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Correlates of prescription opioid therapy in Veterans with chronic pain and history of substance use disorder

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Abstract—Patients with a history of substance use disorder (SUD) are more likely to be prescribed opioid medications for chronic pain than patients without an SUD history; however, little is known about prescription opioid therapy in populations composed exclusively of patients with SUD. This study examined correlates of prescription opioid therapy in 214 Veterans with chronic noncancer pain and an SUD history. Participants completed psychosocial questionnaires and participated in a structured mental health diagnostic interview, and medical diagnoses and opioid pharmacy data were abstracted from their Department of Veterans Affairs electronic medical records. Participants were categorized into three groups based on opioid prescriptions in the past 90 d: no opioid therapy (n = 134), short-term (<90 d) opioid therapy (n = 31), or long-term (>/= 90 d) opioid therapy (n = 49). Relative to participants prescribed no or short-term opioid therapy, participants who were prescribed long-term opioid therapy had a greater number of pain diagnoses; reported higher levels of pain severity, interference, and catastrophizing; and endorsed lower chronic pain self-efficacy. In a multivariate model, number of pain diagnoses and pain interference were associated with a greater likelihood of being prescribed long-term opioid therapy after controlling for demographic and clinical characteristics. Findings highlight the poor pain-related functioning in patients with SUD histories who are prescribed long-term opioid therapy.

Key words: chronic noncancer pain, chronic pain, long-term opioid therapy, opioids, pain, pain interference, prescription opioid therapy, short-term opioid therapy, substance use disorder, Veterans.

INTRODUCTION

More than half of Department of Veterans Affairs (VA) primary care patients report pain, with many reporting chronic pain [1–3]. Relative to patients without chronic pain, patients with chronic pain have increased medical utilization, disability, and lost work productivity and decreased quality of life [1,4–5]. High rates of past and current alcohol and other substance use disorders (SUDs) have also been observed in patients with chronic pain [6–7].

Abbreviations: ANOVA = analysis of variance, BDI-II = Beck Depression Inventory-Second Edition, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition, LOT = long-term opioid therapy, MPI = West Haven-Yale Multidimensional Pain Inventory, NIH = National Institutes of Health, NOT = no opioid therapy, PTSD = posttraumatic stress disorder, SD = standard deviation, SOT = short-term opioid therapy, SUD = substance use disorder, VA = Department of Veterans Affairs.

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Prescription opioid therapy is commonly used to treat chronic pain in both Veteran and non-Veteran patients [8–10]. However, controversy surrounds this practice because recent studies indicate that fewer than half of patients prescribed opioids will experience a clinically significant reduction in pain intensity in the short term, with little improvement in physical function long-term [11–12]. Treating chronic pain with opioid therapy in patients with comorbid SUD may be especially difficult. Persons with chronic pain and SUD histories prescribed opioid therapy are at increased risk of opioid misuse, abuse, and diversion [2,13] as well as opioid overdose and opioid-related death [14–15]. These data have contributed to further controversy over the prescription of opioids to persons with SUD [16–18].

Several studies have identified specific patient demographic and clinical characteristics associated with prescription short-term opioid therapy (SOT) and long-term opioid therapy (LOT) among diverse samples of Veterans with and without SUD histories. These include younger age, male sex, white race, mental health diagnoses (e.g., depressive disorders and posttraumatic stress disorder [PTSD]), specific pain diagnoses (e.g., low back pain, neck or joint pain, arthritis), and greater perceived pain intensity [8–9,19–20]. Notably, Veterans with comorbid chronic pain and SUD, relative to Veterans with chronic pain and no SUD, are also more likely to be prescribed SOT and LOT at high doses [2,8,13,21–22]. No studies, however, have identified correlates of prescription opioid therapy within samples composed exclusively of patients with lifetime SUD histories, and it is unclear whether correlates of opioid therapy identified in previous studies that recruited heterogeneous patient samples will extend to SUD populations. Furthermore, previous studies that examined correlates of prescription opioid therapy have predominantly used administrative data, limiting available data to what were included in and could be extracted from patients' medical records (e.g., demographic characteristics, medical diagnoses).

