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Prevalence and Impact of Comorbid Chronic Pain and Cigarette Smoking among People Living with HIV

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Abstract

Rates of chronic pain and cigarette smoking are each substantially higher among people living with HIV (PLWH) than in the general population. The goal of these analyses was to examine the prevalence and impact of comorbid chronic pain and cigarette smoking among PLWH. Participants included 3289 PLWH (83% male) who were recruited from five HIV clinics. As expected, the prevalence of smoking was higher among PLWH with chronic pain (41.9%), than PLWH without chronic pain (26.6%, $p < .0001$), and the prevalence of chronic pain was higher among current

Declaration of Interest Statement

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smokers (32.9%), than among former (23.6%) or never (17%) smokers (*p*s < .0001). PLWH who endorsed comorbid chronic pain and smoking (vs. nonsmokers without chronic pain) were more likely to report cocaine/crack and cannabis use, be prescribed long-term opioid therapy, and have virologic failure, even after controlling for relevant sociodemographic and substance-related variables (*p*s < .05). These results contribute to a growing empirical literature indicating that chronic pain and cigarette smoking frequently co-occur, and extend this work to a large sample of PLWH. Indeed, PLWH may benefit from interventions that are tailored to address bidirectional pain-smoking effects in the context of HIV.

Keywords

chronic pain; cigarette smoking; substance use

Introduction

Chronic pain is common among people living with HIV (PLWH), with prevalence estimates ranging from 25–85% (e.g., Jiao et al., 2016; Merlin et al., 2018; Miaskowski et al., 2011). PLWH with chronic pain may be at increased risk for virologic failure (Merlin et al., 2018), and the presence/severity of pain among PLWH has been associated with negative health behaviors (e.g., cigarette smoking; Merlin et al., 2012). Like chronic pain, cigarette smoking is highly prevalent among PLWH, with estimates indicating that 47% of PLWH are current smokers (Lindayani, Yeh, Ko, & Ko, 2019). Smokers (vs. nonsmokers) with HIV report poorer adherence with antiretroviral therapy (ART; O'Cleirigh et al., 2015; Shuter & Bernstein, 2008), and are more likely to have a detectable viral load (Hile, Feldman, Alexy, & Irvine, 2016; King et al., 2018; O'Cleirigh et al., 2015) and endorse substance use (O'Cleirigh et al., 2015).

Previous work has documented high rates of comorbidity between chronic pain and cigarette smoking (e.g., Ditre, Brandon, Zale, & Meagher, 2011). The base rate of smoking among persons with chronic pain is approximately 30–42% (vs. ~14% in the general population; Zvolensky et al., 2009), and the prevalence of smoking among treatment-seeking chronic pain patients may be as high as 68% (e.g., Michna et al., 2004). Conversely, the base rate of chronic pain among individuals with tobacco use disorder is approximately 60% (John & Wu, 2020). Ultimate base rates of (1) smoking among individuals with chronic pain and (2) chronic pain among individuals who smoke depend largely on the setting from which the population was derived (e.g., Ditre et al., 2011), and researchers have noted that appropriate base rate information may be derived from clinical and/or setting-specific samples (Elwood, 1993).

Pain and smoking interact in the manner of a positive feedback loop, resulting in greater pain and the maintenance of tobacco dependence (Ditre et al., 2011; Ditre, Zale, & LaRowe, 2019; LaRowe & Ditre, 2020; Zale, Maisto, & Ditre, 2016). Smoking is a risk factor for the development of chronic pain (e.g., Shiri, Karppinen, Leino-Arjas, Solovieva, & Viikari-Juntura, 2010), and lifetime nicotine/tobacco exposure has been positively associated with chronic pain status (Pisinger et al., 2011; Sugiyama et al., 2010), pain severity (De Vita,

Maisto, Ansell, Zale, & Ditre, 2019; Scott, Goldberg, Mayo, Stock, & Poitras, 1999), and pain reactivity (De Vita et al., 2019). Pain can also motivate smoking (e.g., Dhingra et al., 2014; Ditre & Brandon, 2008), and smokers often report using cigarettes for pain-coping (Hooten et al., 2011; Patterson et al., 2012).

