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ORIGINAL PAPER

Prescription of High-Dose Opioids Among People Living with HIV in British Columbia, Canada

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Abstract

People living with HIV (PLHIV) often experience pain for which opioid medications may be prescribed. Thus, these individuals are particularly vulnerable to opioid-related harms, including overdose, misuse, and addiction, particularly when prescribed at high doses. We used a comprehensive linked population-level database of PLHIV in British Columbia (BC) to identify demographic and clinical characteristics associated with being prescribed any high-dose opioid analgesic, defined as > 90 daily morphine milligram equivalents (MME/day). Among PLHIV who were prescribed opioids between 1996 and 2015 (n = 10,780), 28.2% received prescriptions of > 90 MME/day at least once during the study period. Factors positively associated with being prescribed high-dose opioid analgesics included: co-prescription of benzodiazepines (adjusted odds ratio [AOR] = 1.14; 95% confidence interval 1.11–1.17); presence of an AIDS-defining illness (ADI; AOR = 1.78; 95% CI 1.57–2.02); seen by an HIV specialist (AOR = 1.24; 95% CI 1.20–1.29); substance use disorder (AOR = 1.46; 95% CI 1.25–1.71); and more recent calendar year (AOR = 1.05; 95% CI 1.04–1.06). Given the known risks associated with high-dose opioid prescribing, future research efforts should focus on the clinical indication and outcomes associated with these prescribing practices.

Keywords Prescription opioids · Analgesics · Pain · People living with HIV

Introduction

Historically, pain associated with HIV was primarily due to complications of acquired immune deficiency syndrome (AIDS), including infection, HIV-associated neuropathy, or side effects of medications [1, 2]. Despite the advent of highly-active antiretroviral therapy (ART) and the evolution of HIV into a chronic illness, a systematic review demonstrated that the prevalence of pain among PLHIV continues to range between 54 and 83% and has not diminished over time [3]. Current literature suggests the etiology of pain among PLHIV has evolved to become more multifactorial, often associated with comorbid medical conditions, substance use, and psychiatric illnesses in addition to complications related to HIV [4–6]. There is also evidence to suggest that pain continues to be undertreated in certain populations of PLHIV, including women, people who inject drugs, and those with low socioeconomic status [7–9].

Prescription opioids have traditionally featured prominently in chronic pain management. However, in the general population, there are inherent health risks associated with long-term opioid use, including overdose, misuse, and addiction, particularly when prescribed at high doses [10]. There is also preliminary evidence to suggest that opioids may have additional negative consequences among PLHIV, including impaired immune function, increased virologic failure, and disruption of gut homeostasis which may lead

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to accelerated disease progression [11–13]. Due to the above risks as well as equivocal evidence substantiating efficacy, the Infectious Disease Society of America (IDSA) does not recommend opioids as first line therapy for either non-neuropathic or neuropathic chronic pain [10]. This is similar to established recommendations for pain management in the general population, including the *Canadian Guideline for Opioid Therapy and Chronic Non-Cancer Pain* and World Health Organization's Pain Relief Ladder [14, 15].

Opioid prescription rates have increased steadily in the general population in the past several years. Prescription opioid sales have quadrupled since 1999 in the United States, and similarly, Canada experienced a 250% increase in opioid consumption between 2000 and 2014 [16–18]. Unfortunately, the world has also seen a concurrent rise in opioid overdose rates [16, 19, 20]. Literature suggests that there is a direct correlation with opioid dose and overdose rate, with dosages of 50–100 daily morphine milligram equivalents (MME/day) found to increase risk of overdose by factors of 1.9 to 4.6 relative to low dose regimens of < 20 MME/day [21–24]. The US Centers for Disease Control and Prevention as well as the Canadian Medical Association have both recently published guidelines in 2016 and 2017 respectively which caution clinicians to carefully assess risks and benefits when increasing opioid dosing for chronic non-cancer pain. The recommendation is to use caution when prescribing high-risk regimens, such as > 50 MME/day or co-prescribing opioids with benzodiazepines, and clinicians should avoid dosing over 90 MME/day wherever possible [14, 25]. While these guidelines apply to the population in general, there is evidence to suggest that PLHIV as a specific population also have an increased risk of mortality when prescribed over 50 MME/day [26].

