conditions that require the use of other medications, some individuals may choose to remain in undesirable jobs to receive employer benefits or quit their jobs just to qualify for ODSP (Yoong et al. 2015). This has important implications given that employment has been associated with economic stability and overall improved health for people living with HIV (Richardson et al. 2014; Rueda et al. 2011).

Our finding that individuals who inject drugs (Yehia et al. 2016; Burchell et al. 2015; Lourenco et al. 2014) and those with mental health concerns (Yehia et al. 2016) were less likely to be suppressed is consistent with previous literature. Our results further support the need for pragmatic and targeted interventions, such as supportive care and greater access to treatment for substance misuse, which work to continuously engage in care highly vulnerable populations and ensure continuous access to ART (Higa et al. 2016). Smoking was associated with a decreased likelihood of being virally

Table 2 Unadjusted and adjusted factors associated with viral suppression among participants enrolled in the OCS between 2008 and 2013

Variable	Unadjusted PR (95% CI)	Adjusted ⁺ PR (95% CI)
Drug coverage (vs. employer)		
Co-pay	0.98 (0.94–1.02)	0.97 (0.94–1.01)
Ontario Drug Benefit	<i>0.96 (0.93–0.98)</i>	<i>0.98 (0.95–0.99)</i>
Out of pocket	0.96 (0.90–1.03)	0.95 (0.89–1.01)
Trillium	0.99 (0.97–1.02)	1.00 (0.97–1.03)
Age at follow-up (vs. > 35)		
≤ 35	<i>0.95 (0.92–0.99)</i>	<i>0.95 (0.91–0.99)</i>
Sex/orientation (vs. male: MSM)		
Male: non-MSM/unknown	<i>0.97 (0.93–0.99)</i>	
Female	<i>0.96 (0.93–0.99)</i>	
Ethnicity/race (vs. white)		
ACB	0.99 (0.96–1.02)	
Indigenous	0.98 (0.95–1.02)	
Other	1.03 (0.99–1.06)	
Citizenship and immigration (vs. born in Canada)		
Immigrated ≤ 10 years	1.01 (0.98–1.05)	
Immigrated > 10 years	1.01 (0.99–1.04)	
Years since HIV diagnosis (vs. 10+)		
1–< 5	0.97 (0.94–1.00)	
5–< 10	0.98 (0.96–1.01)	
Years on ART (vs. 10+)		
1–< 5	0.99 (0.96–1.01)	1.00 (0.98–1.03)
5–< 10	0.99 (0.96–1.01)	0.99 (0.97–1.02)
Gross personal income (CAD/year) (vs. ≥ \$60,000)		
< \$20,000	0.96 (0.93–0.98)	
\$20,000–< \$40,000	0.97 (0.95–1.00)	
\$40,000–< \$60,000	0.97 (0.95–1.00)	
Education (vs. university degree(s))		
Some high school or less	<i>0.95 (0.92–0.98)</i>	0.98 (0.94–1.01)
Completed high school	0.97 (0.94–1.00)	0.99 (0.95–1.02)
Trade/some college	0.96 (0.93–1.00)	0.98 (0.94–1.01)
College/some university	0.99 (0.97–1.02)	1.00 (0.98–1.03)
Employment status (vs. employed FT/PT)		
Unemployed and seeking	<i>0.97 (0.95–0.99)</i>	1.01 (0.98–1.03)
Not in the labour force	0.99 (0.97–1.02)	1.01 (0.98–1.02)
Disability	0.98 (0.95–1.02)	1.01 (0.98–1.02)
Marital status (vs. single)		
Married/living common-law/committed relationship	1.00 (0.98–1.02)	
Separated/divorced	0.98 (0.94–1.02)	
Widowed	1.03 (0.99–1.06)	
Mental health concerns* (vs. no)		
Yes	<i>0.96 (0.93–0.98)</i>	<i>0.97 (0.95–0.99)</i>
Cigarette smoking (past 30 days) (vs. never smoked)		
Current/occasional smoker	<i>0.95 (0.93–0.98)</i>	<i>0.97 (0.95–0.99)</i>
Former smoker	1.01 (0.99–1.03)	1.01 (0.99–1.03)
Hazardous drinking (past year) (vs. no)		
Yes	1.01 (0.99–1.03)	
Drug use (past 6 months) (vs. no drug use)		
Yes: no injection	1.00 (0.97–1.03)	1.00 (0.97–1.03)
Yes: injection	<i>0.87 (0.80–0.94)</i>	<i>0.90 (0.83–0.97)</i>