Despite high rates of comorbidity and well-documented interrelations between chronic pain and smoking, no previous research has examined the prevalence co-occurring chronic pain and smoking among a large population of PLWH. Moreover, although these conditions have each been independently associated with greater substance use and increased risk for virologic failure among PLWH, no previous work has tested associations between pain-smoking comorbidity and risk for these outcomes. The goals of this study were to test the following hypotheses among PLWH recruited from 5 clinical care sites across the United States: (1) the prevalence of current smoking will be higher among PLWH who endorsed chronic pain (vs. no chronic pain), (2) the prevalence of chronic pain will be higher among PLWH who are current smokers (vs. former/never smokers), (3) PLWH with comorbid chronic pain and smoking (vs. neither condition) will be at a greater risk for endorsing high-risk drinking, cannabis use, and cocaine use, being prescribed long-term opioid therapy (LTOT), and virologic failure. Although not a primary goal of this paper, we also examined whether chronic pain alone (i.e., in the absence of smoking) and smoking alone (i.e., in the absence of chronic pain) were independently associated with each outcome (relative to no chronic pain or smoking).

Method

Setting, Study Population, and Data Collection

This study was embedded in the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS), a large ongoing prospective cohort study of PLWH in routine clinical care in the United States (Kitahata et al., 2008), and data were collected from July 2015 and July 2016 (Merlin et al., 2018). CNICS sites are patient-centered medical homes that provide primary and specialty care for PLWH. All patients at these sites with a diagnosis of HIV/AIDS are invited to participate in the CNICS cohort, and recruitment is ongoing. Demographic/clinical data are collected from the electronic medical record and other institutional sources, and PLWH complete the self-report measures on a computer or tablet approximately every 4–6 months (Crane et al., 2007; Fredericksen et al., 2012). Five CNICS sites contributed data to these analyses: Fenway Health in Boston, the University of Alabama at Birmingham (UAB), University of California, San Diego (UCSD), University of North Carolina (UNC), and University of Washington (UW). These analyses only included data collected during the first CNICS clinical assessment that included pain measures.

Measures

Chronic Pain.—Participants were asked to indicate: (1) whether they have pain that has lasted for more than 3 months, and (2) the severity of their pain during the past week (none, very mild, mild, moderate, severe, and very severe; Merlin et al., 2015). Given that greater than mild pain is considered to be clinically significant (Moore, Straube, & Aldington, 2013), PLWH who reported at least moderate pain in the last week, in addition to pain

lasting 3 months or longer, were classified as having current chronic pain. This approach is consistent with previous research (e.g., Merlin et al., 2018).

Cigarette Smoking.—Smoking status was assessed using the CNICS smoking questionnaire (Zyambo et al., 2015) and was categorized as: current smoking, former smoking (i.e., >20 cigarettes in one's lifetime but no current smoking), and never smoking (i.e., <20 cigarettes in one's lifetime). Current smokers further indicated the number of years that they have smoked cigarettes (response options: 0–5 years, 6–10 years, 11–15 years, 16–20 years, > 20 years), and the number of cigarettes they smoke per day (response options: <½ pack a day, ½ - 1 pack a day, 1–2 packs a day, >2 packs a day).

Substance Use.—Participants completed the Alcohol Use Disorders Identification Test – Consumption (AUDIT-C; Bush, Kivlahan, McDonell, Fihn, & Bradley, 1998). High-risk drinking behavior was defined as scores ≥4 for males and ≥3 for females. Past three-month cocaine/crack and nonmedical cannabis use were assessed using the Alcohol, Smoking, and Substance Involvement Screening Test (World Health Organization, 2002). Illicit substance use was defined as endorsing past three-month use of methamphetamine/crystal, cocaine/crack, or opioids (nonmedical use).

Treatment-Related Variables.—Long-term opioid use (LTOT) was defined as opioid therapy for ≥90 consecutive days based on medical record data (Merlin et al., 2016). Viral load and $CD4^+$ T-cell count were also available in the CNICS data repository from the EMR. Consistent with previous work (e.g., Jittamala, Puthanakit, Chaiinseeard, & Sirisanthana, 2009; Merlin et al., 2018), virologic failure was defined as plasma HIV RNA >1000 copies/mL without a repeated test within 30 days that found <1000 copies/mL. We chose this cut-off, which is higher than cut-offs often recommended by clinical guidelines (50 or 200 copies/mL), to maximize the specificity of identifying virologic failure among individuals with "no-shows" who may not return for a confirmatory viral load.

