

Adherence to Clinical Guidelines for Opioid Therapy for Chronic Pain in Patients with Substance Use Disorder

Benjamin J. Morasco, PhD¹, Jonathan P. Duckart, MPS², and Steven K. Dobscha, MD^{1,2}

¹Mental Health and Clinical Neurosciences Division, Portland VA Medical Center, and Department of Psychiatry, Oregon Health & Science University, Portland, OR, USA; ²Portland Center for the Study of Chronic, Comorbid Mental and Physical Disorders, Portland VA Medical Center, Portland, OR, USA.

BACKGROUND: Patients with chronic non-cancer pain (CNCP) have high rates of substance use disorders (SUD). SUD complicates pain treatment and may lead to worse outcomes. However, little information is available describing adherence to opioid treatment guidelines for CNCP generally, or guideline adherence for patients with comorbid SUD.

OBJECTIVE: Examine adherence to clinical guidelines for opioid therapy over 12 months, comparing patients with SUD diagnoses made during the prior year to patients without SUD.

DESIGN: Cohort study.

PARTICIPANTS: Administrative data were collected from veterans with CNCP receiving treatment within a Veterans Affairs regional healthcare network who were prescribed chronic opioid therapy in 2008 (n=5814).

KEY RESULTS: Twenty percent of CNCP patients prescribed chronic opioid therapy had a prior-year diagnosis of SUD. Patients with SUD were more likely to have pain diagnoses and psychiatric comorbidities. In adjusted analyses, patients with SUD were more likely than those without SUD to have had a mental health appointment (29.7% versus 17.2%, OR=1.49, 95% CI=1.26–1.77) and a urine drug screen (UDS) (47.0% versus 18.2%, OR=3.53, 95% CI=3.06–4.06) over 12 months. There were no significant differences between groups on receiving more intensive treatment in primary care (63.4% versus 61.0%), long-acting opioids (26.9% versus 26.0%), prescriptions for antidepressants (88.2% versus 85.8%, among patients with depression), or participating in physical therapy (30.6% versus 28.6%). Only 35% of patients with SUD received substance abuse treatment.

CONCLUSIONS: CNCP patients with SUD were more likely to have mental health appointments and receive UDS monitoring, but not more likely to participate in other aspects of pain care compared to those without SUD. Given data suggesting patients with comorbid SUD may need more intensive treatment to achieve improvements in pain-related function, SUD patients may be at high risk for poor outcomes.

KEY WORDS: chronic pain; substance use disorder; opioids; treatment guidelines; medical utilization.

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INTRODUCTION

Chronic non-cancer pain (CNCP) is a debilitating illness that affects up to 35% of primary care patients.¹ It is the most frequent reason for medical visits and the direct economic impact of chronic back pain alone has been estimated to be as high as \$86 billion annually, with indirect costs exceeding hundreds of billion dollars.²

Providing treatment for CNCP is challenging and many patients continue to experience persistent pain and disability. The use of prescription opioid medications has increased^{3,4} and chronic opioid therapy is now the most common treatment for CNCP.⁵ Clinical guidelines for managing patients with CNCP include recommendations for assessment and follow-up, dose changes, supplementary treatment, managing adverse events, and special approaches for high-risk patients.^{6–8}

CNCP patients with comorbid substance use disorder (SUD) who receive chronic opioid therapy are considered a high-risk group. There is a disproportionately high prevalence of SUDs among CNCP patients.⁹ Although rates vary by setting and type of substance being assessed, approximately 10% of CNCP in primary care^{10,11} and 10–30% of patients in specialty pain clinics^{12–14} have a current SUD. CNCP patients with a history of SUD are more likely to receive opioids for CNCP and at higher daily dose than patients without history of SUD.^{15–17}

Guidelines for CNCP state that history of SUD is not a contraindication for treatment.⁶ However, patients with CNCP and a history of SUD are at increased risk for medication misuse^{18–20}, and treatment guidelines recommend that patients with a history of SUD receive more intensive monitoring and treatment. Guidelines published by the Department of Veterans Affairs (VA) indicate that opioid therapy is contraindicated for patients with an active SUD who are not in treatment.⁷

