Opioid misuse among persons with HIV engaged in care in the Southeastern US

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ABSTRACT

The prevalence of opioid misuse by people living with HIV (PLWH) during the current US opioid epidemic has not been fully described. Among a cohort of persons engaged in HIV care in North Carolina, we examined the prevalence of and risk factors for opioid misuse, defined as self-reported "street" opioid use (e.g., heroin) or nonmedical prescription opioid use on a patient reported outcomes survey. Recent (past three-month) opioid misuse among 1,440 PLWH in care 2012–2017 was 2% (95% CI 2-3%) and lifetime misuse 15% (13-16%). Persons reporting lifetime or recent misuse more commonly had hepatitis C and reported injecting drugs. In multivariable logistic regression models, male-to-male sexual contact was inversely associated with recent or lifetime misuse. White/non-Hispanic race/ethnicity was associated with lifetime misuse and CD4 count and viral load were not associated with opioid misuse. Among 32 persons reporting recent misuse, 81% had a contemporaneous viral load <50 copies/mL. In this cohort of PLWH engaged in care, recent opioid misuse prevalence was similar to general population estimates. Assessments of opioid misuse among PLWH not in care are urgently needed to fully characterize the impact of opioids on all PLWH.

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Introduction

The opioid epidemic has substantially impacted public health in the United States (US). In addition to mounting drug overdose deaths, opioids have also been linked to outbreaks of HIV from injection drug use (IDU), increases in hepatitis C and hospitalizations for severe bacterial infections, such as infective endocarditis (Centers for Disease Control and Prevention, 2017; Cranston et al., 2019; Peters et al., 2016; Ronan & Herzig, 2016). According to national data, IDU-associated HIV diagnoses are no longer declining in the US, and are increasing among persons who are White, young, and reside in the Midwest. (Lyss, Zhang, & Oster, 2018).

North Carolina (NC) has been significantly impacted by the opioid crisis. Annual unintentional opioid overdose deaths have skyrocketed from 109 in 1999 to 1,384 in 2016 (Kansagra & Cohen, 2018). Markers of widespread IDU are apparent in NC, including sharp rises in hepatitis C diagnoses and a twelve-fold increase in IDU-related infective endocarditis (Kansagra & Cohen, 2018; Schranz, Fleischauer, Chu, Wu, & Rosen, 2019). However, new HIV diagnoses have remained stable from 2013–2017 (15.2-16.3 per 100,000), and the proportion with IDU or combined IDU and male-to-male sexual contact (MSM) as a risk factor have also been essentially unchanged (North Carolina HIV/STD/Hepatitis Surveillance Unit, 2018).

The impact of the opioid epidemic on persons already living with HIV (PLWH) has not been well defined. Although substance use disorders were found to be highly prevalent among PLWH, present in 48% of persons in a large multicenter cohort of persons in care, opioid use disorder was the least common, affecting only 4% (Hartzler et al., 2017). Other studies have generated conflicting estimates of the prevalence of past-year opioid misuse among PLWH ranging from 3 to 12% (Lemons et al., 2019; Turner et al., 2016). Yet, PLWH may be at especially high risk of opioid misuse, as they are frequently prescribed opioids for chronic pain and receive higher doses than other populations. (Brunet, Napravnik, Heine, Leone, & Eron, 2017; Edelman et al., 2013).

Opioid misuse among PLWH poses a risk to both patient and public health. Recent data has linked opioid misuse to lower rates of viral suppression (Lemons et al., 2019). Substance misuse is associated with adverse outcomes among PLWH, such as non-receipt of antiretroviral therapy, poor retention in care and mortality (DeLorenze, Weisner, Tsai, Satre, & Quesenberry, 2011; Meyer, Althoff, & Altice, 2013; Rebeiro et al.,

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2013). Improving HIV outcomes, such as viral suppression, among persons who misuse opioids can also help stem ongoing transmission of HIV. PLWH who misuse opioids and are not virally suppressed may pose a greater risk at introducing HIV into networks of HIV-uninfected persons who use drugs. Substance misuse has been linked to higher-risk sexual practices, such as condomless sex, in addition to IDU (Clayton, Lowry, August, & Jones, 2016; Friedman et al., 2017). Understanding opioid misuse among PLWH in the setting of the current opioid epidemic is foundational to identifying opportunities to improve care and enhance pathways for delivering medications for opioid use disorder.