The current study examined correlates of prescription opioid therapy in VA patients with chronic pain and lifetime SUD histories using data available in patients' medical records integrated with well-validated measures of psychopathology, substance use, and pain-related variables obtained through self-report questionnaires and clinical interviews. Based on prior research, we hypothesized that patients with more severe depressive and PTSD-related symptoms, an active SUD, and poor pain-related coping and functioning would be more likely to be prescribed LOT to manage pain. We further hypothesized that these relationships would remain significant even after controlling for demographic characteristics that have been associated with prescription opioid therapy in previous studies.

METHODS

Participants and Procedures

Participants consisted of a sample from a larger study at a single VA medical center in the Pacific Northwest that examined the relationship between chronic pain, hepatitis C virus infection, and substance abuse [23]. Participants were recruited by posted advertisements in the medical center, letters sent to patients with scheduled primary care appointments, announcements in mental health classes, and referral by clinicians in the medical center's Hepatology Clinic. Participants completed a single research appointment consisting of a clinical interview and completion of self-administered questionnaires. They received a $30 store gift card as compensation.

Eligible participants met the following study inclusion criteria: history of being tested for hepatitis C regardless of the result of the test (62% of enrolled participants were hepatitis C positive), age 18 yr or older, and English literacy. Patients with hepatitis C have high rates of chronic pain [24–25] and SUD [26], making this sample ideal for examining prescription opioid therapy in patients with both chronic pain and SUD histories. A total of 375 patients were screened for study eligibility, and 284 participants enrolled in the larger study between March 2009 and August 2011. Reasons for study exclusion included age greater than 70 yr (n = 1), pending litigation or disability compensation for pain (n = 28), presence of advanced liver disease (n = 50), current suicidal ideation (n = 2), current untreated psychotic-spectrum disorder (e.g., schizophrenia) or bipolar disorder (n = 2), cognitive impairment that precluded participation (n = 2), being a non-Veteran (n = 3), and incomplete responses to eligibility screening questions (n = 3).

Data Collection

Demographic Characteristics

Self-administered questionnaires assessed participant demographic characteristics, including age, sex, race, marital status, years of education, and annual income.

Pain Measures

Participants completed several well-validated and commonly used pain measures. Participants' perception of pain severity and the extent to which pain interferes with their lives was assessed with the West Haven-Yale Multidimensional Pain Inventory (MPI) severity scale (3 items) and interference scale (11 items) [27]. Pain severity and interference are widely used measures in studies of pain and have been recommended through expert consensus as core outcome measures in pain clinical trials [28]. MPI severity and interference scores range from 0 to 6, with scores lower than 2 indicating no or mild pain severity or interference, scores between 2 and 4 indicating moderate pain severity or interference, and scores higher than 4 representing severe pain severity or interference [29]. Pain-related catastrophizing was assessed with the 13-item Pain Catastrophizing Scale [30]. The Pain Catastrophizing Scale includes items that assess exaggerated negative orientation toward pain. Self-efficacy for managing pain was assessed with the 22-item Chronic Pain Self-Efficacy Scale [31], which measures individuals' beliefs about the extent to which they can manage their pain. Items on all pain measures used in the current study use numeric rating scales, and items are summed or averaged within scales to produce scale scores.

Mental Health Functioning

The 21-item Beck Depression Inventory-Second Edition (BDI-II) [32] assessed depressive symptom severity in the past 2 wk. The PTSD Checklist-Civilian Version [33] is commonly used in VA studies that examine symptoms of PTSD and evaluates the extent to which respondents experienced each of 17 PTSD-related symptoms in the past 1 mo. We chose to use the civilian rather than military version of the PTSD Checklist in order to assess current symptoms associated with "stressful life experiences." Prior research has demonstrated good psychometric characteristics of the PTSD Checklist-Civilian Version among Veterans [34–35]. For the current study, participants were classified as meeting criteria for PTSD if they responded affirmatively to an index trauma question and scored at least 50 on the PTSD Checklist. Scores above this cutoff are indicative of clinically significant PTSD symptoms [36].

