ORIGINAL RESEARCH

Factors associated with prescription opioid misuse in a cross-sectional cohort of patients with chronic non-cancer pain

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Objective: To examine demographic features, psychosocial characteristics, pain-specific behavioral factors, substance abuse history, sleep, and indicators of overall physical function as predictors of opioid misuse in patients presenting for new patient evaluation at a tertiary pain clinic.

Methods: Overall, 625 patients with chronic non-cancer pain prospectively completed the Collaborative Health Outcomes Information Registry, assessing pain catastrophizing, National Institutes of Health Patient-Reported Outcomes Measurement Information System standardized measures (pain intensity, pain behavior, pain interference, physical function, sleep disturbance, sleep-related impairment, anger, depression, anxiety, and fatigue), and substance use history. Additional information regarding current opioid prescriptions and opioid misuse was examined through retrospective chart review.

Results: In all, 41 (6.6%) patients presented with some indication of prescription opioid misuse. In the final multivariable logistic regression model, those with a history of illicit drug use (odds ratio [OR] 5.45, 95% confidence interval [CI] 2.48–11.98, $p<0.0001$) and a current opioid prescription (OR 4.06, 95% CI 1.62–10.18, $p=0.003$) were at elevated risk for opioid misuse. Conversely, every 1-h increase in average hours of nightly sleep decreased the risk of opioid misuse by 20% (OR 0.80, 95% CI 0.66–0.97, $p=0.02$).

Conclusion: These findings indicate the importance of considering substance use history, current opioid prescriptions, and sleep in universal screening of patients with chronic non-cancer pain for opioid misuse. Future work should target longitudinal studies to verify the causal relationships between these variables and subsequent opioid misuse.

Keywords: sleep, pain catastrophizing, patient-reported outcomes, mood substance use

Introduction

The use of prescription opioids in chronic non-cancer pain populations has been a point of considerable debate in recent years. The risk of misuse of these medications is among the many concerns. Opioid misuse may result in severe health consequences including overdose and contribute to the development of opioid dependence. However, there is a lack of clarity in current estimates of opioid misuse in chronic non-cancer pain populations.[1] Some estimates suggest that up to 60% of patients with chronic pain and a current opioid regimen may be susceptible to misuse of their medications;[2] the most common form of misuse seems to be a pattern of occasional medication overuse, although more severe forms of misuse, such as diversion of medications or crushing, snorting, or chewing opioids, seem to be much less common.[2] Due to the lack of evidence for long-term efficacy of these medications and, further, the concerns that opioids may prime patients for greater physical and psychosocial problems, there has

been an increased interest in determining the risk factors for problematic opioid use in the context of chronic non-cancer pain to aid universal screening efforts.

There are myriad demographic, physical, and psychosocial factors that have been identified as salient predictors for opioid misuse in chronic pain.[3] Cross-sectional studies have suggested that younger, male patients are at increased risk of opioid misuse.[4,5] Patients reporting higher levels of pain severity and pain-related interference tend to be prescribed higher doses of opioids[6] and show an elevated risk of opioid misuse in prospective studies.[7] Other physical factors, such as the presence of concurrent physical illnesses,[8] substance use,[9,10] and degree of pain-related limitation,[4] also seem to be significant predictors of problematic opioid use in people with chronic pain.

Indicators of general and pain-specific psychological distress are key predictors of opioid misuse in cross-sectional and prospective studies. Patients who have concurrent mental health diagnoses[5] and those who report higher levels of psychological distress, such as elevated symptoms of anxiety and depression, tend to be at higher risk of opioid misuse[11–14] and are more likely to be diagnosed with an opioid use disorder.[4] Similarly, patients who evince a greater tendency toward pain catastrophizing, a mental set related to pain that is characterized by feelings of helplessness and persistent and unrealistic beliefs about pain and its consequences, are vulnerable to misuse of opioids.[15,16] High levels of pain catastrophizing may also amplify the risks of opioid misuse for patients with a history of a substance use disorder.[7] Current research highlights the association between general and pain-specific measures of psychological distress and opioid misuse, but it is unclear which of these aspects of mood is most predictive of subsequent medication misuse.