In light of these recent changes in clinical care guidance, this paper examines the trends of current high-dose opioid prescription in British Columbia (BC) among PLHIV. Given the high prevalence of chronic pain among the PLHIV, yet how little is known about the factors that drive high-dose opioid prescriptions for PLHIV, this study also aims to identify demographic and clinical characteristics associated with being prescribed high-dose opioid regimens. We anticipate that these findings will provide evidence to guide the safe and effective management of pain among PLHIV by identifying specific subpopulations who may derive substantial benefit from targeted clinical or policy interventions.

Methods

Study Population

This study was constructed using data from the seek and treat for optimal prevention (STOP) of HIV/AIDS in BC cohort, which is based on a provincial-level linkage of several health administrative databases and disease registries. A detailed description of this cohort can be found elsewhere [27, 28]. In brief, the STOP HIV/AIDS in BC cohort includes the following databases: (1) the BC Centre for Excellence in HIV/AIDS' drug treatment program, which gathers information on antiretroviral therapy dispensations, CD4 cell count measurements, viral load and resistance testing [29]; (2) the BC Centre for Disease Control's HIV testing database, which captures HIV testing and new HIV diagnoses from the BC Public Health Microbiology and Reference Laboratory [30, 31]; (3) the Medical Services Plan (MSP) which documents physician billing services [32]; (4) the Discharge Abstract Database (DAD), which captures information on all hospitalizations within the province [33]; (5) the BC PharmaNet database, which records non-ART-related drug dispensations [32]; and (6) the BC Vital Statistics database, which provides information on deaths [34]. For the present study, we considered all individuals identified as HIV-positive who were prescribed at least one opioid during the study period from January 1st, 1996 to March 31st, 2015. HIV positivity was determined using a validated algorithm [28]. This study was approved by the University of British Columbia–Providence Health Care's Research Ethics Board.

Measures

Consistent with regional and international guidelines, the primary outcome for this study was high-dose opioid regimens, defined in two ways: (a) > 90 MME/day and (b) > 50 MME/day. Overlapping prescriptions in a given dispensation period for each patient were summed to calculate a total MME dose. We chose these cut-off points based on the Canadian Medical Association *Guideline for Opioid Therapy and Chronic Non-cancer Pain* and the U.S. Centers for Disease Control and Prevention *Guidelines for Prescribing Opioids for Chronic Pain* [14, 25]. PharmaNet data was used to obtain prescription dispensation dates and dosage of all opioid agonist and opioid partial agonist prescriptions filled by our study population. Methadone and buprenorphine/naloxone were excluded as these medications are more commonly prescribed for opioid dependence rather than pain in BC, and the inclusion of these specific medications would likely bias our results. For consistency, we converted to morphine milligram equivalents using a standardized conversion chart [35].

We also considered a number of explanatory variables that we hypothesized were associated with high-risk opioid prescribing, and included: age (per 10 year increase); sex (male vs. female); viral load (log10 copies/mL categorized into ranges of < 2.70, 2.70–3.99, 4.00–4.99, and ≥ 5.00) within 6 months prior to dispensation of a high-dose opioid;

CD4 cell count (per 100 cells/mL) within 6 months prior to dispensation of a high-dose opioid; HCV positive serostatus (yes vs. no); history of a substance use disorder based on ICD-9/10 codes, prescriptions of methadone or buprenorphine/naloxone, or identification as a high risk group in the BC-CfE or BCCDC databases, either through self-report or physician-report (yes vs. unknown vs. no); co-prescription of benzodiazepine(s) overlapping opioid prescription by at least 1 day (yes vs. no); documented diagnosis of acute or chronic pain, based on medical service billing and hospitalization records as defined by ICD-9/10 codes (yes vs. no), those with at least one reported AIDS-defining illness during the study period (yes vs. no); those on anti-retroviral treatment at the time of opioid prescription (yes vs. no); and whether the opioid prescriber was an HIV specialist, defined as having previously treated at least five HIV patients as the first prescribing doctor (yes vs. no). We selected these variables a priori based on previous literature [36–38].