Substance Use Disorders

To obtain detailed SUD histories, trained interviewers administered the SUD module of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) [37], which has demonstrated excellent psychometric properties [38]. This interview identifies patients' lifetime histories of alcohol and non-alcohol substance abuse and dependence that are consistent with DSM-IV diagnostic criteria. The Structured Clinical Interview was modified for the current study to allow for separate diagnoses of prescription opioid use disorder and illicit (e.g., heroin) opioid use disorder. Consistent with DSM-IV diagnostic criteria, participants who met criteria in the prior month for substance abuse or dependence were coded as having an active SUD. Participants who previously met criteria for substance abuse or dependence, but not in the past month, were coded as having a lifetime SUD history. For participants who met diagnostic criteria for a lifetime SUD history, we did not distinguish between those in early versus sustained remission or partial versus full remission. We used these definitions of active and lifetime SUD history to align with DSM-IV diagnostic criteria and because a purpose of the parent study was to identify the proportion of patients with current SUD symptoms that required clinical attention.

Pain Diagnoses and Opioid Prescriptions

Pain diagnoses and opioid pharmacy data were extracted from patients' electronic medical records using the Veterans Integrated Service Network-20 Data Warehouse. The Data Warehouse contains extracts of data from clinical records of regional VA facilities and national VA databases. Diagnostic data were obtained using International Classification of Diseases, 9th Edition, Clinical Modification codes listed in medical encounter data for the 5 yr preceding study assessment. Pain diagnoses included neck or joint pain, low back pain, arthritis, migraine headache, neuropathy, and fibromyalgia. Electronic medical record data also identified participants who had current opioid prescriptions from this medical center. Opioid type included codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, and propoxyphene. Notably, no participants were prescribed methadone as part of an opioid substitution program. We abstracted data on opioid type and duration in the past 90 d. Type of opioid prescribed was categorized into short-acting only (codeine, hydrocodone, hydromorphone, morphine, oxycodone, oxymorphone, and propoxyphene), long-acting only (fentanyl, methadone, and sustained-release hydromorphone, morphine, oxycodone, and oxymorphone), or concurrent short- and long-acting [39–40].

Statistical Analyses

This study included a subset of 214 participants from the larger sample who had one or more chronic pain diagnoses in the electronic medical record and met criteria for one or more active or lifetime SUDs based on the structured diagnostic interview. To identify correlates of prescription opioid therapy, we categorized participants into three groups: (1) no opioid therapy (NOT) in the past 90 d (n = 134), (2) SOT (<90 d duration; n = 31), or (3) LOT (≥90 d duration; n = 49). Similar definitions of SOT and LOT have been used in prior studies [8,20,41–42].

We conducted bivariate analyses using analysis of variance (ANOVA) for continuous variables and chi-square tests of association for categorical variables to compare demographic characteristics, mental health functioning, pain variables, and SUD diagnoses between the three opioid therapy groups. Significant omnibus ANOVA tests were followed with Fisher least significant difference pairwise comparisons. We also compared type of prescribed opioid between those on SOT versus LOT using chi-square tests of association. We next conducted a hierarchical multinomial logistic regression analysis to identify clinical and pain-related variables most strongly associated with NOT versus SOT versus LOT in the past 90 d. The goal of this analysis was to test the hypothesized correlates of prescription opioid therapy. The first step of this model controlled for demographic characteristics that have demonstrated associations with receipt of prescription opioid therapy in prior studies (age, sex, race) [8–9,19]. In the second step, we included depression symptom severity, PTSD diagnosis, and active SUD diagnosis. Data screening procedures identified high intercorrelations between five pain variables: number of pain diagnoses, pain severity, pain interference, pain catastrophizing, and chronic pain self-efficacy (see **Table 1** for variable correlations). We thus performed a backward stepwise elimination procedure for the pain variables in the third step of the model, retaining variables in the model that were significant at the $p < 0.10$ level. We chose this cutoff criterion to ensure retention of pain variables most strongly correlated with prescription opioid therapy while maintaining model parsimony [43]. All analyses employed two-tailed tests of significance.