Statistical Analyses

First, we used chi-square tests to examine the frequencies of current, former, and never smoking at each level of the chronic pain status variable (i.e., chronic pain vs. no chronic pain). We also examined the frequency of current smoking at each level of past-week pain severity. Second, we examined the frequency of chronic pain at each level of the smoking status variable. Among current smokers, we also examined the frequencies of responses for (1) number of years smoked and (2) cigarettes smoked per day at each level of chronic pain status. Third, multivariable logistic regression models (run as fixed effects models in which clinic was treated as a fixed effect) were used to test associations between a four-group chronic pain and smoking variable – comorbid chronic pain and smoking, chronic pain alone, smoking alone, and no chronic pain or smoking (reference group) – and likelihood of endorsing high-risk alcohol use, cannabis use, cocaine use, long-term opioid treatment (LTOT), and virologic failure. The primary goal of this paper was to test whether PLWH who have comorbid chronic pain and smoking are also at greater risk for substance use, LTOT, and virologic failure than PLWH nonsmokers with no chronic pain. However, given that both chronic pain and smoking have previously been associated with poorer substance

and health-related outcomes among PLWH (e.g., Merlin et al., 2018; O'Cleirigh et al., 2015), we also examined whether chronic pain alone (i.e., in the absence of smoking) and smoking alone (i.e., in the absence of chronic pain) were independently associated with each outcome (relative to no chronic pain or smoking). Each model accounted for sex, age, race, illicit substance use, and all other outcome variables (i.e., high-risk alcohol use, recent cannabis use, recent cocaine use, LTOT, and virologic failure) aside from the outcome being assessed.

Results

Participant Characteristics

Participants were 3289 PLWH from five HIV clinical care sites across the US (see Table 1). The majority were male (83%), over one-third were non-Hispanic Black, and the mean $CD4^+$ T-cell count was 585 cells/mm^3. Approximately 60% endorsed current (30%) or former smoking (29%). The majority of current smokers (76%) reported smoking for more than 10 years, and 51% reported smoking ≥10 cigarettes per day (CPD), with 11% smoking >20 CPD. Nearly one-third (31.6%) of the sample endorsed at least moderate past-week pain, and almost one-quarter (23.7%) met criteria for chronic pain. Overall, 10% of the sample endorsed comorbid chronic pain and cigarette smoking.

Prevalence of Smoking

The prevalence of current smoking was 41.9% among PLWH with chronic pain, compared to 26.6% among PLWH without chronic pain ($p<.0001$; Figure 1). The prevalence of current smoking was 25.3% among those without past-week pain, 25.1% among those with very mild or mild pain, 39.4% among those with moderate pain, and 44.0% among those with severe/very severe pain, X^2 (6, $N = 3289$)=115.44, $p<.0001$ (Figure 1).

Prevalence of Chronic Pain

The prevalence of chronic pain was 32.9% among current smokers, compared to 23.6% among former smokers, and 17% among never smokers (ps<.0001; Figure 2). The prevalence of chronic pain was 29.75% among those smoking <10 CPD, 34.01% among those smoking 10–20 CPD, 42.72% among those smoking 20–40 CPD, and 66.7% among those smoking >40 CPD, X^2 (3, $N = 987$)=9.96, $p=.0189$ (Figure 2). The prevalence of chronic pain was 20.95% among those who reported smoking for 0–5 years, 23.48% for 6–10 years, 26.57% for 11–15 years, 32% for 16–20 years, and 40.51% for >20 years, X^2 (4, $N = 987$)=26.16, $p<.0001$ (Figure 2).

Correlates of Comorbid Chronic Pain and Smoking

Comorbid chronic pain and smoking was not associated with high-risk drinking ($p>.05$; Table 2, Figure 3). However, PLWH who endorsed comorbid chronic pain and smoking were more than twice as likely to report cocaine/crack use (*AOR*=2.49, *95% CI*: 1.16-.33) and over 1.5 times as likely to report cannabis use (*AOR*=1.77, *95% CI*: 1.23–2.54), when compared to nonsmokers without chronic pain. Smoking alone was also associated with a greater likelihood of endorsing cocaine/crack (*AOR*=2.16, *95% CI*: 1.24–3.75) and cannabis (*AOR*=1.97, *95% CI*: 1.53–2.54) use.