In this study, we estimated the prevalence of recent and lifetime opioid misuse in a large cohort of PLWH in NC. We examined demographic and clinical factors associated with opioid misuse, and the prevalence of viral suppression among persons misusing opioids.

Methods

The University of North Carolina (UNC) Center for AIDS Research HIV Clinical Cohort (UCHCC) collects longitudinal clinical and demographic data on patients ≥18 years of age seen for HIV care at UNC (Napravnik et al., 2006). For this study, we included all patients in care from April 2012 to December 2017. Since April 2012, patients also complete computer-based patient reported outcomes (PRO) surveys at four to six month intervals during clinical visits (Fredericksen et al., 2012). The PROs include the modified Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), a brief instrument developed by the World Health Organization to screen for substance use in primary care. ASSIST questions pertaining to illicit or prescription opioid misuse ask about lifetime and past three-month misuse (Supplemental Table 1).

Opioid misuse was defined as a response to either "street" opioid use, such as heroin, or nonmedical use of prescription opioids. Participants were categorized as recent (any use in the past three months), ever (lifetime but not past three months) and never opioid misuse. Opioid misuse was the condition of interest, not opioid use disorder, which is the psychiatric diagnosis for a problematic pattern of opioid use. We chose opioid misuse in order to broadly capture any participants at-risk for drug-related HIV transmission, which may include sexual transmission among drug using partners, or transmission via IDU. Lifetime IDU was based on PRO questions. MSM as transmission risk factor was determined at the time of entry to care at UNC. Hepatitis C status was based on abstracted diagnoses indicating infection at any point during the study period or prior. Viral suppression at PRO date was defined by the nearest HIV RNA six months prior or three months after being <50 copies/mL. CD4 count was determined by the nearest CD4 twelve months prior or six months after the PRO date.

We included data from the latest PRO reporting recent opioid misuse. For those who reported lifetime misuse but not recent misuse, we included the latest PRO reporting lifetime misuse. For patients never reporting any opioid misuse, the most recent PRO was included. To estimate age and length of time in care for all patients we used data most proximal to September 16, 2016 (the median date of PRO completion). This was done to avoid making never misuse patients appear to have older age and more years in care, since they were evaluated based upon their most recent PRO available.

Unadjusted and multivariable logistic regression models were created to evaluate the association between demographic and clinical factors with (1) recent opioid misuse, and (2) either recent or lifetime opioid misuse. Multivariable models adjusted for age, gender, race/ethnicity, MSM, years in care, CD4 cell count and viral suppression. Analyses were performed with SAS v9.4 (SAS Institute, Cary, NC). The study was approved by the UNC institutional review board.

Results

Of 2,170 participants in care during the study period, 1,545 completed at least one PRO. A total of 3,420 PROs were completed; however, we excluded 433 PROs due to nonresponse to questions pertaining to lifetime opioid misuse. Most (>69%) of the PROs with missing opioid misuse responses also had missing information on other survey questions indicating the PRO survey was not completed.

1,440 unique participants completed at least one eligible PRO during the study period and were included in the analysis. Of those, 35 or 2% (95% confidence interval 2-3%) reported opioid misuse in the past three months, 210 or 15% (13-16%) reported ever misusing opioids in their life (but not in the past three months), and 1,195 or 83% (81-85%) never misused opioids (Table 1). Patients reporting lifetime misuse were older than those reporting recent or never misuse (median age 53, 51, 48 years, respectively). Black/non-Hispanic was the most common race/ethnicity in all groups, comprising 56% overall. Median years in care differed between recent misuse (5), lifetime misuse (11) and never misuse (8). Self-reported lifetime IDU was more common in recent (33%) or ever misuse (30%) vs. never misuse (5%). Of persons reporting recent or lifetime opioid misuse, 81% and 90%, respectively, were

Table 1. Demographic and clinical characteristics of persons living with HIV, stratified by self-reported opioid misuse.[a]