RESULTS

This sample of 214 Veteran patients with chronic pain and SUD histories was composed predominantly of white (76%) male (94%) individuals. Of the participants, 60 percent had annual incomes less than $15,000 and 78 percent had a high school education or greater. Nearly all participants (95%) met diagnostic criteria for a lifetime alcohol use disorder, and many also met criteria for a lifetime cannabis use disorder (64%), lifetime cocaine use disorder (59%), and lifetime stimulant use disorder (54%). Thirty-nine percent of participants met criteria for a lifetime opioid use disorder and of these, 61 percent (n = 51) reported prior abuse of prescription opioids. Seventeen percent of participants (n = 36) met criteria for

Table 1.
Bivariate correlations between demographic, clinical, and pain variables.

Covariate	1	2	3	4	5	6	7	8	9	10	11
Demographic											
Age	1.00	—	—	—	—	—	—	—	—	—	—
Sex (Male = 0, Female = 1)	–0.11	1.00	—	—	—	—	—	—	—	—	—
Race (Minority = 0, White = 1)	–0.05	–0.03	1.00	—	—	—	—	—	—	—	—
Clinical											
BDI-II Depression Severity	–0.11	0.04	0.04	1.00	—	—	—	—	—	—	—
PTSD Diagnosis (No = 0, Yes, = 1)	–0.07	–0.02	0.05	0.51*	1.00	—	—	—	—	—	—
Active SUD Diagnosis (No = 0, Yes = 1)	–0.07	–0.07	–0.07	0.14†	0.18*	1.00	—	—	—	—	—
Pain											
No. of Pain Diagnoses	0.15†	–0.03	0.01	0.19*	0.11	–0.07	1.00	—	—	—	—
Pain Severity	0.13	0.05	–0.03	0.32*	0.21*	0.06	0.33*	1.00	—	—	—
Pain Interference	0.15†	–0.01	–0.01	0.43*	0.33*	0.08	0.32*	0.81*	1.00	—	—
Pain Catastrophizing	–0.05	–0.01	0.08	0.57*	0.37*	0.16†	0.24*	0.63*	0.66*	1.00	—
Chronic Pain Self-Efficacy	–0.12	–0.01	0.04	–0.35*	–0.12	–0.08	–0.25*	–0.48*	–0.56*	–0.53*	1.00

*$p < 0.01$.
†$p < 0.05$.
BDI-II = Beck Depression Inventory-Second Edition, No. = number, PTSD = posttraumatic stress disorder, SUD = substance use disorder.

an active SUD; the most common active SUD diagnoses included alcohol (64%, $n = 23$) and cannabis (22%, $n = 8$) use disorders. Only 17 percent ($n = 6$) of participants with an active SUD met diagnostic criteria for an opioid use disorder; half of these participants ($n = 3$) met criteria for illicit opioid use disorder, while the other half ($n = 3$) met criteria for prescription opioid use disorder. Nineteen participants (9%) were receiving specialty SUD treatment at the time of study assessment.

The most common pain syndromes in the sample were neck or joint pain (82%), low back pain (66%), and arthritis (57%). Having multiple pain syndromes was the norm rather than the exception; 74 percent of participants had at least two chronic pain diagnoses, with a mean ± standard deviation (SD) of 2.5 ± 1.3 pain diagnoses in the entire sample. Thirty-seven percent of participants ($n = 80$) were prescribed opioid therapy in the past 90 d, with 61 percent of those ($n = 49$) prescribed LOT. Among participants prescribed opioids, 85 percent were prescribed short-acting opioids only, 6 percent were prescribed long-acting opioids only, and 9 percent were prescribed both short- and long-acting opioids. The most commonly prescribed opioids were hydrocodone (65% prescribed SOT and 61% prescribed LOT) and oxycodone (26% prescribed SOT and 43% prescribed LOT). The mean ± SD BDI-II score in the sample was 17.1 ± 12.5, with 47 percent scoring above 17, which is representative of clinically significant depressive symptoms [32]. Of the participants, 114 (53%) were prescribed antidepressant medication at the time of study assessment. Thirty-two percent met criteria for PTSD based on PTSD Checklist scores.