There is also a significant relationship between an individual's substance abuse history and their vulnerability to aberrant opioid use. A history of prior substance abuse,[11,17] recent use of illicit drugs,[17] prior opioid abuse,[4] prior legal problems related to drug or alcohol use,[17] and prior treatment for a substance use disorder[4] are characteristics of patients who are at high risk of opioid misuse. Similarly, opioid misuse has been linked to the severity of associated withdrawal symptoms.[4]

In short, a diverse set of factors predict problematic use of prescription opioids in individuals with chronic pain. However, there remains a need to characterize these risk factors across a variety of settings to support universal screening efforts. Many prior studies have been conducted through the use of administrative data,[9] veteran samples (which are

predominantly male),[5] population-based data sets[10,18] that provide valuable incidence data, and primary care settings.[17] The current study sought to contribute to the existing literature by comprehensively characterizing a tertiary care pain clinic sample of 625 patients using the Collaborative Health Outcomes Information Registry (CHOIR), which provides deep phenotypic data across a variety of domains. We examined demographic features, psychosocial characteristics, pain-specific behavioral factors, substance abuse history, sleep, and indicators of overall physical function as predictors of opioid misuse. We identified significant predictors of opioid misuse through multivariable logistic regression to determine the factors most strongly associated with problematic opioid use. Opioid misuse was defined as either 1) taking an opioid in a manner or dose other than prescribed or 2) taking someone else's opioid prescription, even if for a legitimate medical complaint such as pain.

Methods
Design and setting
This cross-sectional cohort study with retrospective chart review examined a large sample of adult patients with chronic non-cancer pain. Patients presenting for new patient consultation at the Stanford Outpatient Pain Management Center, a large tertiary academic pain clinic, with chronic non-cancer pain, were included. Data were extracted for patients with new patient visits between January 2014 and May 2014. All study procedures were approved by the Stanford University School of Medicine Institutional Review Board (IRB). Informed consent was waived by the Stanford University School of Medicine IRB as CHOIR data were initially collected for clinical care. The IRB approved a retrospective chart review combined with CHOIR data extraction for the purposes of this project.

Data collection
Data were collected using the CHOIR system (http://choir. stanford.edu.laneproxy.stanford.edu), which is an open-source, open platform health outcome registry, and learning health system. CHOIR consists of Patient-Reported Outcomes Measurement Information Systems (PROMIS) item banks developed by the National Institutes of Health (NIH), as well as legacy instruments used to assess domains of physical, psychological, and social functioning.[19] Use of computerized adaptive testing reduces participant burden through the selection of a subset of items from an item bank until measurement meets preset criteria for standard errors.[19] The survey was administered 5 days prior to a patient's scheduled

new patient consultation. Patients also had the option to complete CHOIR using a tablet computer at the clinic. All CHOIR assessments including sociodemographic variables, the Pain Catastrophizing Scale (PCS), characterization of sleep, average pain intensity, pain duration, NIH PROMIS standardized measures, and substance use history were directly inputted by patients electronically. Data extraction from CHOIR and the Stanford Hospital and Clinics electronic medical record (EMR) system was checked by 2 independent statisticians for completeness and accuracy prior to data analysis.

Opioid prescription

Patients self-reported all current opioid prescription data verbally to clinic staff during their medical visit. Opioid data were extracted through retrospective chart review in a stepwise manner. Step 1 involved recording current opioid medications for the new patient clinic visit from physician documentation (the clinical note) in the EMR. If data were absent in step 1, step 2 was employed, in which opioid data were extracted from the EMR medication list. Step 2 was employed for <10% of the extracted opioid prescription data. Data collection screened for codeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, oxycodone, oxymorphone, tramadol, and buprenorphine. As many new patients are referred from outside the Stanford Health Care system, no information is located in the EMR medication list until it has been updated based on patient self-report during the patients' first visit. Physician documentation from the new patient clinic visits often provides more reliable and in-depth information regarding current opioid use and prescriptions. Also, the EMR medication list may contain multiple opioids, but the patient may only be taking 1 opioid. As such, the first step was to examine physician documentation from the new patient clinic visit. Any opioid prescription was recorded as a binary variable. In other words, patients with any self-reported opioid prescriptions or opioid prescriptions on their EMR medication list were classified as having any opioid prescription.

