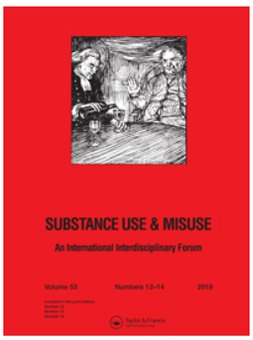

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ORIGINAL ARTICLE

Associations between Pain-Related Anxiety, Gender, and Prescription Opioid Misuse among Tobacco Smokers Living with HIV/AIDS

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ABSTRACT

Background: People living with HIV/AIDS (PLWHA) who smoke cigarettes are vulnerable to greater pain and aberrant use of prescription pain medications. Prescription opioid misuse is highly prevalent among PLWHA and can lead to a variety of adverse outcomes. Pain-related anxiety, which has been implicated in the maintenance of both pain and tobacco dependence, may also play a role in prescription pain medication misuse. *Objectives*: This study aimed to test associations between pain-related anxiety and prescription opioid misuse. We hypothesized that, among those prescribed opioid medication, pain-related anxiety would be positively associated with current opioid misuse, and stated intentions to misuse prescription opioids in the future. We further hypothesized that these relations would be more pronounced among males (vs. females). *Methods*: Participants included 61 PLWHA daily tobacco smokers with pain. Hierarchical regressions were used to test interactions between gender and pain-related anxiety on current and intended opioid misuse among those prescribed opioid medications. *Results*: There was a significant interactive effect of pain-related anxiety and gender on opioid misuse, such that pain-related anxiety was positively associated with current opioid misuse among male (but not female) participants who were prescribed opioid medications. Among both males and females, pain-related anxiety was positively associated with intention to misuse prescription pain medications in the future. *Conclusions/Importance*: Additional research into the role of pain-related anxiety in prescription opioid misuse is warranted. This type of work may inform the development of tailored interventions for PLWHA smokers who are prescribed opioid pain medications.

KEYWORDS
Pain; pain-related anxiety; opioid; opioid misuse; smoking

Over 35 million people worldwide are infected with the Human Immunodeficiency Virus (HIV; Joint United Nations Programme on HIV/AIDS, 2016). Persons living with HIV/AIDS (PLWHA) endure numerous stressors, including physical pain (e.g., Breitbart, Gatchel, & Turk, 1999; Marcus, Kerns, Rosenfeld, & Breitbart, 2000). Pain in PLWHA is generally chronic (Marcus et al., 2000), and a recent review indicated that up to 83% of PLWHA endorse past three-month pain (Parker, Stein, & Jelsma, 2014). Effective pain management is an important consideration for improving health outcomes and quality of life for PLWHA, and opioid medications are commonly prescribed (e.g., Hansen et al., 2011).

PLWHA who smoke tobacco cigarettes are particularly vulnerable to both pain and prescription opioid misuse, and this may be due, in part, to complex nicotine-opioid interactions (Shi, Weingarten, Mantilla, Hooten, & Warner, 2010). The prevalence of tobacco smoking among PLWHA (45–74%; Vidrine, 2009) is substantially greater than in the general population (15.1%; Jamal et al., 2016), and regular smoking may lead to greater sensitivity to pain via dysregulation of the endogenous opioid system (Shi et al., 2010). Relative to nonsmokers, current tobacco smokers are more likely to report severe pain (Ackerman & Ahmad, 2007; Creekmore, Lugo, & Weiland, 2004), be prescribed opioid medications (Dobscha, Morasco, Duckart, Macey, & Deyo, 2013), and misuse opioids (Michna et al., 2004; Tetrault et al., 2008). Aberrant opioid use (e.g., problematic medication use patterns, addiction, poor response to medication, and signs of intoxication; Butler et al., 2007) is especially prevalent among PLWHA (Hansen et al., 2011; Tsao, Dobalian, & Stein, 2005), with rates of misuse as high as 62% (Robinson-Papp, Elliott, Simpson, Morgello, & Bank, 2012). Prescription opioid misuse can result in physiological dependence, withdrawal, impairments in functioning, and overdose (Vowles et al., 2015). Among PLWHA, prescription opioid misuse has also been associated with poor antiretroviral adherence (e.g., Jeevanjee et al., 2014; Robinson-Papp et al., 2012), which

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can lead to an increased HIV-1 RNA viral load and risk of progression from HIV to AIDS (e.g., Bangsberg et al., 2001; Low-Beer, Yip, O'shaughnessy, Hogg, & Montaner, 2000; Paterson et al., 2000).