Little data have been published on the extent to which providers adhere to opioid treatment recommendations generally, or for patients considered at high risk. The purpose of this study was to examine adherence to opioid therapy guidelines for CNCP patients based on SUD status. Results from a recent systematic review indicate there is little information available to guide clinicians who treat CNCP in patients with comorbid

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SUD.⁹ In this study, we compare implementation of guideline suggested clinical care in: 1) veterans with CNCP who are receiving chronic opioid therapy and have a SUD, and 2) veterans with CNCP receiving chronic opioid therapy and do not have a SUD diagnosis.

METHODS

Participants

All data were obtained for veterans receiving medical care at a VA facility in the Pacific Northwest (Washington, Oregon, Idaho, and Alaska) in 2008. Data were extracted from the Veterans Integrated Service Network (VISN)-20 Data Warehouse²¹ after approval by the Institutional Review Board at the Portland VA Medical Center. The Data Warehouse contains extracts of data from the main clinical software packages of regional facilities and two national VA databases.

Patients were eligible if they received care within VISN-20 during 2008. To identify patients with CNCP, we reviewed electronic medical record pain Numeric Rating Scores (NRS) which are routinely administered during ambulatory visits. Pain intensity is rated on a scale of 0–10, where 0=no pain and 10=worst pain imaginable.²² As part of the VA “Pain as the 5th Vital Sign” initiative, NRS are routinely collected at outpatient medical visits; over 95% of veterans with an outpatient visit in VISN-20 in 2008 had a NRS. We defined CNCP as being present when patients had pain intensity scores ≥ 4 on the NRS in three or more different months (for patients whose first pain score occurred in November or December, the first two months of 2009 were considered). This is consistent with definitions that require at least three months duration.²³ We chose NRS scores ≥ 4 as indicating moderate to severe pain because it is consistent with prior research and aligns with VA clinical practice and policy regarding indication for further pain assessment.²⁴ To be included, patients must have been prescribed chronic opioid therapy, defined as 90 or more consecutive days.^{10,25} We identified 28,556 potentially eligible patients. Patients were excluded if they had any cancer diagnosis within the last six years ($n=6,234$), surgery within the past six months ($n=1,597$), enrollment in a VA opioid substitution program ($n=456$), or death in 2008 ($n=592$). We retained the 5,814 patients who were prescribed opioids for 90 or more consecutive days. A portion of these data have been reported in a report of factors associated with prescriptions for high doses of opioids.²⁶

We created an index date for all patients to be used as a reference for data collection. The index date was the earliest date in 2008 at the beginning of a 90 consecutive day episode of opioid use.

Demographic, Diagnostic, Pharmacy, and Medical Utilization Data

The independent variable was having a SUD documented within 12 months prior to the index date. All alcohol use disorders, illicit SUDs, and prescription drug use disorders were included. Inpatient and outpatient diagnoses were based

on the International Classification of Diseases, Clinical Modification–9th Revision (ICD-9-CM). This may include some patients whose SUD is in remission but whose provider noted it because the patient’s history of SUD may be relevant to current care.

Demographic data included age, gender, race, marital status, and VA service-connected status. We collected ICD-9-CM diagnoses of common psychiatric disorders. Past-year inpatient hospitalization and outpatient diagnoses were used to calculate a Charlson Comorbidity score²⁷, a standardized technique that uses diagnostic codes to provide a measure of illness severity.^{28,29}

Pharmacy data were reviewed for one year after the index date to obtain prescriptions of opioids and non-opioid analgesics. Each opioid prescription was converted to a morphine equivalent.²⁶

We extracted medical utilization data from services considered important in management with opioid therapy for one year after the index date. This included data from primary care, physical therapy, orthopedics, mental health, and substance abuse treatment. Data were also collected on the frequency and results of urine drug screen (UDS) administrations.

Statistical Analyses

CNCP patients with a SUD diagnosis made within one year prior to the index date were compared to patients who did not have a SUD diagnosis. Chi-square tests were used for categorical variables and analysis of variance for linear variables.