PLWH who endorsed comorbid chronic pain and smoking were 10 times as likely to be prescribed LTOT (vs. nonsmokers without chronic pain; *AOR*=10.0, *95% CI*: 6.79–14.70; Table 2, Figure 3). As expected, chronic pain alone was also associated with a greater likelihood of being prescribed LTOT (*AOR*=6.75, *95% CI*: 4.87–9.37). Among PLWH with chronic pain, current smokers (vs. never smokers) were over 50% more likely to be prescribed LTOT (*AOR*=1.51, *95% CI*: 1.02, 2.24). In addition, PLWH who endorsed comorbid chronic pain and smoking were over 2.5 times as likely to have virologic failure (vs. nonsmokers without chronic pain; *AOR*=2.54, *95% CI*: 1.58–4.08; Table 2, Figure 3). Neither chronic pain nor smoking status were independently associated with virologic failure (*p*s>.05).

Discussion

This study examined the prevalence/impact of comorbid chronic pain and cigarette smoking among a large population of PLWH. Overall, 10% of the sample reported comorbid chronic pain and smoking. The prevalence of smoking was 57% higher among PLWH with chronic pain (vs. without chronic pain) and increased with greater past-week pain severity. Similarly, the prevalence of chronic pain was nearly twice as high among current (vs. never) smokers, and increased as a function of both the number of years smoked and cigarettes smoked per day. Results further indicated that PLWH with comorbid chronic pain and smoking (vs. PLWH nonsmokers with no pain) were significantly more likely to endorse cocaine/crack and cannabis use, be prescribed long-term opioid treatment, and meet criteria for virologic failure.

These results contribute to a growing literature indicating that chronic pain and smoking frequently co-occur, and extend prior findings by providing novel evidence of significant pain-smoking comorbidity among PLWH. Rates of chronic pain were greater among those smoking more cigarettes per day and for longer durations, suggesting that the prevalence of chronic pain among smokers living with HIV may increase in a dose-dependent manner. This pattern of findings is consistent with evidence that lifetime exposure to cigarettes is positively associated with risk for developing persistent pain (Pisinger et al., 2011; Sugiyama et al., 2010), although causal interpretation of the current results is precluded by the cross-sectional nature of the data. An alternative explanation for these findings stems from evidence that smokers with pain often report using cigarettes for pain-coping (Patterson et al., 2012), and, relative to their pain-free counterparts, are less likely to initiate a quit attempt and more likely to lapse/relapse to smoking if they do attempt cessation (Ditre, Heckman, LaRowe, & Powers, 2020). Consistent with this prior work, we also observed that the prevalence of smoking was higher among those who endorsed greater pain severity. Nicotine can confer acute analgesic effects (Ditre, Heckman, Zale, Kosiba, & Maisto, 2016), and greater pain severity may increase the propensity to use cigarettes to self-medicate pain symptoms among PLWH. Increased pain during acute nicotine/tobacco abstinence (Ditre, Zale, LaRowe, Kosiba, & De Vita, 2018; LaRowe, Kosiba, Zale, & Ditre, 2018) may further perpetuate pain-smoking comorbidity.

Results also indicated that comorbid chronic pain and smoking was associated with a greater risk for substance use and poorer health-related outcomes. Pain and smoking have been

independently associated with substance use (e.g., Merlin et al., 2012; O'Cleirigh et al., 2015) and virologic failure (e.g., Hile et al., 2016; Merlin et al., 2018; O'Cleirigh et al., 2015), and this is the first study to demonstrate that comorbid chronic pain and smoking may also be associated with these outcomes. Examination of Table 2 indicates that the odds of cocaine/crack use, long-term opioid treatment, and virologic failure were higher among PLWH with comorbid chronic pain and smoking, than among those who endorsed smoking alone or chronic pain alone. This suggests that the negative impact of comorbid chronic pain and smoking on cocaine/cannabis use, long-term opioid treatment, and viral suppression may be even greater than the risks imposed by either condition alone. Contrary to expectation, comorbid chronic pain and smoking was not associated with likelihood of endorsing high-risk alcohol use. It is possible that PLWH may have underreported the quantity/frequency of their drinking, and previous work has noted that research participants may respond to questions about alcohol use differently when data is collected in a clinical setting (vs. traditional research setting) to avoid jeopardizing their ability to receive future prescriptions (Saffier, Colombo, Brown, Mundt, & Fleming, 2007).