	Total n (%)	Recent (past 3 months) n (%)	Ever n (%)	Never n (%)
Total	1440	35 (2)	210 (15)	1,195 (83)
Age, median (IQR)	49 (38-56)	51 (34-55)	53 (43-60)	48 (38-55)
Male Gender	1,038 (72)	26 (74)	155 (74)	857 (72)
Race/Ethnicity				
Black/non-Hispanic	802 (56)	21 (60)	104 (50)	677 (57)
White/non-Hispanic	490 (34)	12 (34)	88 (42)	390 (33)
Hispanic, Other, Unknown	148 (10)	2 (6)	18 (9)	128 (11)
MSM[b]				
No	611 (42)	17 (49)	96 (46)	498 (42)
Yes	728 (51)	13 (37)	98 (47)	617 (52)
Lifetime Injection Drug Use[c]	102 (12)	11 (33)	62 (30)	29 (5)
Hepatitis C[d]	208 (14)	9 (26)	69 (33)	130 (11)
Years in care, median (IQR)[e]	9 (4-16)	5 (2-15)	11 (5-17)	8 (4-15)
CD4 cell count, median (IQR)[f]	626 (436-853)	646 (366-950)	640 (410-858)	626 (440-850)
Viral Suppression[g]				
Suppressed	1,193 (87)	26 (81)	182 (90)	985 (87)
Not Suppressed, on ART	147 (11)	6 (19)	16 (8)	125 (11)
Not Suppressed, not on ART	31 (2)	0	5 (2)	26 (2)

Table 1 Legend: Results include clinical data and patient reported outcomes drawn from the University of North Carolina Center for AIDS Research Clinical Cohort from April 2012 to December 2017.

[a]Prescription and illicit opioid misuse were assessed via self-report on the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) measure.

[b]MSM, men who have sex with men, as transmission risk factor is based on abstraction from chart review. MSM was unknown for 101 participants (5, 16 and 80 for recent, lifetime and never misuse, respectively).

[c]Injection drug use as self-reported on the ASSIST measure. Responses were missing for 612 participants (2, 6 and 604 for recent, lifetime and never misuse, respectively).

[d]Hepatitis C defined as ever being diagnosed with Hepatitis C by the end of the study period, as per information abstracted from the medical record.

[e]Since years in care was centered on September 16, 2016, 14 participants were coded as −1 year in care (0, 2 and 12 for recent, lifetime and never misuse, respectively).

[f]CD4 count measured as cells/mm^3. CD4 count results were missing for 45 participants (0, 6 and 39 for recent, lifetime and never misuse, respectively).

[g]Viral suppression as determined by HIV RNA <50 copies/mL. ART, antiretroviral therapy, known use at the time of PRO response. Combined HIV RNA and ART status was missing for 69 participants (3, 7 and 59 for recent, lifetime and never misuse, respectively).

virally suppressed. The median CD4 cell count and proportion of persons who were virally suppressed did not differ across strata of opioid misuse.

In univariate models, patients reporting injection drug use were more likely to report recent opioid misuse (OR 3.87, 95% CI 1.82-8.24, Table 2). In multivariable models, recent opioid misuse was inversely associated with MSM (OR 0.33, 95% CI 0.12-0.86), but not associated with any other characteristic. When examining recent or lifetime opioid misuse in univariate models, older patients had an OR of 1.22 per ten-year increase in age (95% CI 1.08-1.37) and White/non-Hispanic race/ethnicity had an OR of 1.39 compared to Black/non-Hispanic individuals (95% CI 1.04-1.86). Injection drug use (8.62, 5.42-13.72), hepatitis C infection (3.83, 2.77-5.29) and years in care (1.02, 1.00-1.04) were also associated with reporting either recent or lifetime opioid misuse. In multivariable models, MSM was inversely associated with recent or lifetime misuse (0.54, 0.36-0.81). White/non-Hispanic race/ethnicity (1.72, 1.23-2.40) was still associated with reporting either recent or lifetime misuse in multivariable models.

In a sensitivity analysis using gender and MSM risk as a combined variable in adjusted models, compared to MSM, heterosexual men were more likely to report recent misuse (3.07, 1.17-8.04) and recent or lifetime misuse (1.85, 1.22-2.79), but there was no association with women. To estimate the potential impact of adjusting for hepatitis C infection and lifetime IDU, we conducted two additional sensitivity analyses. In one analysis including hepatitis C infection as a covariate, adjusted estimates were similar to the main findings for both recent misuse and recent or lifetime misuse, but less precise, with an OR of recent or lifetime misuse for MSM of 0.66 (0.43-1.01). Hepatitis C was associated with recent or ever misuse use (3.53, 2.41-5.16) but not recent misuse (1.45, 0.51-4.11). In a subgroup analysis of patients with lifetime IDU and other covariates available (N = 721), in adjusted models also including both hepatitis C infection and lifetime IDU, all estimates were similar to the main findings but less precise, with an OR comparing White/non-Hispanic to Black/non-Hispanic patients of 1.45 (0.97-2.15). In that model IDU was strongly associated with recent (4.21, 1.49-11.93) and recent or lifetime misuse (6.71, 3.90-11.53) but hepatitis C was no longer associated with either timeframe of opioid misuse.