Statistical Analyses

First, we performed preliminary summary statistics on our study population to determine the frequency and proportion of being prescribed > 90 MME/day, and stratified the data by year of dispensation. We also conducted a test for linear trend on these proportions. Next, we performed baseline descriptive statistics on our study sample, stratified by the main outcome, > 90 MME/day. Bivariable and multivariable generalized estimating equation (GEE) models were then developed to determine demographic and clinical factors associated with being prescribed > 90 MME/day. Only those variables that were associated with a statistical difference ($p < 0.10$) in bivariable analyses were retained in the multivariable analysis. The most parsimonious model was chosen using the quasilikelihood under independence criterion (QIC). The variance inflation factor (VIF) was small for all variables and there were no issues with multicollinearity. As a sensitivity analysis, we built a second multivariable GEE model with > 50 MME/day as the outcome, using similar statistical procedures as described above. All analyses were performed using SAS software Version 9.4 (SAS Institute, Cary, NC).

Results

We identified 10,780 PLHIV who were prescribed at least one opioid during the study period from January 1996 to March 2015. The majority of participants were male (8719; 80.9%) and the median age was 38 years old (Quartile [Q]1–Q3 = 31–46). Further details on participant characteristics are displayed in Table 1. Of all opioid prescriptions dispensed among our study population (n = 209,026), the median dose was 31.5 MME/day (Q1–Q3 = 19.3–40.1). A total of 3043 (28.2%) participants received a prescription of > 90 MME/day and 6149 (57.0%) participants received a prescription of > 50 MME/day at least once during the study period. When stratified by year of dispensation to statistically examine the proportion of high-risk dosing regimens over time using the Mann–Kendall trend test, a highly significant positive linear relationship was demonstrated for both > 90 MME/day prescriptions (p value < 0.001) and > 50 MME/day prescriptions (p value < 0.001).

Table 2 presents results from bivariable and multivariable GEE analyses for the main outcome, high-dose opioid prescription of > 90 MME/day. We excluded diagnosis

Table 1 Characteristics of study sample at baseline

Characteristic	Total (%) (n = 10,780)	Prescription > 90 MME/day at the first prescription		p Value
		Yes (%) (n = 218)	No (%) (n = 10,562)	
Male sex	8719 (80.9)	181 (2.1)	8538 (97.9)	0.416
Co-prescription of benzodiazepine and opioid	1004 (9.3)	43 (4.3)	961 (95.7)	< 0.001
Positive HCV serostatus	3537 (43.4)	80 (2.3)	3457 (97.7)	0.007
AIDS-defining illness	2428 (22.5)	69 (2.8)	2539 (97.1)	0.001
ARV treatment at prescription	328 (3.0)	15 (4.6)	313 (95.4)	< 0.001
HIV specialist as prescriber	2343 (21.7)	67 (2.9)	2276 (97.1)	0.001
Substance use disorder	4140 (46.0)	100 (2.4)	4040 (97.6)	0.047
Baseline age (median, Q1–Q3)	38 (31, 46)	38 (32, 45)	38 (31, 46)	0.795
Viral load (log10 copies/mL) (median, Q1–Q3)	3.0 (2.7, 4.5)	3.9 (2.7, 4.9)	3.0 (2.7, 4.5)	0.044
CD4 cell count (cell/mm^3) (median, Q1–Q3)	360 (200, 530)	220 (60, 430)	360 (210, 540)	< 0.001
Year of dispensation (median, Q1–Q3)	1999 (1996, 2004)	2000 (1996, 2005)	1999 (1996, 2004)	0.511

Q quartile, *HCV* hepatitis C virus, *ARV* antiretroviral

Table 2 Bivariable and multivariable generalized estimating equation modeling of factors associated with being prescribed > 90 MME/day

Characteristic	Odds ratio (OR)	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Baseline age (per 10-year increase)	0.99 (0.94–1.05)	–
Sex (male vs. female)	1.09 (0.93–1.28)	–
Co-prescription of benzodiazepine and opioid (yes vs. no)	1.15 (1.13–1.18)*	1.14 (1.11–1.17)*
Positive HCV serostatus		
Yes versus no	1.25 (1.06–1.47)	–
Unknown versus no	1.12 (0.93–1.35)	–
AIDS-defining illness (yes vs. no)	1.92 (1.71–2.16)*	1.78 (1.57–2.02)*
ARV treatment at prescription (yes. vs. no)	0.87 (0.83–0.91)*	0.87 (0.83–0.91)*
HIV specialist as prescriber	1.29 (1.25–1.34)*	1.24 (1.20–1.29)*
Substance use disorder		
Yes versus no	1.35 (1.15–1.57)*	1.46 (1.25–1.71)*
Unknown versus no	0.80 (0.64–1.01)	1.02 (0.81–1.29)
CD4 cell count (per 100 cells/mm^3)	0.99 (0.98–1.00)	–
Viral load (log10 copies/mL)†		
Continuous	0.97 (0.94–0.99)*	–
2.70–3.99 versus < 2.70	0.89 (0.85–0.94)*	0.97 (0.92–1.03)
4.00–4.99 versus < 2.70	0.91 (0.86–0.95)*	1.02 (0.97–1.07)
≥ 5.00 versus < 2.70	0.94 (0.89–1.00)	1.05 (0.99–1.12)
Unknown versus < 2.70	0.78 (0.74–0.83)*	0.96 (0.91–1.02)
Year of dispensation	1.05 (1.05–1.06)*	1.05 (1.04–1.06)*