Prescription opioid misuse

The EMR pertaining to a patient's new patient clinic visit was reviewed by an anesthesiology resident physician. Subsequent independent verification was completed by a pain medicine specialist. Referral documents were reviewed for referring provider concerns regarding opioid misuse behaviors (eg, early medication refill requests, obtaining opioids from multiple providers or pharmacies, taking a friend or family member's opioids, and inconsistent urine drug testing). Second, new

patient visit pain physician documentation was reviewed for indicators of opioid misuse. The 4 A's of opioid use are routinely recorded in reference to analgesia, activity level, aberrant behaviors, and adverse effects associated with opioid therapy. Opioid misuse was defined as either 1) taking an opioid in a manner or dose other than prescribed or 2) taking someone else's opioid prescription, even if for a legitimate medical complaint such as pain. This definition was adopted from the National Institute on Drug Abuse criteria for misuse of prescription drugs.[20]

PROMIS instruments

PROMIS pain intensity was assessed on a modified numerical rating scale.[21] Respondents were asked to rate their average pain intensity over the previous 7 days on a scale of 0–10. NIH PROMIS item banks[22] for pain behavior, pain interference, physical function, sleep disturbance, sleep-related impairment, anger, depression, anxiety, and fatigue were administered using the CHOIR-Computerized Adaptive Testing algorithm. Detailed description of PROMIS item banks are available online (http://www.nihpromis.org/measures/domainframework1). PROMIS instruments utilize item response theory yielding standardized T-scores (mean=50, standard deviation [SD] =10)[23]; these scores are normed on a large sample of the US population.[22] The pain behavior item bank measures an array of self-reported pain behaviors including distorted ambulation, facial/audible expressions, help-seeking behavior, reclining, minimizing movement, isolating oneself, increased body tension, avoiding physical contact with others, and massaging a painful area.[24] Higher T-scores represent increased pain behaviors. The pain interference item bank measures the negative effect of pain on physical, mental, and social functioning in a range comparable to the majority of people who have pain.[23] Higher T-scores represent increased pain interference with functioning. The physical function item bank measures self-reported functioning of extremities (dexterity and walking), axial regions (neck and back), and activities of daily living.[25] Higher T-scores represent increased physical functioning. Thus, a score of 60 represents higher than average physical functioning. The sleep disturbance item bank measures perceived sleep quality, depth, and restoration.[26] Higher T-scores represent increased sleep disturbance. The sleep-related impairment item bank measures self-reported alertness, sleepiness, and fatigue during waking hours, and the perceived functional impairments during wakefulness that are attributed to sleep problems or impaired alertness.[26] Higher T-scores represent increased sleep-related impairment. The PROMIS item banks

for anger measure angry mood (irritability and frustration), negative social cognitions, and efforts to control anger.[27] The item bank for depression measures negative mood, negative views of self (worthlessness and self-criticism), social cognition (loneliness), and decreased positive affect and engagement (loss of interest, meaning, and purpose).[27] The item bank for anxiety measures self-reported fear, anxious misery (worry and dread), hyperarousal, and somatic symptoms of arousal (racing heart and dizziness).[27] The item bank for fatigue measures the frequency, duration, and intensity of fatigue in addition to its impact on physical, mental, and social functioning.[28]

Pain catastrophizing

Pain catastrophizing was measured with the PCS.[29] The PCS asks respondents to rate how frequently they respond to pain in a manner consistent with each of the 13 statements presented (eg, "It's awful and I feel that it overwhelms me."). Each item is rated on a 5-point scale ranging from 0 ("not at all") to 4 ("always"). A total PCS score is computed by summing the 13 items (range =0–52) with higher scores reflecting higher levels of catastrophizing. The PCS was administered electronically as part of CHOIR and completed by the patient.

Analytic plan

SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) was used for all analyses. A *t*-test was used to compare all continuous variables, and chi-square test was used to compare all categorical variables between patients with opioid misuse and without misuse. Prescription opioid misuse was analyzed as a distinct dependent variable in the logistic regression analyses. SAS PROC LOGISTIC was used for logistic regression, calculation of odds ratios (ORs), and model building. Listwise deletion was used for handling missing data. The linearity assumption of all significant predictors was met by plotting a linear relationship of the independent variable to the log odds.