Discussion

In this cohort of PLWH who are engaged in HIV care, prevalence of self-reported recent opioid misuse was

Table 2. Univariate and multivariable models of the association between demographic and clinic factors and recent or lifetime opioid misuse.

	Unadjusted Odds Ratio (95% CI)		Adjusted Odds Ratio (95% CI)	
	Recent	Recent or Ever	Recent	Recent or Ever
Age, per 10-year increase	0.84 (0.64-1.10)	1.22 (1.08-1.37)	0.80 (0.57-1.13)	1.06 (0.92-1.22)
Male Gender	1.12 (0.52-2.42)	1.12 (0.82-1.52)	1.73 (0.64-4.62)	1.54 (0.99-2.38)
Race/Ethnicity				
Black/non-Hispanic	1	1	1	1
White/non-Hispanic	0.93 (0.46-1.92)	1.39 (1.04-1.86)	1.28 (0.56-2.93)	1.72 (1.23-2.40)
Hispanic, Other, Unknown	0.51 (0.12-2.20)	0.85 (0.51-1.41)	0.58 (0.13-2.59)	0.97 (0.55-1.70)
MSM[a]				
No	1	1	1	1
Yes	0.64 (0.31-1.32)	0.79 (0.60-1.06)	0.33 (0.12-0.86)	0.54 (0.36-0.81)
Lifetime Injection Drug Use[b]	3.87 (1.82-8.24)	8.62 (5.42-13.72)	-	-
Hepatitis C[c]	2.10 (0.97-4.54)	3.83 (2.77-5.29)	-	-
Years in care	0.96 (0.91-1.01)	1.02 (1.00-1.04)	0.97 (0.91-1.03)	1.02 (1.00-1.04)
CD4 count, per 100-cell/μL increase[d]	1.01 (0.91-1.12)	1.00 (0.96-1.04)	0.98 (0.86-1.11)	1.00 (0.95-1.05)
Viral Suppression[e]				
Not Suppressed	1	1	1	1
Suppressed	0.72 (0.29-1.76)	1.24 (0.81-1.89)	0.85 (0.32-2.29)	1.07 (0.68-1.69)

Table 2 Legend: Results include clinical data and patient reported outcomes drawn from the University of North Carolina Center for AIDS Research Clinical Cohort from April 2012 to December 2017.

[a]MSM, men who have sex with men, as transmission risk factor is based on abstraction from chart review. MSM was unknown for 101 participants (5, 16 and 80 for recent, lifetime and never misuse, respectively).

[b]Injection drug use as self-reported on the ASSIST measure. Responses were missing for 612 participants (33, 204 and 591 for recent, lifetime and never misuse, respectively).

[c]Hepatitis C defined as ever being diagnosed with Hepatitis C by the end of the study period, as per information abstracted from the medical record.

[d]CD4 count modeled linearly. CD4 count results were missing for 45 participants (0, 6 and 39 for recent, lifetime and never misuse, respectively).

[e]Viral suppression as determined by HIV RNA <50 copies/mL. HIV RNA was missing for 48 participants (3, 5 and 40 for recent, lifetime and never misuse, respectively).

2% between 2012 and 2017. White/non-Hispanic race/ethnicity was associated with recent or lifetime opioid misuse, and MSM contact was inversely associated with recent or lifetime misuse. In sensitivity analyses, compared to MSM, heterosexual men were more likely to report recent or lifetime misuse. Among 32 persons reporting recent opioid misuse with available viral loads, 81% were recently virally suppressed. Viral suppression and CD4 count were not associated with opioid misuse.

Opioid misuse among PLWH in this cohort was generally consistent with estimates in the overall population in North Carolina. In the 2015–2016 National Surveys on Drug Use and Health (NSDUH), 4.7% and 0.4% of persons over 18 years of age reported past-year prescription pain reliever and heroin use, respectively (Substance Abuse and Mental Health Services Administration, 2018).