To inform the development of tailored cognitive-behavioral treatments for PLWHA smokers, it is important to identify factors that may be associated with the misuse of prescription opioids. One cognitive-affective factor of increasing theoretical and clinical interest is pain-related anxiety, which reflects a tendency to respond to pain with anxiety or fear (McCracken, Zayfert, & Gross, 1992). Pain-related anxiety has been identified as a risk factor in the transition from acute to chronic pain (e.g., Boersma & Linton, 2006), and greater pain-related anxiety has been related to more severe pain and maladaptive coping (McCracken, Gross, Sorg, & Edmands, 1993). Pain-related anxiety has also been positively associated with tobacco dependence (Ditre, Langdon, Kosiba, Zale, & Zvolensky, 2015; Ditre, Zale, Kosiba, & Zvolensky, 2013), the use of tobacco to cope with pain (Patterson et al., 2012), expectations that smoking can alleviate negative affect (Gonzalez, Hogan, McLeish, & Zvolensky, 2010), and greater self-reported barriers to smoking cessation (Ditre et al., 2015). Most recently, higher pain-related anxiety was shown to predict early lapse and relapse to smoking following a quit attempt (LaRowe, Langdon, Zvolensky, Zale, & Ditre, 2017).

Given its specificity to pain-relevant phenomena (including escape/avoidance behaviors), and demonstrated associations with both pain and tobacco smoking, there is reason to suspect that pain-related anxiety may play an important role in the misuse of prescription opioids among PLWHA smokers. Further, associations between pain-related anxiety and opioid misuse may differ as a function of gender: pain-related anxiety is associated with greater pain intensity and poorer adjustment to chronic pain, an association that has been shown to be stronger among men than women (e.g., Edwards, Augustson, & Fillingim, 2000; Robinson et al., 2005). Further, some evidence suggests that males (vs. females) are more likely to respond to anxiety with externalizing behaviors, such as substance use (e.g., Altemus, Sarvaiya, & Epperson, 2014; Marmorstein, 2007).

The primary goal of this study was to conduct the first test of cross-sectional relations between pain-related anxiety and prescription opioid misuse among PLWHA smokers with co-occurring pain. A second goal was to examine the interactive effects of pain-related anxiety and gender on prescription opioid misuse. Specifically, we hypothesized that greater pain-related anxiety would be positively associated with current prescription opioid misuse, and greater self-reported intention to misuse prescription opioids in the future among participants who were prescribed opioid medications. We further hypothesized that these effects would be stronger among male (vs. female) participants.

Method

Participants

Participants were recruited from a university hospital-based outpatient infectious disease clinic in central New York for a study examining the efficacy of a computer-based personalized feedback intervention (PFI) for tobacco cigarette smokers with pain and HIV/AIDS. More specifically, the primary study aimed to adapt and pilot test a brief PFI designed to increase motivation, confidence, and intention to quit smoking, and decrease positive attitudes and intentions toward the misuse of prescription analgesic medications. The study aimed to recruit a sample of older adults given that pain is more prevalent among this population (McMahon, Koltzenburg, Tracey, & Turk, 2013). To be included in the study, participants were required to endorse current tobacco cigarette smoking, current use of prescription pain medication, and age greater than 30. Participants were excluded if they reported currently attempting to quit smoking or an inability to speak and read English. A total of 61 participants met these inclusion/exclusion criteria, attended a baseline assessment, and completed the measure of pain-related anxiety. Although the current study aimed to examine associations between pain-related anxiety, gender, and opioid misuse among the subsample of participants who were prescribed opioid pain medication, participants taking nonopioid pain medications were included in the total sample to test for differences in pain-related anxiety as a function of opioid use (vs. nonopioid pain medication use).