In order to construct a generalizable multivariable model of prescription opioid misuse in patients presenting with chronic non-cancer pain, we chose not to constrict the model to a number of preselected variables a priori. All significant variables in univariate analysis were considered for inclusion in the final multivariable model. Sensitivity analyses of this method of multivariable model selection included comparison of results between automated stepwise, backward, and forward variable selection algorithms. The criterion for selection or retention in the model building algorithms was a significance level of 0.05. Comparisons of

−2 LogL scores of models generated from automated stepwise, backward, and forward variable selection algorithms confirmed optimal model fit of the final multivariable model. These analyses also allowed examination for potential errors in model building.

A post hoc power analysis was conducted by using SAS Power and Sample Size 14.1 (SAS Institute Inc.). PROC POWER for logistic regression with a binary response was used with an alpha =0.05, response probability =0.066, corresponding ORs noted in Table 1, probability of illicit drug use history =0.1, probability of any opioid prescription =0.54, average hours of sleep =5.4 (SD =1.9), and sample size of 625. This test yielded 99.7% power for the specified multivariable model in Table 1.

Results
General demographics
Overall, 41 (6.6%) of 625 patients presented with a history of prescription opioid misuse at their first visit to a tertiary pain management center (Table 2). Also, a significantly higher percentage of patients with opioid misuse was male compared to those without misuse (56% vs 37%, *p*=0.02). Those with opioid misuse were more likely to be Caucasian and slightly younger in the sample. Similarly, a higher percentage of patients with opioid misuse was more likely to be divorced, separated, or single. No differences were noted in education level.

Pain behaviors
Patients exhibiting opioid misuse had significantly reduced physical functioning, and higher PCS scores (Table 3). They also reported significantly reduced average hours of nightly sleep (4.8 vs 5.9, *p*=0.0009) with concomitant significant increases in sleep disturbance and sleep-related impairment. Both groups were similar in terms of reported pain level, pain duration, pain behaviors, and pain interference.

Psychosocial measures
Patients exhibiting prescription opioid misuse reported higher levels of anxiety, depression, and anger on NIH PROMIS instruments. Also, a higher percentage of those with opioid

Table 1 Multivariable regression analysis of variables associated with misuse of prescription opioids

Variables	OR (95% CI)	*p*-value
Any opioid prescription	4.06 (1.62–10.18)	0.003
Average hours of sleep	0.80 (0.66–0.97)	0.02
History of illicit drug use	5.45 (2.48–11.98)	<0.0001

Abbreviations: OR, odds ratio; CI confidence interval.

Table 2 General demographics

Variables	No prescription opioid misuse	Prescription opioid misuse	p-value[a]
Sex*,[b]			0.02
Female	368 (63)	18 (44)	
Male	216 (37)	23 (56)	
Marital status*,[b]			0.01
Divorced/separated	86 (15)	12 (29)	
Married/cohabitating	343 (59)	16 (39)	
Widowed	25 (4)	0	
Never married	129 (22)	13 (32)	
Education*,[b]			0.05
No high school diploma	60 (10)	5 (12)	
High school diploma or GED	58 (10)	10 (24)	
Some college, associate's degree or bachelor's degree	348 (60)	22(54)	
Graduate degree	110 (19)	4 (10)	
Unknown	2 (<1)	0 (0)	
Race*,§,[b]			0.002
Caucasian	366 (63)	36 (90)	
Other	179 (31)	4 (10)	
Unknown	36 (6)	0 (0)	
Age (mean, SD)	49.2 (16.5)	44.4 (14.2)	0.07
Any opioid prescription[b]	305 (52)	35 (85)	<0.0001

Notes: *Less than 1% of participants missing responses for these variables due to lack of survey completion. §Due to limitations of the EMR used, Hispanic is subsumed in either Caucasian or other categories. [a]Chi-square test for categorical variables, t-test for continuous variables; [b]number (%).
Abbreviations: SD, standard deviation; EMR, electronic medical record; GED, General Education Department.

misuse was receiving disability (46% vs 29%, $p=0.03$). In addition, fewer patients reporting opioid misuse were currently working compared to patients with no opioid misuse history (22% vs 35%).