Among PLWH, existing estimates of opioid misuse vary widely. We found a slightly lower prevalence of misuse than in a large study of over 28,000 PLWH in the US through the Medical Monitoring Project, which observed a prevalence of opioid misuse of 3.3% over a past twelve-month period (Lemons et al., 2019). That study found that a lower proportion of persons misusing opioids were virally suppressed (59%), compared with those not misusing opioids (69%). An evaluation of PLWH at two clinics in Ohio found that 11-12% reported non-medical use of prescription opioids over the prior year, a proportion that is over twice the estimate of 4.6% in the general Ohio population (Substance Abuse and Mental Health Services Administration, 2018; Turner et al., 2016). Another study in two HIV clinics in Atlanta and Boston found that, among PLWH prescribed chronic opioids, 43% scored highly on a measure assessing risk of past 30-day prescription opioid misuse, and 5% reported illicit opioid use in the past year (Colasanti et al., 2018). Since previous studies have typically captured the prevalence of past-year misuse, our findings add additional information about the prevalence of even more recent opioid misuse. These variations in the frequency of opioid misuse within different populations of PLWH may relate to regional differences in socioeconomic contexts, drug use practices and physician opioid prescribing, although further information is needed.

Half of our study population included persons with a history of MSM, and we found that MSM was strongly inversely associated with misusing opioids recently. However, MSM, substance misuse and HIV do intersect in NC, where roughly half of all new IDU-associated HIV diagnoses from 2013–2017 included MSM as a co-risk factor for transmission (North Carolina HIV/STD/Hepatitis Surveillance Unit, 2018). HIV diagnoses among persons with both MSM and IDU as risk factors may represent use of drugs other than opioids, such as methamphetamine, which is the most commonly injected drug among MSM who are not HIV-infected (Finlayson et al., 2011).

The demographic profile of PLWH reporting opioid misuse in our study differed from the general population affected by opioid overdoses in NC. In 2017, overdose deaths were primarily White (86%), men (67%) and aged 25–45 (55%) (Kaiser Family Foundation, n.d.). Accordingly, this matched the profile of those involved in a recent outbreak of HIV in another state linked to injected opioids (Peters et al., 2016), in which persons involved were largely young and white. Our population, which was primarily middle-aged and Black, should call attention to other demographic groups impacted by opioids. Further, our population represents persons with existing HIV diagnoses and who are engaged in care. The proportion of PLWH in our study with suppressed HIV RNA did not meaningfully differ by strata of opioid misuse and was particularly high (81-90%), exceeding the proportion of PLWH who are virally suppressed in North Carolina overall (62%) (North Carolina HIV/STD/Hepatitis Surveillance Unit, 2018). In addition to indicating good clinical outcomes, this finding suggests that only a small proportion of PLWH engaged in care who misuse opioids may be at-risk of contributing to HIV transmission.

The strengths of this study include surveys on substance use among almost 1,500 patients combined with clinical data, and being located in a US region severely affected by both the HIV and opioid epidemics. We relied on self-reported drug use behaviors. Although persons might be reluctant to disclose these behaviors in a survey, prior work using this questionnaire in a similar setting suggests that PROs likely provide more reliable data on substance use than electronic health records (Kozak et al., 2012). Due to the nature of the data collected by the modified ASSIST survey, our analysis focused on 3-month and lifetime use, which makes direct comparisons to the general population in the NSDUH challenging, and does not explicitly ask about current use. Lastly, this study included PLWH attending routine HIV care visits, and our findings may not be generalizable to PLWH who are not engaged in care. Out-of-care PLWH may have a higher prevalence of ongoing opioid misuse and be less likely to be virally suppressed, which would have important implications for HIV transmission.

In summary, in this cohort of PLWH engaged in clinical care in the Southeastern US, prevalence of recent opioid misuse was 2.4%. Persons reporting recent or lifetime opioid misuse were largely virally suppressed and had similar CD4 counts than those who never misused opioids. Further studies evaluating opioid misuse, IDU and viral suppression specifically among patients not engaged in care are needed to elucidate the impact of the opioid epidemic on PLWH across the spectrum of engagement in care.

Disclosure statement

JJE is ad hoc consultant to ViiV healthcare, Gilead Sciences, Merck and Janssen; and investigator on research contracts to the University of North Carolina from ViiV Healthcare, Gilead Sciences and Janssen. All other authors declare no conflicts.

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