Measures

Pain-related anxiety

Pain-related anxiety was assessed using the Pain Anxiety Symptom Scale-20 item (PASS-20; McCracken & Dhingra, 2002). The PASS-20 uses a 6-point Likert scale ranging from *never* (0) to *always* (5) to assess how often participants engage in various pain-relevant thoughts and behaviors. The PASS-20 measures four components of pain-related anxiety, including a cognitive factor (e.g., "I can't think straight when in pain"), an escape and avoidance factor (e.g., "I avoid important activities when I hurt"), a fear factor (e.g., "When I feel pain, I am afraid that something terrible will happen"), and a physiological anxiety factor (e.g., "Pain seems to cause my heart to pound or race"). The PASS-20 demonstrated excellent internal consistency in the current sample ($\alpha = .96$).

Current use of pain medication

Approved medical staff extracted data regarding current pain medication use via medical chart review. Prescription pain medications were classified as either opioid medications (e.g., hydrocodone, oxycodone, morphine, tramadol) or nonopioid medications (e.g., pregabalin, gabapentin, naproxen).

Current opioid misuse and intention to misuse opioids in the future

Current opioid misuse was assessed using the well-established Current Opioid Misuse Measure (COMM; Butler et al., 2007). The COMM has evinced strong diagnostic performance characteristics among individuals with co-occurring pain (Meltzer et al., 2011). The COMM consists of 17 items and uses a 5-point Likert scale ranging from *never* (0) to *very often* (4) to assess how often participants have engaged in various aberrant medication related behaviors (e.g., going to someone other than the prescribing physician to get sufficient relief from medications) in the past 30 days. Items are summed to compute a total score. Given that researchers have noted the importance of practicing caution when interpreting COMM cut-off scores for diagnostic purposes (e.g., Butler et al., 2007; Meltzer et al., 2011), we tested COMM scores as a continuous variable. The COMM demonstrated good internal consistency in the current sample ($\alpha = .85$).

To measure intentions for future opioid misuse, we adapted the COMM (i.e., COMM-Intention; Appendix 1) to assess how likely it is that participants will engage in aberrant medication use behaviors in the next 30 days. The COMM-Intention measure consisted of 10 items and utilized a 5-point Likert scale ranging from *extremely unlikely* (1) to *extremely likely* (5). Seven items from the COMM were excluded from the COMM-Intention measure because they could not be adapted to assess how likely it is that the participant would engage in that behavior over the next 30 days (e.g., "In the past 30 days, how often have you seriously thought about hurting yourself?"). The COMM-Intention measure demonstrated excellent internal consistency in the current sample ($\alpha = .91$). Importantly, the correlation between COMM and COMM-Intention scores was $r = .66$ ($p < .01$), indicating that although these measures were positively correlated, the COMM-Intention measure conveys information about intended misuse of opioids that is not captured by the COMM.

Characteristic pain intensity

Pain intensity was assessed using the characteristic pain intensity subscale of the Graded Chronic Pain Scale (GCPS; Von Korff, Ormel, Keefe, & Dworkin, 1992). The GCPS provides a reliable and valid method of assessing global pain severity across a range of chronically painful conditions. Participants rated the intensity of their pain *right now*, their *worst* pain in the past 24 hours, and their pain *on average* during the past 24 hours using separate 0–10 numerical rating scales. Consistent with GCPS scoring instructions, these items were averaged and multiplied by 100 to yield a continuous composite score (range 0–100) of characteristic pain intensity/severity. This measure demonstrated excellent internal consistency in the current sample ($\alpha = .93$).

HIV/AIDS symptom count

The AIDS Clinical Trial Group Symptom Distress Module (SDM) is a 20-item measure used to assess HIV/AIDS symptoms (Justice et al., 2001). Participants indicated whether they have experienced 20 different symptoms (e.g., fatigue or loss of energy, feeling dizzy or lightheaded) over the past two weeks, and subsequently rated the degree to which they have been bothered by each symptom on a scale ranging from *it doesn't bother me* (1) to *it bothers me a lot* (4). The SDM has demonstrated excellent construct validity (Justice et al., 2001).

Sociodemographic and smoking characteristics

A range of sociodemographic (e.g., age, gender, race/ethnicity, education, and income) and smoking characteristics (e.g., number of cigarettes smoked per day, number of years smoking, and tobacco dependence) were assessed via self-report. Tobacco dependence was assessed using the Heaviness of Smoking Index (HSI; Heatherton, Kozlowski, Frecker, Rickert, & Robinson, 1989), which is comprised of two items (i.e., "How soon after you wake up do you smoke your first cigarette?" and "How many cigarettes per day do you smoke?"; Heatherton et al., 1989).