CI confidence interval, *HCV* hepatitis C virus, *ARV* antiretroviral

*Significant at $p < 0.05$

†Viral load was treated as categorical for the multivariable model due to a high proportion of missing observations within 6 months of initial opioid dispensation date

of acute or chronic pain from further analysis given that only a small proportion (0.002%) had a diagnosis on file using ICD-9/10 codes. We believed this was likely due to a systems-level issue of under-documentation of pain diagnoses which could have potentially led to large variability and inconclusive results. In multivariable analyses, participants who were co-prescribed a benzodiazepine (adjusted odds ratio [AOR] = 1.14, 95% confidence interval [CI]: 1.11–1.17), those with an AIDS-defining illness (AOR 1.78, 95% CI 1.57–2.02), those whose opioid was prescribed by an HIV specialist (AOR 1.24, 95% CI 1.20–1.29), and those who were identified as having a history of any kind of substance use disorder (AOR 1.46, 95% CI 1.25–1.71) were more likely to receive a prescription for > 90 MME/day. We also found that year of dispensation was a significant continuous variable, whereby participants who received opioids 1 year later were more likely to receive a high-dose prescription compared to the year before (AOR 1.05, 95% CI 1.04–1.06). Of note, HCV serostatus was not included in multivariable analysis as it was found to be highly collinear with a history of substance use disorder. In addition, we found that participants who were on antiretroviral treatment at the time of opioid prescription were less likely to receive a prescription for > 90 MME/day (AOR 0.87, 95% CI 0.83–0.91).

Bivariable and multivariable GEE analyses for the secondary outcome of opioid analgesia regimen of > 50 MME/day are displayed in Table 3. Those more likely to receive > 50 MME/day in multivariable analysis included: males (AOR 1.13; 95% CI 1.00–1.27), participants with co-prescription of benzodiazepines (AOR = 1.19, 95% CI 1.16–1.23), those with an AIDS-defining illness (AOR 1.71, 95% CI 1.53–1.90), those with a viral load ≥ 5.00 (AOR 1.11, 95% CI 1.04–1.19), those who received opioids in a more recent calendar year (AOR 1.06, 95% CI 1.05–1.06), as well as those who were prescribed > 50 MME/day by an HIV specialist (AOR 1.10, 95% CI 1.05–1.15). Participants who were on antiretroviral treatment at the time of opioid prescription were less likely to receive a prescription for > 50 MME/day (AOR 0.87, 95% CI 0.83–0.90).

Table 3 Bivariable and multivariable generalized estimating equation modeling of factors associated with being prescribed > 50 MME/day

Characteristic	Odds Ratio (OR)	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Baseline age (per 10-year increase)	1.01 (0.97–1.05)	–
Sex (male vs. female)	1.17 (1.05–1.32)*	1.13 (1.00–1.27)*
Co-prescription of benzodiazepine and opioid (yes vs. no)	1.18 (1.14–1.21)*	1.19 (1.16–1.23)*
Positive HCV serostatus		
Yes versus no	0.95 (0.85–1.06)	–
Unknown versus no	0.91 (0.80–1.04)	–
AIDS-defining illness (yes vs. no)	1.89 (1.71–2.10)*	1.71 (1.53–1.90)*
ARV treatment at prescription (yes vs. no)	0.87 (0.84–0.91)*	0.87 (0.83–0.90)*
HIV specialist as prescriber	1.19 (1.14–1.24)*	1.10 (1.05–1.15)*
Substance use disorder		
Yes versus no	0.99 (0.89–1.11)	–
Unknown versus no	0.83 (0.71–0.97)*	–
CD4 cell count (per 100 cells/mm^3)	0.98 (0.97–1.00)	–
Viral load (log10 copies/mL)†		
Continuous*	0.95 (0.93–0.97)*	–
2.70–3.99 versus < 2.70	0.85 (0.81–0.90)*	1.00 (0.95–1.06)
4.00–4.99 versus < 2.70	0.87 (0.82–0.91)*	1.05 (0.99–1.11)
≥ 5.00 versus < 2.70	0.92 (0.86–0.97)*	1.11 (1.04–1.19)*
Unknown versus < 2.70	0.69 (0.65–0.73)*	0.92 (0.87–0.99)*
Year of dispensation	1.06 (1.05–1.06)*	1.06 (1.05–1.06)*