Substance use

A significantly higher percentage of patients with opioid misuse had an opioid prescription (85% vs 52%, $p<0.0001$). Of note, substance use measures were globally increased in those reporting opioid misuse compared to patients with no opioid misuse history. Patients with opioid misuse behavior were more likely to be current smokers and have a history of alcohol abuse. A significantly higher percentage of patients with opioid misuse reported a history of illicit drug use (39% vs 8%, $p≤0.001$) as well as a history of drug or alcohol treatment in the past.

Univariate analyses

Univariate logistic regression analyses revealed a number of covariates potentially associated with patients presenting with signs of opioid misuse (Table 4). These variables included substance use measures of current smoking, a history of illicit drug or alcohol abuse, and a history of drug or alcohol treatment (Table 4). Also, covariates such as having an opioid prescription, higher levels of anxiety, decreased nightly hours

of sleep, and elevated sleep disturbance were considered for inclusion in the final multivariable model.

Multivariable analysis

In all, 14 variables were considered for inclusion in the final multivariable model. Only 3 variables remained in the final multivariable model of factors associated with prescription opioid misuse through the automated variable selection algorithms (Table 1). Patients with a history of illicit drug use exhibited significantly elevated odds of opioid misuse (OR 5.45, 95% confidence interval [CI] 2.48–11.98, $p<0.0001$). Patients with an opioid prescription were >4 times as likely to exhibit signs of opioid misuse (OR 4.06, 95% CI 1.62–10.18, $p=0.003$). An association with poor sleep remained as every 1-h increase in average hours of nightly sleep decreased the odds of opioid misuse by 20% (OR 0.80, 95% CI 0.66–0.97, $p=0.02$).

Given the possibility of collinearity or multicollinearity among the predictor variables (eg, collinearity of average hours of sleep with anxiety or depression), collinearity diagnostics of all 14 variables considered for inclusion in the final multivariable model were carried out (Table 5). As evidenced by variance inflation factors well below 10 or conversely tolerance values well above 0.1, collinearity does not seem to be an issue among the variables examined.

Table 3 Differences in pain behaviors, psychosocial measures, and substance use between patients with and without prescription opioid misuse

Variables	No prescription opioid misuse	Prescription opioid misuse	p-value
Pain behaviors			
PCS score	23.7 (12.3)	29.1 (12.9)	0.008§
Average pain (NRS)	6.0 (2.1)	6.1 (2.4)	0.6§
Pain duration (years)	6.4 (8.5)	7.8 (7.2)	0.4§
Pain behavior+	60.9 (3.3)	61.7 (3.8)	0.2§
Pain interference+	67.5 (6.2)	68.2 (5.3)	0.5§
Physical function+	34.5 (7.6)	31.9 (6.0)	0.03§
Sleep disturbance+	58.8 (9.3)	63 (11.3)	0.006§
Sleep-related impairment+	58.6 (9.6)	61.5 (10.4)	0.07§
Average hours of sleep	5.9 (1.9)	4.8 (1.8)	0.0009§
Psychosocial measures			
Anger+	53.7 (10.7)	58.6 (12.6)	0.006§
Depression+	58.0 (9.8)	62.3 (10)	0.007§
Anxiety+	59.2 (9.8)	63.8 (10.6)	0.004§
Fatigue+	62.8 (9.6)	63.8 (9.8)	0.5§
Currently working (n,%)	202 (35)	9 (22)	0.12*
Receiving disability (n,%)	172 (29)	19 (46)	0.03*
Substance use			
Current smoker (n, %)	60 (10)	14 (34)	<0.0001*
Any opioid prescription (n, %)	305 (52)	35 (85)	<0.0001
History of illicit drug use (n, %)	46 (8)	16 (39)	<0.001*
History of alcohol abuse (n, %)	28 (5)	7 (17)	0.005*
Any drug or alcohol treatment (n, %)	22 (4)	6 (15)	0.007*

Note: *chi-square test; §t-test; +NIH PROMIS measure.
Abbreviations: NIH, National Institutes of Health; PROMIS, Patient-Reported Outcomes Measurement Information Systems; PCS, Pain Catastrophizing Scale; NRS, numerical rating scale.

Furthermore, the largest condition number (index of the global instability of the regression coefficients) was 4.5 and well below the threshold of 10 or more, which would be an indication of instability.