An important implication of this study is that comorbid chronic pain and smoking may increase risk for deleterious outcomes among PLWH. Therefore, reducing pain severity and promoting smoking cessation should be critical treatment goals. Several integrated pain-smoking interventions have been developed (e.g., Hooten, LaRowe, Zale, Ditre, & Warner, 2018; Zale, Maisto, De Vita, Hooten, & Ditre, 2020), including a brief computer-based personalized feedback intervention that was administered to smokers living with pain and HIV (Ditre et al., 2019). This intervention (which included psychoeducation regarding pain-smoking interrelations and addressed pain-smoking perceptions/expectancies) increased knowledge of pain-smoking interrelations and increased confidence/intention to quit among heavier smokers. Future research is needed to develop/test treatments that support long-term abstinence among PLWH with comorbid chronic pain and tobacco dependence. Preliminary work using integrated treatment platforms to address smoking cessation in the context of other co-morbidities among PLWH has shown promise (O'Cleirigh et al., 2018). Integrated interventions may also benefit from including pharmacological cessation aids (e.g., nicotine replacement therapy, varenicline, bupropion), which may have unique utility in the context of pain (Bagdas et al., 2018; Hatsukami et al., 2007; LaRowe & Ditre, 2020; Mills et al., 2012; Shah & Moradimehr, 2010; Zale & Ditre, 2013).

Several limitations should be noted. First, results are cross-sectional and preclude causal/temporal interpretation. Future prospective studies should clarify directional pathways between chronic pain and smoking among PLWH, and determine whether poorer substance- and health-related outcomes in this population are a consequence or correlate of comorbid chronic pain and smoking. Second, chronic pain status, smoking status, high-risk drinking behavior, and cannabis/cocaine use were all assessed via self-report. Future work could include medical chart verification of chronic pain status and biochemical indices of substance use (e.g., cotinine levels, exhaled CO, urine drug screens; Glasgow et al., 1993, Markway & Baker, 2011). Third, use of other tobacco products (e.g., cigar, cigarillo) was not assessed, and future work should include a more comprehensive assessment of nicotine/tobacco use. Fourth, the majority of participants were male, and although this is consistent with epidemiological estimates for HIV prevalence in the US (e.g., Moore, 2011), future

work should examine a more gender-balanced sample that permits tests of sex differences in the prevalence/impact of comorbid chronic pain and smoking. Finally, the majority of PLWH had an undetectable viral load, and future research should examine these associations among PLWH whose viral load is not suppressed.

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Data Availability Statement

The data that support the findings of this study are available upon reasonable request.

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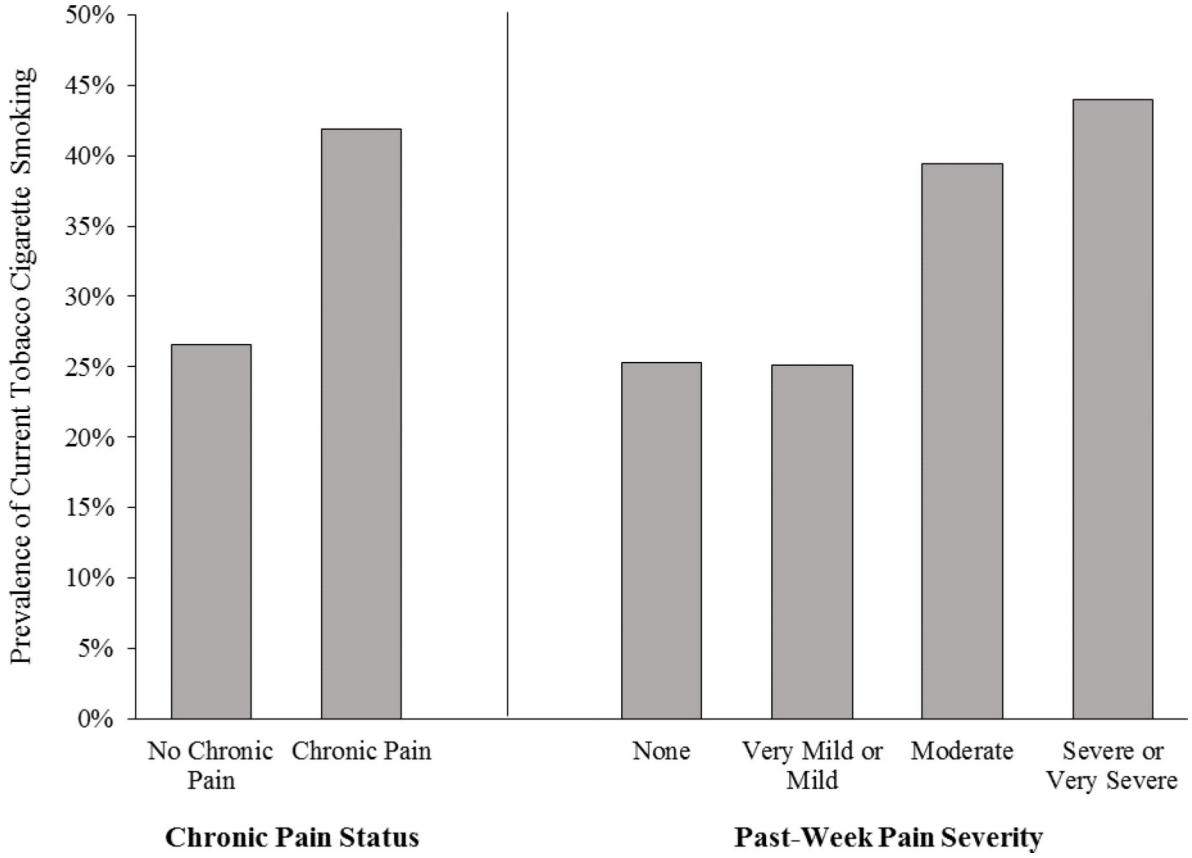