Data analytic strategy

First, relations between pain-related anxiety, sociodemographic, smoking, and pain variables as a function of current prescription opioid use were examined using Chi-square and *t*-tests. We also conducted a series of bivariate correlations to test associations between pain-related anxiety, current opioid use, COMM and COMM-Intention scores, and sociodemographic, pain, and smoking characteristics (associations between continuous variables and dichotomous variables were tested using point-biserial correlations; Tate, 1954). Notably, among participants who were prescribed opioid medications, PASS-20 scores were positively associated with both COMM ($r = .45$) and COMM-Intention ($r = .53$) scores ($ps < .01$). COMM and COMM-Intention scores were also significantly correlated with Hispanic ethnicity

($r = .39$ and $r = .27$, respectively) and income ($r = -.32$ and $r = -.26$, respectively). Significant correlations were also observed between PASS total scores and education ($r = -.30$), income ($r = -.38$), and characteristic pain intensity ($r = .36$). Based on these observations, all subsequent analyses controlled for the influence of ethnicity, income, education, and characteristic pain intensity.

Second, we conducted separate hierarchical regressions to test the interaction between gender and pain-related anxiety on COMM and COMM-Intention scores among participants who were prescribed opioid medications. For each of the hierarchical regression models, predictors were entered in the following order: Step 1 (ethnicity, income, education, characteristic pain intensity); Step 2 (gender); Step 3 (pain-related anxiety); Step 4 (gender × pain-related anxiety interaction). We assessed the relative contribution of each predictor variable to the observed variance in continuous COMM scores by examining change in R squared (ΔR^2) and squared semipartial correlations (sr^2) at each step of the models. Significant interactions were probed by testing the conditional effects of pain-related anxiety at each level of gender using the PROCESS Macro for SPSS (Hayes, 2012).

Results

Participant characteristics

Participants included 61 PLWHA smokers with co-occurring pain (44.3% female; $M_{age} = 50.89$, $SD = 7.80$, range: 32–67), who reported smoking 12.85 cigarettes per day ($SD = 11.25$). The mean HSI score was 2.72 ($SD = 1.46$), indicating a moderate level of tobacco dependence (e.g., Chaiton, Cohen, McDonald, & Bondy, 2007). Nearly half of the sample (45.9%) identified as black or African American. All participants reported an annual income below $50,000, 47.5% reported earning less than $10,000 per year, and only 3 participants (4.9%) completed four years of college.

Participants reported experiencing an average of nearly 13 HIV/AIDS symptoms over the past two weeks ($M = 12.79$, $SD = 6.28$). The most frequently reported symptoms included "fatigue or loss of energy," "pain, numbness, or tingling in the hands or feet," "difficulty falling or staying asleep," and "muscle aches or joint pain." The vast majority of participants (95.1%) endorsed pain lasting longer than 3 months, which is a commonly used cutoff for indexing chronic pain (e.g., Merskey, 1986). Half of the sample (49.2%) endorsed neck/back pain as primary, and over one-third endorsed lower extremity (i.e., leg, hip, or foot) pain (36.1%). The mean characteristic pain intensity score was high ($M = 53.83$, $SD = 31.76$; Von Korff, Dworkin, & Le Resche, 1990), and the mean PASS-20 total score was 41.97 ($SD = 26.10$; range: 0–96). More than half (53.2%) of participants scored ≥30 on the PASS-20, indicating that they are at risk of responding to pain with significant anxiety and participating in a self-perpetuating cycle that maintains chronic pain (Abrams, Carleton, & Asmundson, 2007).