Discussion

The current study sought to characterize demographic, physical, and psychosocial factors associated with misuse of opioid medications in a sample of 625 patients with chronic pain presenting for new patient consultation at a tertiary pain management center. Overall, 6.6% of patients presented with a history of prescription opioid misuse far exceeding the national prevalence of 1.9% among US adults.[30] In addition to opioid prescription status and a history of illicit drug use, the present analyses also highlighted sleep as a salient factor in discriminating between patients who exhibited some indication of opioid misuse and those who did not. Problematic sleep has been identified as a salient reason for opioid misuse

Table 4 Univariate logistic regression analyses of variables associated with misuse of prescription opioids

Variables	OR (95% CI)	p-value
PCS score	1.04 (1.01–1.06)	0.008
Physical function+	0.95 (0.91–1.00)	0.03
Average pain (NRS)	1.04 (0.90–1.21)	0.6
Pain duration (years)	1.02 (0.98–1.05)	0.4
Pain behavior+	1.08 (0.97–1.22)	0.2
Pain interference+	1.02 (0.97–1.07)	0.5
Sleep disturbance+	1.05 (1.01–1.09)	0.006
Average hours of sleep	0.73 (0.60–0.88)	0.001
Anger+	1.04 (1.01–1.07)	0.006
Depression+	1.05 (1.01–1.08)	0.007
Anxiety+	1.05 (1.02–1.09)	0.005
Fatigue+	1.01 (0.98–1.05)	0.5
Currently working	0.52 (0.25–1.12)	0.09
Receiving disability	2.07 (1.09–3.9)	0.03
Current smoker	4.51 (2.24–9.07)	<0.0001
History of illicit drug use	7.49 (3.73–15.01)	<0.0001
History of alcohol abuse	4.09 (1.67–10.03)	0.002
Any drug or alcohol treatment	4.38 (1.67–11.50)	0.003
Age	0.98 (0.96–1.00)	0.07
Female sex	0.46 (0.24–0.87)	0.02
Any opioid prescription	5.34 (2.21–12.90)	0.0002

Note: +NIH PROMIS measure.
Abbreviations: NIH, National Institutes of Health; PROMIS, Patient-Reported Outcomes Measurement Information Systems; PCS, Pain Catastrophizing Scale; NRS, numerical rating scale.

Table 5 Tolerance and variance inflation factors of variables used for multivariable model building

Variables	Tolerance	Variance inflation
PCS	0.52	1.91
Physical function	0.80	1.25
Sleep disturbance	0.53	1.89
Average hours of sleep	0.62	1.61
Anger	0.41	2.43
Depression	0.29	3.42
Anxiety	0.29	3.50
Receiving disability	0.91	1.10
Current smoker	0.88	1.13
History of illicit drug use	0.77	1.30
History of alcohol abuse	0.77	1.30
Any drug or alcohol treatment	0.77	1.30
Any opioid prescription	0.91	1.10
Female sex	0.93	1.08

Abbreviation: PCS, Pain Catastrophizing Scale.

in some patients with chronic pain,[31] but this factor has not been included consistently in prior studies.

Despite preliminary indications of group differences between patients misusing and not misusing opioids (eg, different rates of disability and poorer physical and psychological function) in the single-predictor models, functional measures, pain characteristics (average pain intensity and pain duration), or psychological variables were not found to be significant predictors of opioid misuse in this multivariable

logistic regression model. Instead, the results of the multivariable logistic regression analyses highlighted a smaller set of key predictors of opioid misuse. The finding that patients with a current opioid prescription were more likely to be misusing opioids echoes prior research;[5] those patients who had routine (and medically sanctioned) access to opioids were more likely to misuse these medications. Similarly, indications of prior illicit drug use remained a significant predictor of opioid misuse, above and beyond other physical and psychosocial factors: this finding, too, reflects a replication of prior studies that have highlighted a history of substance abuse[4,11] as a key risk factor for opioid misuse.

The present study results revealed a novel predictor of opioid misuse that has remained relatively unexamined in prior studies: reduced sleep duration. Although opioid misuse status was not directly related to functional deficits related to sleep disruption (eg, fatigue and sleep-related impairment), patients who misused opioids in the sample reported fewer hours of sleep per night. Prior evidence suggests that there may be a reciprocal relationship between sleep disruption and opioid use: while some patients with pain may be more likely to misuse opioids for the purposes of stress management or sleep improvement,[31] it also seems that opioid use may have deleterious effects for physiological processes underlying sleep.[32] Consequently, continued focus on aspects of pain and psychological processes that affect sleep may provide an important, but thus far understudied, target in the effective prevention of opioid misuse.