Figure 1.

Prevalence of Current Tobacco Cigarette Smoking as a Function of Chronic Pain Status and Past-Week Pain Severity among 3289 People Living with HIV in Clinical Care at 5 Sites in the United States

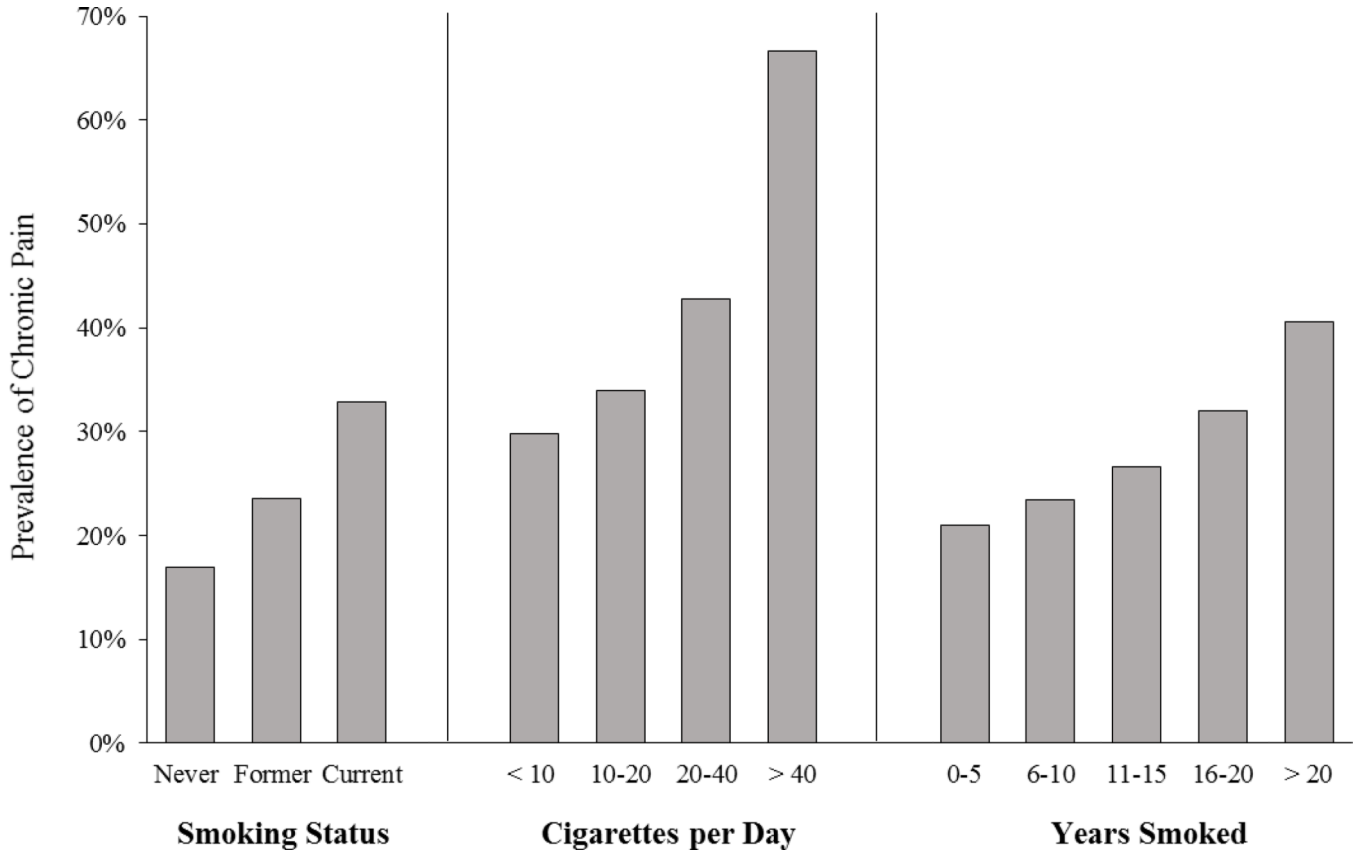

Figure 2.

Prevalence of Chronic Pain as a Function of Tobacco Cigarette Smoking among 3289 People Living with HIV in Clinical care at 5 Sites in the United States

Note. Rates of chronic pain as a function of cigarettes per day and years smoked are among current smokers.