Bivariate Correlates of Prescription Opioid Therapy

Table 2 provides data comparing participants in the three groups (NOT, SOT, and LOT) on demographic characteristics, mental health variables, SUD variables, pain-related variables, and type of opioid therapy received. Difference trends in depression, receipt of antidepressant medication, and PTSD were observed across the three groups, suggesting increasing depressive symptom severity and PTSD prevalence and receipt of antidepressant medication for participants prescribed opioid therapy, particularly LOT; however, these results did not reach statistical significance. Participants prescribed LOT reported poorer pain-related function and had more pain diagnoses. Specifically, participants prescribed LOT, relative to those prescribed NOT or SOT, reported greater pain severity, pain interference, pain catastrophizing, and lower self-efficacy to manage pain. Pain severity and interference were also higher in participants prescribed SOT relative to those prescribed NOT. Participants prescribed LOT had more pain diagnoses relative to those prescribed NOT or SOT. No differences in demographic or SUD variables were observed between participants prescribed NOT, SOT, or LOT.

Notably, among the 80 participants prescribed opioid therapy in the past 90 d, those prescribed LOT were less likely than those prescribed SOT to be prescribed short-acting opioids only (78% vs 97%, $p = 0.05$). However, only 22 percent of participants prescribed LOT were prescribed long-acting opioids.

Multivariate Model of Any Prescription Opioid Therapy

A multivariate hierarchical multinomial logistic regression model identified correlates of NOT ($n = 134$) versus SOT ($n = 31$) versus LOT ($n = 49$). This model controlled for age, sex, and race in the first model step. The overall step was nonsignificant (step 1 $\chi^2(6) = 2.06$, $p = 0.91$), as were each of the individual demographic covariates. The second model step, which included depressive symptom severity, PTSD diagnosis, and active SUD diagnosis, was also nonsignificant (step 2 $\chi^2(6) = 9.39$, $p = 0.15$), as were each of the mental health and SUD covariates. Candidate pain variables included in the stepwise elimination procedure in the final model step included number of pain diagnoses, pain severity, pain interference, pain catastrophizing, and chronic pain self-efficacy. The overall model step was significant (step 3 $\chi^2(4) = 37.98$, $p < 0.001$). Only number of pain diagnoses ($\chi^2(2) = 7.78$, $p = 0.02$) and pain interference ($\chi^2(2) = 24.83$, $p < 0.001$) were retained in the final model. Specifically, an increased number of pain diagnoses and greater pain interference were associated with a greater likelihood of being prescribed LOT versus NOT or SOT. Number of pain diagnoses and pain interference were unrelated to the likelihood of being prescribed SOT versus NOT. **Table 3** lists final model statistics.

DISCUSSION

This study examined correlates of prescription opioid therapy for chronic pain in a sample composed entirely of patients with lifetime SUD histories. More than one-third

Table 2.
Comparison of demographic and clinical characteristics based on receipt of opioid therapy. Data presented as mean ± standard deviation or frequency (%).