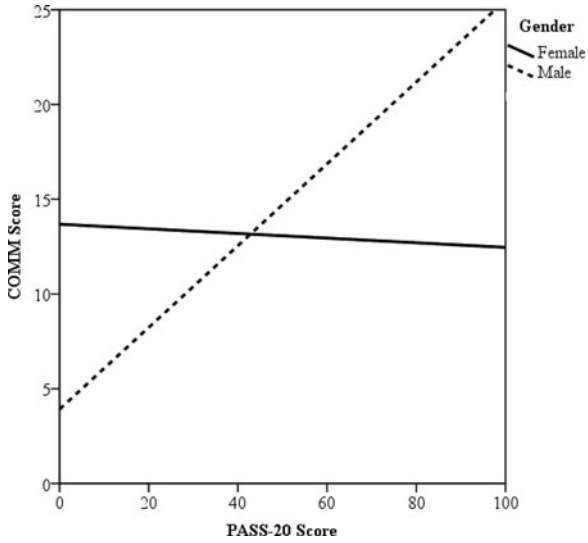

Figure 1. Conditional effects of PASS-20 scores on COMM scores as a function of gender.

More than half of the sample (57.4%) was prescribed opioid pain medication (vs. nonopioid pain medication; $n = 13$ tramadol, $n = 11$ oxycodone, $n = 8$ hydrocodone, $n = 2$ morphine, $n = 2$ Percocet, $n = 1$ fentanyl, $n = 1$ Vicodin, $n = 1$ codeine, $n = 1$ Demerol), and 4 participants were prescribed more than one opioid medication. Current prescription opioid use (yes/no) was not associated with pain-related anxiety or any other sociodemographic, smoking, or pain variable. Additional sociodemographic and clinical data are presented in Table 1.

Pain-related anxiety and current opioid misuse

Among participants who were prescribed opioid medications, hierarchical regression analyses (controlling for the effects of ethnicity, income, education, characteristic pain intensity, gender, and pain-related anxiety) revealed a significant gender x PASS-20 interaction that was positively associated with COMM scores (Step 4: $\beta = .228$, $p = .014$; Figure 1). As shown in Table 2, examination of the ΔR^2 statistic at Step 4 revealed that the interaction between gender and PASS-20 scores accounted for approximately 9% of unique variance in COMM scores. The interaction was probed by testing the conditional effects of pain-related anxiety at each level of gender (i.e., male and

Table 1. Sociodemographic, smoking, and pain characteristics.

	Opioids[a] $n = 35$ n (%)	Nonopioids[b] $n = 26$ n (%)	Total $N = 61$ n (%)
Gender			
Female	16 (45.7%)	11 (42.3%)	27 (44.3%)
Race			
White	17 (48.6%)	9 (34.6%)	26 (42.6%)
Black or African American	15 (42.9%)	13 (50.0%)	28 (45.9%)
American Indian/Alaska Native	3 (8.6%)	4 (15.4%)	7 (11.5%)
Ethnicity			
Hispanic	5 (14.3%)	2 (7.7%)	7 (11.5%)
Income			
< $10,000	17 (48.6%)	12 (46.2%)	29 (47.5%)
$10,000 – $29,000	12 (34.3%)	12 (46.2%)	24 (39.3%)
$30,000 – $49,000	6 (17.1%)	2 (7.7%)	8 (13.1%)
Education			
Did not graduate high school	9 (25.7%)	13 (50.0%)	22 (36.1%)
High school graduate	9 (25.7%)	6 (23.1%)	15 (24.6%)
Some college	8 (22.9%)	2 (7.7%)	10 (16.4%)
Technical school/Associate's degree	6 (17.1%)	5 (19.2%)	11 (18.0%)
4-year college degree	2 (5.7%)	0 (0.0%)	2 (3.3%)
School beyond 4-year college degree	1 (2.9%)	0 (0.0%)	1 (1.6%)
Primary Pain Location			
Neck/Back	17 (48.6%)	13 (50.0%)	30 (49.2%)
Lower Extremity	12 (34.3%)	10 (38.5%)	22 (36.1%)
Upper Extremity	3 (8.6%)	2 (7.7%)	5 (8.2%)
Chest	0 (0.0%)	1 (3.8%)	1 (1.6%)
Stomach	1 (2.9%)	0 (0.0%)	1 (1.6%)
Head	2 (5.7%)	0 (0.0%)	2 (3.3%)
Pain Duration			
< 3 months	2 (5.7%)	1 (3.8%)	3 (4.9%)
3–12 months	6 (17.1%)	4 (15.4%)	10 (16.4%)
> 12 months	27 (77.1%)	21 (80.8%)	48 (78.7%)
	M (SD)	M (SD)	M (SD)
Age	50.74 (8.29)	51.08 (7.24)	50.89 (7.80)
Characteristic pain intensity[c]	55.43 (33.06)	51.67 (30.42)	53.83 (31.76)
Cigarettes per day	11.83 (8.82)	14.23 (13.94)	12.85 (11.25)
HSI score[d]	2.63 (1.44)	2.85 (1.52)	2.72 (1.46)
Pain-related anxiety[e]	38.26 (27.44)	46.96 (23.78)	41.97 (26.10)