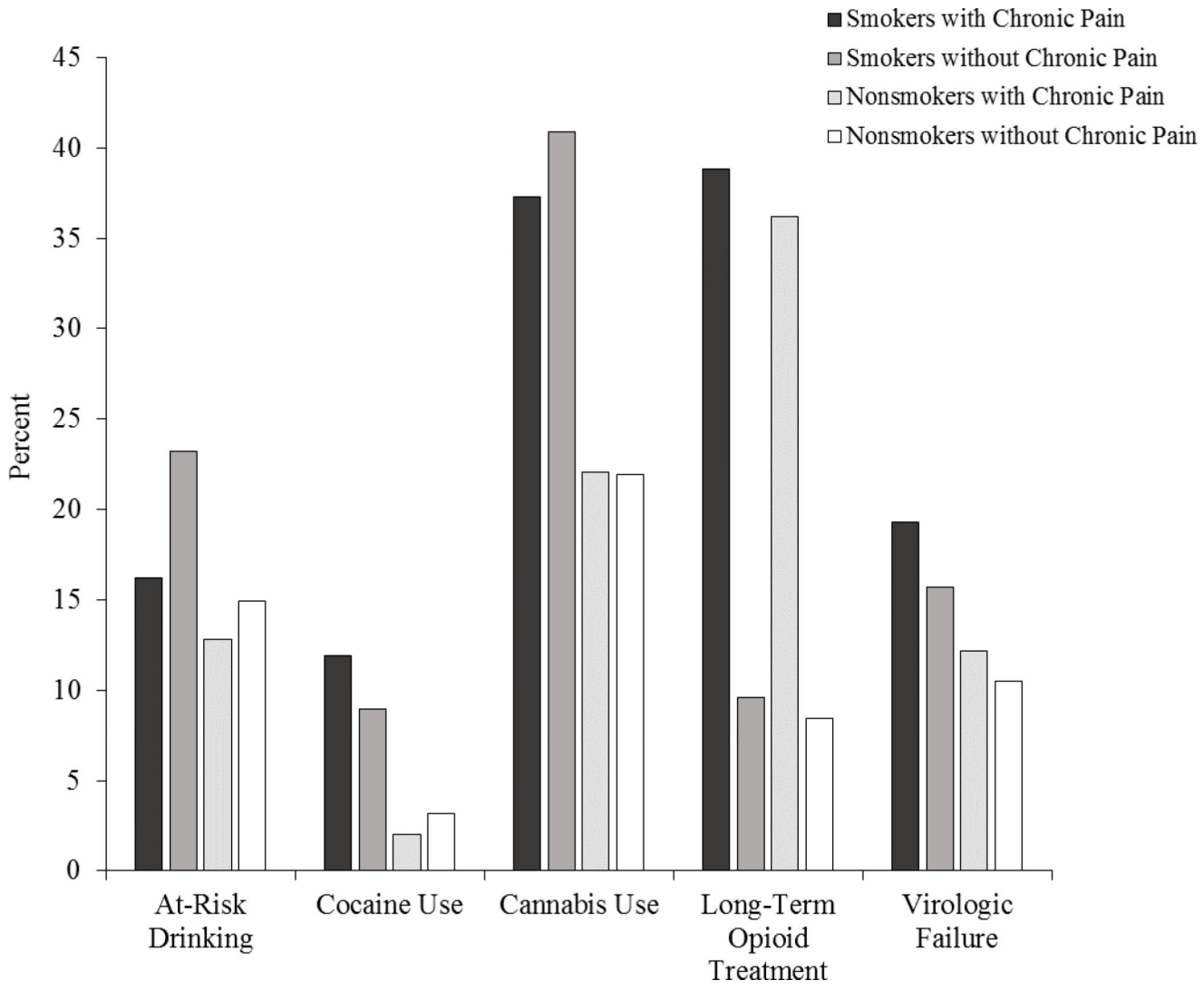

Figure 3.

Substance Use and Treatment-Related Outcomes as a Function of Pain/Smoking Group among 3289 People Living with HIV in clinical care at 5 Sites in the United States

Table 1

Sociodemographic, Smoking, and Pain Characteristics among 3289 People Living with HIV in Clinical Care at 5 sites in the United States

	Total N = 3289
	***n* (%)**
Age	
≥ 50	1429 (43.4%)
Sex	
Female	558 (17.0%)
Race/Ethnicity	
White	1569 (47.7%)
Black	1231 (37.4%)
Hispanic	366 (11.1%)
Other	489 (14.9%)
Site	
Fenway Health	107 (3.3%)
UAB	1566 (47.6%)
UCSD	1054 (32.0%)
UNC	116 (3.5%)
UW	446 (13.6%)
Chronic Pain Status	
At least moderate chronic pain	780 (23.7%)
Less than moderate chronic pain	2509 (76.3%)
Tobacco Smoking Status	
Current smoker	995 (30.3%)
Former smoker	953 (29.0%)
Never smoker	1341 (40.8%)
Alcohol Use	
High-risk drinking	541 (16.4%)
Not high-risk drinking	2748 (83.6%)
Illicit Substance Use	
Past three-month drug use	383 (11.6%)
No past three-month drug use	2906 (88.4%)
Long-Term Opioid Therapy	
Yes	511 (15.5%)
No	2778 (84.5%)
Virologic Failure	
HIV RNA >1000 copies/mL	416 (13.4%)
HIV RNA <1000 copies/mL	2683 (86.6%)

Note. UAB = University of Alabama at Birmingham. UCSD = University of California, San Diego. UNC = University of North Caroline. UW = University of Washington.

Table 2