Characteristic	No Opioid Therapy (*n* = 134)	Short-Term Opioid Therapy (*n* = 31)	Long-Term Opioid Therapy (*n* = 49)	*p*-Value
Demographic				
Age (yr)	54.8 ± 8.2	54.2 ± 6.0	55.3 ± 6.4	0.82
Male	128 (95.5)	29 (93.5)	44 (89.8)	0.48
White	103 (76.9)	24 (77.4)	36 (73.5)	0.90
Marital Status				0.75
Single	30 (22.4)	6 (19.4)	13 (26.5)	
Married	28 (20.9)	8 (25.8)	12 (24.5)	
Divorced/Separated	71 (53.0)	15 (48.4)	20 (40.8)	
Widowed	5 (3.7)	2 (6.5)	4 (8.2)	
High School Education or Less	28 (20.9)	8 (25.8)	11 (22.4)	0.82
Annual Income <$15,000	79 (59.0)	22 (71.0)	28 (57.1)	0.40
Mental Health				
BDI-II	15.9 ± 12.4	17.0 ± 10.6	20.6 ± 13.6	0.08
Prescribed Antidepressant Medication	65 (48.5)	16 (51.6)	33 (67.3)	0.08
PTSD Diagnosis	34 (25.4)	13 (41.2)	21 (43.9)	0.06
SUD				
Lifetime SUD Diagnoses				
Alcohol	127 (94.8)	30 (96.8)	47 (95.9)	0.87
Cannabis	85 (63.4)	21 (67.7)	30 (61.2)	0.84
Cocaine	81 (60.4)	21 (67.7)	25 (51.0)	0.36
Stimulants	72 (53.7)	19 (61.3)	24 (49.0)	0.56
Hallucinogens	45 (33.6)	11 (35.5)	14 (28.6)	0.77
Illicit Opioids	39 (29.1)	9 (29.0)	17 (34.7)	0.76
Prescribed Opioids	34 (25.4)	8 (25.8)	9 (18.4)	0.59
Sedatives	31 (23.3)	6 (19.4)	11 (22.4)	0.93
No. of Lifetime SUD Diagnoses	3.8 ± 2.0	4.0 ± 2.2	3.6 ± 1.9	0.64
Active SUD Diagnosis	19 (14.1)	7 (22.6)	10 (20.4)	0.38
Receiving Specialty SUD Care	0 (0.0)	10 (32.3)	9 (18.4)	0.16
Pain				
Pain Diagnoses				
Neck or Joint Pain	106 (79.1)[a]	23 (74.2)[a]	46 (93.9)[b]	0.04
Low Back Pain	81 (60.4)[a]	18 (58.1)[a]	42 (85.7)[b]	<0.01
Arthritis	68 (50.7)[a]	19 (61.3)[a,b]	36 (73.5)[b]	0.02
Migraine Headache	25 (18.7)	5 (16.1)	12 (24.5)	0.59
Neuropathy	13 (9.7)	4 (12.9)	5 (10.2)	0.87
Fibromyalgia	11 (8.2)[a]	1 (3.2)[a]	9 (18.4)[b]	0.05
No. of Pain Diagnoses	2.3 ± 1.2[a]	2.3 ± 1.1[a]	3.1 ± 1.2[b]	<0.01
MPI Pain Severity	2.8 ± 1.6[a]	3.4 ± 1.4[b]	4.2 ± 1.0[c]	<0.01
MPI Pain Interference	3.1 ± 1.8[a]	3.7 ± 1.4[b]	4.7 ± 1.0[c]	<0.01
Chronic Pain Self-Efficacy Scale	1,450.6 ± 429.0[a]	1,353.9 ± 350.1[a]	1,137.6 ± 347.4[b]	<0.01
Pain Catastrophizing Scale	19.7 ± 12.8[a]	22.5 ± 13.4[a]	28.7 ± 11.7[b]	<0.01
Prescribed Opioid Therapy				
Type of Opioid				0.05
Short-Acting Only	NA	30 (96.8)	38 (77.6)	
Long-Acting Only	NA	1 (3.2)	4 (8.2)	
Both Short- and Long-Acting	NA	0 (0.0)	7 (14.3)	

Note: Values with different superscript letters significantly differ at $p < 0.05$ level.
*Based on PTSD Checklist.
BDI-II = Beck Depression Inventory-Second Edition, MPI = West Haven-Yale Multidimensional Pain Inventory, NA = not applicable, No. = number, PTSD = post-traumatic stress disorder, SUD = substance use disorder.

Table 3.
Final multivariate model examining correlates of opioid therapy. Data presented as odds ratio (95% confidence interval).