Odds ratios (OR) and 95% confidence intervals (95% CI) were derived using generalized estimating equations (GEE) to identify whether a SUD diagnosis was associated with outcome variables. This methodology accounted for within-site correlations among the eight different VA facilities. We specified a model-based estimator covariance matrix because we were accounting for less than 20 facilities. We controlled for the effects of variables that may be associated with treatment utilization. Categorical variables (gender, major depressive disorder diagnosis, SUD) were entered as predictors, while linear variables (age, average NRS score) were entered as covariates. A separate GEE model was constructed for each outcome variable.

For the GEE models, outcome variables were identified *a priori* that were considered most critical for receiving guideline concordant care. For each outcome variable described below, we provide a grade for the strength of the recommendation (strong, weak) and for quality of the evidence (high, moderate, poor), which are based on published guidelines for chronic opioid therapy.⁶ Treatment recommendations for CNCP with comorbid SUD suggest “more intensive” follow-up and monitoring by primary care (strong recommendation, low-quality evidence).⁶ We therefore examined whether patients met with their primary care provider four or more times in one year; four appointments was chosen because a frequency analysis indicated this was the median number of appointments. Whether patients were prescribed a long-acting opioid was included, as this is a common recommendation (strong recommendation, low-quality evidence); however, there are not high quality empirical studies available to support the use of long-acting versus short-acting opioids.³⁰ Physical

therapy was measured because it is helpful for improving function and a common treatment recommendation is to participate in multidisciplinary treatment, including physical therapy (strong recommendation, moderate-quality evidence).³¹ We evaluated whether patients provided a UDS in the year after the index date as it is recommended that patients on chronic opioid therapy provide annual UDS (weak recommendation, low-quality evidence); more intensive UDS monitoring is recommended in patients with SUD (strong recommendation, low-quality evidence).⁶ We assessed whether patients attended a mental health visit (for patients with a current axis I psychiatric disorder), or received a prescription for antidepressant medication (for patients with major depression or dysthymia). These outcome variables were utilized because mental health interventions are associated with improvements in pain-related function (strong recommendation, moderate-quality evidence).^{32,33}

RESULTS

Of the 5,814 participants, 19.5% (n=1,136) had a SUD diagnosis, which included abuse or dependence of alcohol (n=829, 73.0%), cannabis (n=184, 16.2%), cocaine (n=128, 11.3%), opioids (n=172, 15.1%), amphetamines (n=86, 7.6%), polysubstance (n=81, 7.1%), or other substance (n=257, 22.6%). There were statistically significant differences between groups on demographic characteristics (Table 1). Patients with SUD were younger (52.9 versus 55.5 years), more often male (92.6% versus 89.8%), and less likely to be married (33.4% versus 49.7%) than patients without SUD. Patients with SUD had greater pain NRS (6.7 versus 6.6) than patients without SUD, though the clinical difference between groups was small.

Table 2 displays differences between groups on pain and psychiatric diagnoses. Patients with SUD were more likely to be diagnosed with low back pain, migraine headache, and neck or joint pain than those without SUD. The proportion of patients with three or more documented pain diagnoses significantly differed between groups (31.0% versus 26.7%, *p*=0.004). Patients with SUD were more likely to be diagnosed with every psychiatric disorder assessed, with the exception of sleep disorders than those without SUD.

There was no significant difference between groups in the average daily dose of opioids in morphine equivalent (57.2 versus 56.6 mg). Figure 1 displays comparisons on types of opioid medications that were prescribed. Patients with SUD were more likely to receive oxycodone (35.7% versus 30.2%), and less likely to be prescribed hydrocodone (53.9% versus 59.3%) and fentanyl (1.0% versus 1.9%) than those without SUD. The groups did not differ in likelihood of being prescribed short-acting (85.7% versus 87.8%) or long acting (26.9% versus 26.0%) opioids. There was no difference in the rates of prescriptions for high doses of opioids (defined as ≥ 180 mg morphine equivalent; 9.2% versus 8.0%). Patients with SUD were more likely to receive concurrent prescriptions for antidepressants (73.0% versus 61.7%), benzodiazepines (27.2% versus 22.5%), and NSAID/acetaminophen (68.6% versus 61.8%) than patients without SUD (Fig. 2).