Note. [a]Prescription opioid medications included tramadol, oxycodone, hydrocodone, morphine, Percocet, fentanyl, Vicodin, codeine, and Demerol; [b]Prescription nonopioid medications included acetaminophen, ibuprofen, gabapentin, pregabalin, naproxen, and cannabis; [c]Graded Chronic Pain Scale – Characteristic Pain Intensity Subscale; [d]Heaviness of Smoking Index; [e]Pain Anxiety Symptoms Scale – 20 item; no statistically significant ($p < .05$) differences in any sociodemographic, smoking, or pain characteristic were observed between those who were prescribed opioid medications and those who were prescribed nonopioid pain medications.

Table 2. Associations between gender, pain-related anxiety, and current opioid misuse.

	Model 1			Model 2			Model 3			Model 4		
Variable	β	t	p	β	t	p	β	t	p	β	t	p
Ethnicity	16.596	4.402	<.001	16.216	4.059	<.001	16.258	4.441	<.001	15.138	.572	<.001
Income	− .302	− .228	.821	− .421	− .302	.764	.391	.298	.768	.762	.633	.532
Education Status	.354	.307	.821	.335	.286	.777	.287	.267	.791	.440	.449	.657
Characteristic Pain Intensity	.098	2.418	.022	101	2.403	.023	.075	.263	1.880	.050	1.344	.190
Gender				.943	.332	.742	− .477	− .179	.859	− 9.762	− 2.272	.031
PASS-20[a]							.119	2.554	.016	− .012	− .186	.854
Gender x PASS-20										.228	2.615	.014
R^2		.464			.466			.567			*.655*	
ΔR^2		.464			.002			.101			.087	
F for ΔR^2		6.497**			.110			6.523*			6.837*	

Note: β = standardized beta weights; [a]Pain Anxiety Symptom Scale – 20 Item; *$p < .05$, **$p < 01$.

Table 3. Conditional effects of pain-related anxiety on current opioid misuse.

Gender	B	*p*	95% CI
Male	.216	<.001	.100 – .331
Female	–.012	.854	–.147 – .113

female). As shown in Table 3, PASS-20 scores were positively associated with COMM scores among male ($p < .001$), but not female smokers ($p = .854$).

Pain-related anxiety and intention to misuse opioids in the future

As shown in Table 4, the gender x PASS-20 interaction term was not associated with COMM-Intention scores (Step 4: $\beta = .151$, $p = .635$) among the subsample of participants who were prescribed opioid medications. Thus, we examined the main effects of gender and pain-related anxiety at the second and third steps of the model. Results revealed a positive association between PASS-20 scores and COMM-Intention scores (Step 3: $\beta = .510$, $p = .001$), again, after controlling for ethnicity, income, education, characteristic pain intensity, and gender. Examination of the ΔR^2 statistic at Step 3 revealed that pain-related anxiety accounted for nearly 22% of the unique variance in COMM-Intention scores. There was no effect of gender on COMM-Intention scores (Step 2: $\beta = .025$, $p = .883$).

Discussion

This is the first study to examine associations between pain-related anxiety, gender, and prescription opioid misuse. Analyses were conducted among a sample of PLWHA who endorsed moderate dependence on tobacco smoking, and high levels of pain intensity and pain-related anxiety. Over half of the sample was prescribed opioid pain medications, and most of these reported aberrant opioid use behaviors, including taking someone else's pain medications and using pain medication for symptoms other than for pain. Among male (but not female) participants who were prescribed opioid pain medications, pain-related anxiety was found to be positively associated with current opioid misuse. Pain-related anxiety was also positively associated with self-reported intention to misuse opioids in the future among all participants who were prescribed opioids, accounting for nearly 22% of variance in COMM-Intention scores.