Relationship between Comorbid Chronic Pain and Smoking, and Substance- and Treatment-Relevant Variables

High-Risk Alcohol Use		
Variable	**Adjusted OR (95% CI)**	***p***
Pain/Smoking Group		0.03
Chronic Pain and Smoking	1.03 (.064,1.65)	
Chronic Pain Alone	0.87 (0.57,1.32)	
Smoking Alone	1.52 (1.13, 2.05)	
No Chronic Pain/Smoking	1	
Cocaine/Crack Use		
Variable	**Adjusted OR (95% CI)**	***p***
Pain/Smoking Group		0.01
Chronic Pain and Smoking	2.49 (1.16,5.33)	
Chronic Pain Alone	0.81 (0.30,2.19)	
Smoking Alone	2.16 (1.24, 3.75)	
No Chronic Pain/Smoking	1	
Cannabis Use		
Variable	**Adjusted OR (95% CI)**	***p***
Pain/Smoking Group		< .01
Chronic Pain and Smoking	1.77 (1.23, 2.54)	
Chronic Pain Alone	1.09 (0.78, 1.54)	
Smoking Alone	1.97 (1.53, 2.54)	
No Chronic Pain/Smoking	1	
Long-Term Opioid Treatment		
Variable	**Adjusted OR (95% CI)**	***p***
Pain/Smoking Group		< .01
Chronic Pain and Smoking	10.0 (6.79, 14.70)	
Chronic Pain Alone	6.75 (4.87, 9.37)	
Smoking Alone	1.19 (0.79, 1.80)	
No Chronic Pain/Smoking	1	
Virologic Failure		
Variable	**Adjusted OR (95% CI)**	***p***
Pain/Smoking Group		< .01
Chronic Pain and Smoking	2.54 (1.58, 4.08)	
Chronic Pain Alone	1.48 (0.93, 2.36)	
Smoking Alone	1.21 (0.82, 1.79)	
No Chronic Pain/Smoking	1	

Note. Covariates in each model included clinic location, sex, age, race, and all other outcomes.