MSM men who have sex with other men, PR prevalence ratio, CI confidence interval

*A participant was defined as having mental health concerns if they scored ≥ 22 on the 10-item Kessler Psychological Distress Scale or ≥ 23 on the Center for Epidemiologic Studies Depression Scale (CES_D scale)

+Adjusted for all variables shown and site

p-value < 0.05 italicized

suppressed; this is consistent with previous literature (Hile et al. 2016). A smoking prevalence of two to three times greater than the general population has been demonstrated among people living with HIV (Hile et al. 2016; Mdodo et al. 2015). Smoking has also been associated with suboptimal adherence (Hile et al. 2016) and higher viral load counts (Cropsey et al. 2016). In our setting, smoking is common among more marginalized and vulnerable populations. Specifically, in our cohort, it has been previously demonstrated that smokers were more likely to be unemployed, have lower education levels, be heavy drinkers and report depression (Bekele et al. 2017). Given that smoking status and drug coverage were highly correlated in the current study, with 62.4% of participants on ODB being smokers, there is need for increased awareness of the benefits of smoking cessation in the context of patchwork drug coverage for people living with HIV in our setting. While race/ethnicity has been shown to play a role in terms of ART access and suppression in the US (Ludema et al. 2016), we did not observe any impact on suppression in this study. This may reflect different healthcare systems and greater equity in our setting in terms of access and ethnicity.

There are several limitations to this study. Misclassification of drug coverage was possible given that it was missing for at least 1 year in 40–50% of participants. To address this, we used multiple imputation methods to examine the sensitivity of our findings to our assumed missing data mechanisms. We considered a wide variety of missing data models (both under the assumption that drug coverage categories were missing at random and under a variety of plausible missing not at random missing data models in which the relative probability of imputing each drug category, in turn, was increased by a range of multiplicative factors) and explored the impact of these different assumptions on our results. After employing these different multiple imputation methods, we found that our point estimates and confidence intervals were not substantially altered, which indicates that our findings are robust and our conclusions were not affected by how we chose to accommodate for the missing data. Furthermore, there was no association between the likelihood of being virally suppressed and an indicator of missing data, so it was not surprising that we observed no indication of bias in our complete case analysis. We also limited our analysis to participants who initiated ART before or during the year with no evidence of having stopped in the given year. Individuals who stopped ART in a given year were more likely to report paying out of pocket and therefore likely to have financial challenges related to poor drug coverage. However, given that only 7% of participants had evidence of stopping ART, we are limited in the sample size to explore this. However, future studies will work to explore and describe

the unique challenges of participants who stop ART. Our ability to see the effects of gaps in ART on viral suppression may be limited given that we only looked at the last viral load (VL) in each year. Blips due to gaps in ART which occurred between those annual VL would not have been captured. However, we used the last VL in the year, as recommended in two recent systematic reviews (Medland et al. 2015; Richardson et al. 2014). Future analyses will explore hospitalizations through linkages to the Institute for Clinical Evaluative Sciences and whether type of drug coverage impacts the likelihood of stopping ART and retention in care. Finally, this is an “in care” and closely monitored cohort of research volunteers, thus our findings may therefore not generalize to non-volunteers or those receiving care in other settings.

Our findings may inform HIV care policy and practice guidelines. Even in a setting with universal public insurance for medically necessary physician and hospital services (as well as a number of other ancillary health services), a lack of universal coverage for ART was associated with inadequate viral suppression. People living with HIV in Ontario continue to face difficulty accessing ART. Given the pivotal place of ART in optimizing HIV treatment outcomes and reducing population-level transmission, strategies that can improve access and reduce financial barriers, including universal coverage for ART, require further exploration in our setting.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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