CI confidence interval, *HCV* hepatitis C virus, *ARV* antiretroviral

*Significant at $p < 0.05$

†Viral load was treated as categorical for the multivariable model due to a high proportion of missing observations within 6 months of initial opioid dispensation date

Discussion

During our study period, we found that over one quarter of PLHIV who received prescription opioid analgesics were prescribed a high-risk dosing regimen of > 90 MME/day and over half were prescribed > 50 MME/day. To the best of our knowledge, the few available studies which examined trends of high-dose opioid prescription among PLHIV examined the US Veteran population and used > 120 MME/day as the cutoff point, making them somewhat difficult to compare with our study. Nevertheless, these studies found that 5–8% of participants receiving opioids were prescribed > 120 MME/day [39, 40]. Despite demographic differences, studies of higher dose opioids in the general population demonstrate similar findings to ours. For example, an analysis of Medicaid patients in Washington State found that 23% of opioid users received > 90 MME/day in 2010 [41] and a study of over 1.2 million disabled United States Medicare beneficiaries on chronic opioid therapy found that 19.8% were prescribed > 100 MME/day [42]. Additionally, we found that there was a trend towards higher opioid dosing over time during our study period, which is consistent with both Canadian and American studies examining opioid prescribing patterns in the general population [43, 44].

Our study demonstrated that presence of an AIDS-defining illness and high viral load, both markers of disease severity, were also positively correlated with high-dose prescription opioid use. This is an expected finding as patients with more advanced disease and AIDS diagnoses generally experience more pain as a consequence of their illness [45–47]. Given an expanding body of literature suggesting that opioids alter immune regulation and may accelerate disease progression, one could speculate whether high-risk opioid dosing contributes to, rather than simply being an effect of, more severe disease [12, 13].

In addition, we found that participants who were on antiretroviral therapy at the time of opioid prescription were less likely to be prescribed high-dose opioids. This was an expected finding as patients on antiretroviral therapy are likely to experience better control of their disease, although evidence is conflicting as to whether the incidence of chronic pain is lower in patients on antiretroviral therapy [3]. There are likely confounding social and structural factors associated with antiretroviral access and adherence that were not captured in our data that may also be protective against

high-dose prescription opioid use [48]. In addition, it is possible that patients on antiretroviral therapy may be more likely to be on methadone maintenance therapy, which was an excluded opioid from our study [49, 50].

We also found that PLHIV who were prescribed high-dose opioids were more likely to have an overlapping benzodiazepine prescription. Co-prescription of benzodiazepines and opioids is well-documented to increase risk of fatal overdose and though concerning, our finding was not unexpected [21, 26, 44, 51, 52]. Previous evidence in the general population has demonstrated that patients prescribed higher doses of opioids were more likely to be prescribed concurrent sedatives [53, 54]. In particular, PLHIV are often co-prescribed these medications because of concurrent issues of mental health, pain, and addiction [36, 55, 56]. However, Weisberg et al. studied concurrent opioid and benzodiazepine use specifically among PLHIV and found that mortality risk was increased for patients receiving both long-term opioids and benzodiazepines when opioid doses were ≥ 20 MME/day, compared to ≥ 50 MME/day when patients were prescribed opioids alone [26]. Their finding suggests a dose-dependent relationship in our population of interest. Our study indicates that PLHIV in BC are at risk of the consequences associated with co-prescription of opioids and sedating medications, which should prompt careful consideration of prescribing practices among clinicians who treat these individuals.