Covariate	NOT* vs SOT	NOT* vs LOT	SOT* vs LOT
Step 1: Demographic			
Age	0.99 (0.93–1.04)	0.98 (0.93–1.04)	0.99 (0.93–1.06)
Sex (Male = 0, Female = 1)	1.34 (0.25–7.04)	2.91 (0.70–12.05)	2.18 (0.33–14.08)
Race (Minority = 0, White = 1)	1.09 (0.42–2.86)	0.98 (0.41–2.34)	0.90 (0.29–2.75)
Step 2: Clinical			
BDI-II Depression Severity	0.98 (0.94–1.02)	0.98 (0.94–1.01)	1.00 (0.95–1.05)
PTSD Diagnosis (No = 0, Yes = 1)	1.86 (0.72–4.83)	1.31 (0.55–3.11)	0.70 (0.23–2.12)
Active SUD Diagnosis (No = 0, Yes = 1)	1.56 (0.79–1.40)	1.59 (0.60–4.24)	1.02 (0.31–3.36)
Step 3: Pain			
No. of Pain Diagnoses	0.95 (0.72–1.26)	1.44 (1.08–1.91)†	1.51 (1.06–2.15)†
MPI Interference Scale	1.30 (0.97–1.73)	2.12 (1.50–3.00)†	1.64 (1.09–2.46)†

Note: Final model $\chi^2(16) = 49.42$, $p < 0.001$, Nagelkerke pseudo $R^2 = 0.25$.
*NOT group served as reference category versus SOT and LOT groups; SOT group served as reference category versus LOT group.
†Association significant at $p < 0.05$ level.
BDI-II = Beck Depression Inventory-Second Edition, LOT = long-term opioid therapy, MPI = West Haven-Yale Multidimensional Pain Inventory, No. = number, NOT = no opioid therapy, PTSD = posttraumatic stress disorder, SOT = short-term opioid therapy, SUD = substance use disorder.

of participants in this sample were prescribed an opioid in the past 90 d. This percentage is slightly lower than the approximately 50 percent identified in a national sample of patients with chronic pain diagnoses seen in the VA during fiscal years 2009 through 2011 [9], the same years in which this study was conducted. This observed difference may be an artifact of the intervals over which prescription opioid therapy were measured in the two studies (i.e., 90 d in the current study vs 12 mo in the national cohort) or the potentially nonrepresentative convenience sample recruited for the current study. Notably, our sample was similar in terms of age, sex, race, and recent SUD diagnoses when compared with a nationally representative sample of 10,159 Veterans with high alcohol consumption [44], indicating the composition of our sample across these variables reflects the broader population of VA patients with SUDs. Nonetheless, additional studies using representative samples are needed that describe recent opioid prescription trends and nonopioid pain treatment use specifically in patients with lifetime SUD histories.

Our bivariate finding that participants with SUD prescribed LOT reported greater pain severity than those prescribed NOT or SOT is consistent with our hypothesis and findings from prior studies of patients with chronic pain [8,20]. Unfortunately, we do not have data documenting participant pain ratings prior to the initiation of opioid therapy to determine whether pain severity reduced as a result of LOT. It is possible that high pain ratings led clinicians to initiate opioid therapy for these participants. Indeed, previous studies demonstrated that patients with SUD are highly sensitive to pain and report greater pain severity relative to those without SUD [45–47]. In one scenario, elevated pain ratings in this group of participants prescribed LOT may represent reductions in pain severity from even higher pain ratings observed prior to opioid therapy initiation, albeit to levels still greater than pain ratings endorsed by those not prescribed opioids. Alternatively, participants prescribed LOT may have experienced near alleviation of pain when first initiating opioid therapy but over time developed opioid tolerance or opioid-induced hyperalgesia related to the chronicity of opioid therapy, resulting in a rebound of pain [48–49]. Longitudinal studies are needed to describe pain trajectories for patients with SUD prescribed opioid therapy for chronic pain to inform clinicians about when to initiate, maintain, and discontinue opioid therapy for those with SUD histories. Ideally, these studies would capture pain intensity and pain-related function prior to opioid initiation, during the course of opioid therapy, and when applicable, following opioid discontinuation.