High pain-related anxiety has been associated with the maintenance of substance use (e.g., Ditre et al., 2015; Hogan, Gonzalez, Howell, Bonn-Miller, & Zvolensky, 2010; LaRowe et al., 2017), and these results indicate that pain-related anxiety may also be associated with opioid misuse among PLWHA smokers with co-occurring (and mostly chronic) pain. Indeed, previous work has observed positive relations between pain-related anxiety, pain, and negative affect among individuals with chronic pain (e.g., Hadjistavropoulos, Asmundson, & Kowalyk, 2004; Vowles, Zvolensky, Gross, & Sperry, 2004). PLWHA smokers with co-occurring pain and high levels of pain-related anxiety may be at increased risk for misusing prescription opioid medications to alleviate both pain and negative affect (vs. PLWHA with low pain-related anxiety; e.g., Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Wall, Melzack, & Bonica, 1994).

Further, an allostatic load model of addiction posits that repeated opponent process cycles of opioid-induced analgesia and withdrawal-induced hyperalgesia can result in dysregulation of overlapping neural substrates to engender a persistent imbalance favoring pain facilitation (Egli, Koob, & Edwards, 2012). Consistent with this model, studies across a variety of populations have found that chronic opioid therapy often leads to opioid-induced hyperalgesia (i.e., a state of enhanced pain sensitization caused by chronic exposure to opioids; Yi & Pryzbylkowski, 2015). A persistent state of nociceptive sensitization could motivate PLWHA smokers with high pain-related anxiety to use opioid medications in an

Table 4. Associations between gender, pain-related anxiety, and intentions for opioid misuse.

	Model 1			Model 2			Model 3			Model 4		
Variable	*β*	*t*	*p*	*β*	*t*	*p*	*β*	*t*	*p*	*β*	*t*	*p*
Ethnicity	.506	3.181	.003	.499	2.955	.006	.501	3.551	.001	.492	3.412	.002
Income	− .281	− 1.506	.142	− .289	− 1.470	.152	− .138	− .817	.421	− .129	− .744	.463
Education Status	.345	1.855	.073	.343	1.815	.080	.333	2.107	.044	.338	2.102	.045
Characteristic Pain Intensity	.126	.790	.436	.130	.791	.435	− .004	− .025	.980	− .022	− .145	.886
Gender				.025	.149	.883	− .087	− .593	.558	− .191	− .726	.474
PASS-20[a]							.510	3.673	.001	.430	1.971	.059
Gender x PASS-20										.151	.479	.635
R^2		.331			.331			.549			.553	
ΔR^2		.331			.001			.217			.004	
F for ΔR^2		3.708*			.022			13.494**			.230	

Note: β = standardized beta weights; [a]Pain Anxiety Symptom Scale – 20 Item; *$p < .05$, **$p < .01$.

aberrant fashion (e.g., take more than is prescribed) to escape/avoid their pain.

Importantly, the positive relation between pain-related anxiety and current opioid misuse was only evident among males. One possible explanation for this finding is that associations between pain-related anxiety and pain intensity tend to be stronger among men than women (e.g., Edwards et al., 2000; Robinson et al., 2005). Thus, male PLWHA smokers with high pain-related anxiety may objectively experience greater pain, and in turn, may be more likely to misuse prescription opioid medications. A second possible explanation can be derived from research showing that associations between anxiety and externalizing behaviors (e.g., substance use) tend to be stronger among males, relative to females (e.g., Altemus et al., 2014; Marmorstein, 2007). Previous work has also shown that females are more likely to respond to pain and anxiety by employing other (nonsubstance related) methods of coping, including social support and positive statements (e.g., Altemus et al., 2014; Keogh, 2006).