Our study adds to the literature by demonstrating that HIV specialists are more likely to prescribe high-dose opioids compared to non-HIV specialists. One possible explanation is that HIV specialists may prioritize retention of care and the patient–physician relationship over guideline-based opioid prescribing practices or they may have less experience in non-opioid chronic pain management and addiction care compared to primary care physicians [57]. It is also possible that there are confounding factors that were not captured by our data. For example, patients with access to an HIV specialist may be more likely to live in an urban setting where opioid prescribing practices may differ from remote areas. Nevertheless, this is a concerning finding and further investigation into opioid prescribing practices of HIV specialists may be useful to examine factors that affect decision-making and identify strategies to ensure safe symptom management.

We found that history of a substance use disorder was associated with receipt of > 90 MME/day. This is consistent with similar studies demonstrating that high-dose opioid prescribing was positively associated with substance use disorders [39, 40]. However, our study did not demonstrate this relationship with receipt of > 50 MME/day. One possible explanation for this discrepancy may be that individuals with a history of a substance use disorder may be more likely to seek concurrent prescriptions for multiple providers, perhaps for misuse or diversion, which could manifest as a higher dispensed MME/day than any one clinician intended to prescribe [58]. Further studies may be warranted to determine whether our finding could be related to patient, provider, or perhaps other factors not captured in the present study.

We also found that males were more likely than females to receive a high-risk opioid dosing regimen of > 50 MME. To the best of our knowledge, this is the first study to demonstrate a relationship between male sex and high-risk prescription opioid dosing specifically in PLHIV. Our finding is consistent with a recent large cohort study of the general population in Ontario, Canada which found that males were more likely to experience escalation to high-dose opioid therapy compared to females [59]. These findings are concerning for a number of reasons. Firstly, the same study by Kaplovich et al. also found that males are twice as likely to die from opioid-related causes. With respect to our population of interest, there is also evidence that men living with HIV are more likely than women living with HIV to misuse prescription opioids [8]. From another perspective, our finding that women are less likely to be prescribed higher dose opioids may also be pertinent to the large body of literature suggesting females living with HIV are more likely than males to be undertreated for pain [7, 8, 46]. While it is difficult to speculate the cause of these discrepancies from existing data, further studies into gender-related factors that influence opioid prescribing patterns are certainly warranted.

Our study has several limitations. Firstly, our main outcome measure of milligram morphine equivalents was obtained using PharmaNet data, which only documents opioids that were dispensed in BC. It does not capture opioids that were dispensed elsewhere or obtained by illicit means. Secondly, our calculation of daily MME using dispensation dates and dosages assumed that study participants were taking their medications as prescribed. We understand that pain medications are often consumed only as needed and thus consumption may be overestimated by pharmacy records. However, there is data to suggest that this method is a valid measure for measuring drug exposure in a population [60]. We also encountered another limitation when we attempted to include chronic and acute pain diagnoses using ICD 9/10 codes in our analysis. We found that the number of instances where pain diagnoses were actually billed by clinicians was staggeringly low (0.002%) and given that rates of pain in the PLHIV population range from 39 to 55% in other studies [4, 5, 61, 62], this variable was removed from further analysis. We suspect physicians are prioritizing other diagnostic codes when billing and thus under-capture pain diagnoses using this measure. In addition, our data could not distinguish whether high doses of opioids were prescribed appropriately or inappropriately. Nevertheless, guidelines caution against prescribing > 90 MME/day so our findings were relevant regardless [14, 25]. It is also important to note that this study was conducted prior to the release of these guidelines

and impact of these recommendations remains to be evaluated. Lastly, our study environment in British Columbia bears unique demographics and health care practices, and our results may not be generalizable to other populations.

In summary, we found that among PLHIV who received opioids, over a quarter received high-dose opioids of > 90 MME per day and a majority received an opioid dosing regimen that is considered by guidelines to be high-risk [14, 25]. We found that PLHIV with comorbid conditions and high HIV disease severity were more likely to be prescribed high-dose daily MME. We also found that those who were co-prescribed benzodiazepines and those who were seen by an HIV specialist were also more likely to be prescribed high-dose daily MME. Our results should be interpreted with caution because there are cases where high-dose opioids are indicated. However, we feel that we have identified several subpopulations that could be targeted with clinical point of care modifications, professional education, or health care policies to effectively reduce the rate of high-dose prescription opioid use among PLHIV. For example, implementing physician alerts to co-prescription of benzodiazepines, mandating screening for substance use disorders when prescribing high-dose opioids, or providing HIV specialists with more robust training in the management of chronic pain are possible interventions which may have a substantial impact on the safety of prescription opioid receipt among PLHIV.

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