Several findings about the type of opioids prescribed to participants in the current study are notable. Hydrocodone and oxycodone, both short-acting opioids, were the most commonly prescribed opioids in the entire sample at 63 and 36 percent, respectively. Prescription rates did not differ between participants prescribed SOT or LOT. Only 22 percent of those prescribed LOT were prescribed

any long-acting opioids, and nearly two-thirds of these participants prescribed long-acting opioids were prescribed a short-acting opioid concomitantly. While a historical diagnosis of SUD by itself would not preclude a patient with chronic pain from being prescribed opioid therapy, VA/Department of Defense opioid therapy guidelines recommend use of long-acting opioids for persistent pain and prescription of any opioid therapy for chronic pain only after other nonopioid analgesic pharmacotherapies and nonpharmacologic pain treatments have insufficiently improved pain-related function [50]. Of additional concern is that oxycodone and, recently, hydrocodone are schedule II controlled substances and prescriptions of these substances are associated with increased risk of opioid overdose death [51]. VA patients with SUD histories are also 2.5 times more likely than those without SUD histories to die by prescription opioid overdose [14], indicating that two of the "riskiest" opioids are being prescribed to this already high-risk group.

A unique contribution of this study was the measurement of patient-reported pain outcomes using well-validated measures not previously included- in studies of prescription opioid therapy and the integration of these data with administrative data available in patient medical records. Notably, average pain severity and interference scores for those in the LOT category fell in the "severe" range while pain severity and interference scores for those in the NOT and SOT categories fell in the "moderate" range. Participants prescribed LOT also endorsed greater pain catastrophizing and had poorer pain coping self-efficacy skills. In our multivariate analysis, pain interference remained the most robust correlate of LOT. Many patients with chronic pain will not experience sustained alleviation of pain, despite trials of analgesic pharmacotherapy and nonpharmacologic pain treatment [52–53]. The emphasis for these patients thus becomes improved quality of life through reduced pain-related disability, improved physical function, and enhanced coping skills [54]. Multifaceted, collaborative pain care approaches that are consistent with a biopsychosocial approach to pain management are needed for patients with comorbid SUD because prescription opioid therapy may be contraindicated for some and ineffective at adequately managing pain in others [55].

Results of this study should be considered in light of its limitations. First, we examined a convenience sample of VA patients from a single VA medical center in the Pacific Northwest who had been tested for hepatitis C virus infection, and despite a similar demographic composition of patients in our sample versus nationally representative samples of VA patients with SUD [44], results may not generalize to this larger population. Second, questionnaire and clinical interview data were cross-sectional, and we obtained pain diagnoses, opioid and antidepressant prescription data, and specialty SUD treatment utilization retrospectively from participants' medical records. As such, causal inferences cannot be drawn from these data. Third, we included participants with a lifetime history of any SUD. Some substances when combined with opioids (e.g., alcohol, benzodiazepines) may confer greater risk of opioid-related adverse events than others (e.g., cannabis). Future studies should examine which SUDs, or combination of SUDs, moderate opioid prescribing practices. Fourth, participants with lifetime SUD histories included individuals in early and partial remission from an active SUD, and receipt of opioid therapy may differ between these individuals and those with SUD in full sustained remission. Fifth, we were unable to verify adherence to prescribed opioid therapy or whether participants obtained opioid prescriptions from non-VA sources. Sixth, we did not evaluate opioid therapy retrospectively beyond 90 d prior to the study assessment. As such, we were unable to assess the duration of continuous opioid therapy for those in the LOT category or determine whether participants in the NOT category had previously been prescribed opioid therapy for pain. Seventh, we did not obtain information about nonopioid pain treatment received in the 90 d prior to the study encounter. It is thus unclear what adjunctive services participants may have been using concurrently with, or as alternatives to, opioids to manage pain. Finally, sample size limitations may have contributed to our failure to obtain statistically significant findings for variables previously shown to be associated with opioid therapy (e.g., PTSD and active SUD diagnoses) [8,20].

CONCLUSIONS

In summary, we found that among a sample of VA patients with chronic pain and lifetime SUD histories, those prescribed opioid therapy, particularly LOT, had higher pain severity and poorer pain-related function and coping. Unfortunately, little is known about the effectiveness of pain treatments for patients with SUD because pain therapy clinical trials have historically excluded

these patients [56]. Additional research is needed to identify evidence-based pain treatments for patients with chronic pain and SUD that reduce pain and improve physical function while minimizing the deleterious consequences of substance misuse and abuse.

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