The current findings may have clinical relevance for PLWHA smokers who are prescribed opioid medications. PASS-20 scores indicated that more than half of the sample was at risk of responding to pain with significant anxiety, a finding that underscores the importance of assessing pain-related anxiety in this population. Moreover, these results suggest that PLWHA smokers who are prescribed opioids may face unique challenges that warrant tailored opioid misuse interventions. Treatments that incorporate psychoeducation, cognitive restructuring, and interoceptive exposure have been shown to decrease pain-related anxiety among persons with chronic pain (e.g., Watt, Stewart, Lefaivre, & Uman, 2006; Wetherell et al., 2011), and these treatments could be adapted for PLWHA smokers. Such treatments could also convey information about the risks of opioid misuse in the context of smoking, pain, and HIV/AIDS, which may aid in the development of discrepancy (Miller & Rollnick, 2012) regarding the misuse of prescription opioids and stated goals for better managing pain and HIV/AIDS symptoms. Additionally, tailored coping skills training, particularly among male PLWHA smokers, could emphasize the substitution of externalizing pain/anxiety coping responses (e.g., smoking and opioid misuse) with more adaptive strategies, such as using coping self-statements and reinterpreting pain sensations (e.g., Haythornthwaite, Menefee, Heinberg, & Clark, 1998).

Several study limitations should be noted. For example, the cross-sectional nature of these analyses precludes causal interpretation. Additionally, although it can be beneficial to study smaller samples during the early stages of hypothesis testing, future work should replicate these findings among a larger sample. It is also important to consider that the sample consisted entirely of current cigarette smokers. Given that smokers comprise a large portion of PLWHA (up to 74%; Vidrine, 2009) and are more likely to misuse opioids (e.g., Michna et al., 2004), this population warrants specific empirical attention. However, future work should extend these findings by testing associations between pain-related anxiety and prescription opioid misuse among a sample of PLWHA that is not restricted to current smoking. This sample was also comprised of older adults ($M_{age} = 50.89$), as pain is more common in this population (e.g., McMahon et al., 2013). Future studies should examine associations between pain-related anxiety and opioid misuse in samples that include both younger and older smokers. Given that opioid use in this study was assessed solely via medical record review, future studies would benefit from incorporating biological assessment of opioid and other substance use via urine toxicology screening, along with comprehensive assessment of substance use history. In addition, future work should examine associations between pain-related anxiety and history of opioid use/misuse (e.g., age of first use, duration of use, dosage), and test whether the use of other substances (e.g., alcohol, cannabis) influences associations between pain-related anxiety and opioid misuse. Finally, this was the first study to assess intentions to misuse prescription opioid medications, and future work should evaluate the predictive utility of the adapted COMM-Intention measure.

In summary, results of this study represent an initial, yet important, step towards better understanding the role of pain-related anxiety in the maintenance of prescription opioid misuse among people living with HIV. No previous research has examined associations between pain-related anxiety, gender, and opioid misuse, and these data provide the first evidence that high levels of pain-related anxiety may be associated with greater current opioid misuse among male PLWHA smokers with co-occurring pain, and with intentions to misuse opioids in the future among both male and female PLWHA smokers with co-occurring pain. This and future work has the potential to inform the development of tailored opioid misuse interventions for PLWHA smokers who experience pain and pain-related anxiety. Future work should also continue to explore gender-specific effects of pain-related anxiety in the context of substance use in general, and prescription opioid misuse in particular.

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Appendix 1.

COMM-Intention

Please answer the questions using the following scale:	Extremely unlikely	Unlikely	Neutral	Likely	Extremely likely
	1	2	3	4	5
1. In the next 30 days, how likely is it that you will go to someone other than your prescribing physician to get sufficient pain relief from medications (e.g., another doctor, the Emergency Room, friends, street sources)?					
2. In the next 30 days, how likely is it that you will take your pain medications differently from how they are prescribed?					
3. In the next 30 days, how likely is it that you will spend a significant amount of your time thinking about opioid medications (e.g., having enough, taking them, dosing schedule)?					
4. In the next 30 days, how likely is it that you will take pain medications belonging to someone else?					
5. In the next 30 days, how likely is it that you will worry about how you're handling your pain medications?					
6. In the next 30 days, how likely is it that others will worry about how you're handling your pain medications?					
7. In the next 30 days, how likely is it that you will take more of your pain medication than prescribed?					
8. In the next 30 days, how likely is it that you will borrow pain medication from someone else?					
9. In the next 30 days, how likely is it that you will use your pain medication for symptoms other than pain (e.g., to help you sleep, improve your mood, or relieve stress)?					
10. In the next 30 days, how likely is it that you will visit the Emergency Room to get pain medication?					