It is notable that many of the affective variables in the current study (depression, anxiety, and anger) did not retain significance in the multivariable model as predictors of opioid misuse. A possibility is that the NIH PROMIS measures used to capture these aspects of mood did not have the discriminative capacity of instruments used in previous research. For example, prior research has suggested specific contributions of self-loathing ideations in opioid use, which were not specifically assessed in PROMIS Depression items.[33]

Similarly, pain catastrophizing was not found to be a significant predictor of opioid misuse in the present sample, which stands in contrast to prior studies demonstrating a relationship between pain catastrophizing and opioid misuse.[15,16] Unlike these prior studies, the current study examined relationships between clinical variables and opioid misuse using a retrospective chart review approach of opioid misuse in a large tertiary care pain clinic. Whereas prior studies have used patient-reported assessments to determine opioid misuse (eg, Screener and Opioid Assessment for Patients with Pain, Revised),[15,16] the opioid misuse variable in the present analyses was constructed using indicators of opioid misuse in patients' EMRs. Although the relative merits of either approach are not being debated, the difference in the present study results may be attributable in part to the broader scope of patients (some of whom may not have been interested or able to participate in a prospective study) that were included due to use of a chart review protocol. In addition, data from all patients who completed CHOIR assessments during the reviewed time period were included, regardless of prior medical or psychiatric diagnoses, whereas some prior studies have excluded data for other conditions, including substance use disorders.[15,16] Consequently, the current sample contains a larger degree of heterogeneity than some prior studies but also more closely mirrors the complexity inherent within the population of patients presenting for care at a tertiary care pain clinic. As a result, we interpret our results as reflecting only the most robust predictors of opioid misuse within a complex group of patients with a diverse set of chronic pain conditions.

Similarly, the current study sample was comprised of patients with a high degree of pain and emotional distress, as well as complex psychosocial histories. This fact is evident in the elevated rate of disability, low daily levels of sleep, and elevations in pain catastrophizing, depression, and anxiety. As a result, our findings may not be as applicable to the general population, where these problems are less common, or to primary care, where pain may not be as severe or long-standing in duration. A second caution concerns the cross-sectional nature of our findings. As these variables were measured concurrently, we cannot infer causality in any of these examined relationships; it may be, for example, that even the most salient of predictors in our multivariable analyses, such as substance abuse problems, may have developed after the onset of pain or after problematic patterns of opioid misuse had already developed. These limitations suggest that our findings should be interpreted as a promising set of results that set the stage for studies that may yield a greater degree of causal inference, such as longitudinal assessment or clinical trials. It should also be noted that the predictors examined in our study were confined almost exclusively to the domain of patient-reported outcomes. Although our outcome variable of opioid misuse status was verified by a physician, this outcome as well as the study predictors were gleaned via patient report or physician report, which may have been subject to biases (eg, concerns about compromising future medical care if problematic behaviors were endorsed, incorrect conclusions based on interpretation of urine drug testing). This concern has been

raised in prior studies using patient report to determine risk of opioid misuse.[31] Consequently, future studies should consider objective measures of aberrant substance use (such as cross-referencing prescription drug monitoring programs or urine drug testing), which have been shown in prior studies to be valid indicators of opioid misuse.[2,17,31]

Conclusion

The current study utilized clinical data from a large and diverse group of patients with chronic pain in a tertiary care pain clinic to identify a broad set of predictors of concurrent opioid misuse. This study adds to the literature on prognostic factors in opioid misuse in chronic pain by replicating some key prior findings (eg, the importance of prior substance use, concurrent opioid prescription) while highlighting some aspects of pain experience that may have been overlooked in prior studies (such as reduced sleep duration). This study emphasizes the importance of replicating these findings in longitudinal and treatment studies and suggests that comprehensive models encompassing pain characteristics, demographic and psychosocial factors will yield the greatest value to future clinical and empirical models of opioid misuse in chronic pain populations.

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Disclosure

The authors report no conflicts of interest in this work.

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