Patients with SUD were more likely to be administered at least one UDS (47.0% versus 18.4%, *p*<0.001) and to have a positive

Table 1. Comparison of Demographic Characteristics by Substance Use Disorder (SUD) Status

	Pain and SUD (n=1,136)	Pain only (n=4,678)	p-value
Age, Mean (SD)	52.9 (9.2)	55.5 (12.4)	< 0.001
Male Gender, N (%)	1052 (92.6%)	4199 (89.8%)	< 0.004
Marital Status			< 0.001
Single/Never Married, N (%)	177 (15.6%)	439 (9.4%)	
Married, N (%)	379 (33.4%)	2327 (49.7%)	
Separated/Divorced, N (%)	507 (44.6%)	1544 (33.0%)	
Widow, N (%)	37 (3.3%)	241 (5.2%)	
Unknown, N (%)	36 (3.2%)	127 (2.7%)	
Race			0.004
Caucasian, N (%)	819 (72.1%)	3285 (70.2%)	
Black, N (%)	94 (8.3%)	289 (6.2%)	
Other, N (%)	24 (2.1%)	138 (2.9%)	
Unknown or Declined, N (%)	199 (17.5%)	966 (20.6%)	
VA Service-Connected, N (%)	71 (6.3%)	240 (5.1%)	0.44
Average Pain Score, Mean (SD)	6.7 (1.3)	6.6 (1.3)	< 0.001
Average Daily Dose Morphine Equivalent (SD)	57.2 (86.1)	56.6 (122.4)	0.87
Range, Median	5 - 897, 32	5 - 5496, 30	
Charlson Comorbidity Score, Mean (SD)	1.17 (1.5)	1.11 (1.5)	0.23

UDS for an illicit substance (14.4% versus 4.6%, *p*<0.001). Of the patients that had at least one UDS, patients with SUD averaged more total administrations (4.2 versus 2.4, *p*<0.001) than patients without SUD. The most common positive UDS results were for cannabis and cocaine, both of which occurred at higher rates among patients with SUD diagnoses (12.1% versus 4.5% and 3.2% versus 0.3%, respectively).

Figure 3 displays unadjusted comparisons between groups analyzing whether or not they received specific medical services. Patients with SUD were more likely to have had mental health and substance abuse appointments (all *p*-values ≤ 0.001) than those without SUD. There was no difference between groups in

Table 2. Comparison of Current Pain and Psychiatric Diagnoses by Substance Use Disorder (SUD) Status

	Pain and SUD (n=1136)	Pain only (n=4678)	p-value
Pain Diagnoses			
Fibromyalgia	60 (5.3%)	259 (5.5%)	0.74
Inflammatory Bowel Disease	28 (2.5%)	79 (1.7%)	0.08
Low Back Pain	696 (61.3%)	2632 (56.3%)	0.002
Migraine Headache	124 (10.9%)	407 (8.7%)	0.02
Neck or Joint Pain	738 (65.0%)	2666 (57.0%)	< 0.001
Neuropathy	71 (6.3%)	338 (7.2%)	0.25
Rheumatism/ Arthritis	500 (44.0%)	2024 (43.3%)	0.65
Psychiatric Diagnoses			
Major Depressive Disorder	606 (53.3%)	1743 (37.3%)	< 0.001
Dysthymic Disorder	93 (8.2%)	240 (5.1%)	< 0.001
Bipolar Disorder	138 (12.1%)	202 (4.3%)	< 0.001
Panic Disorder	50 (4.4%)	136 (2.9%)	0.01
Posttraumatic Stress Disorder	457 (40.2%)	1181 (25.2%)	< 0.001
Other Anxiety Disorder	211 (18.6%)	550 (11.8%)	< 0.001
Schizophrenia	63 (5.5%)	108 (2.3%)	< 0.001
Any Sleep Disorder	128 (11.3%)	452 (9.7%)	0.11
Nicotine Disorder	630 (55.5%)	1257 (26.9%)	< 0.001

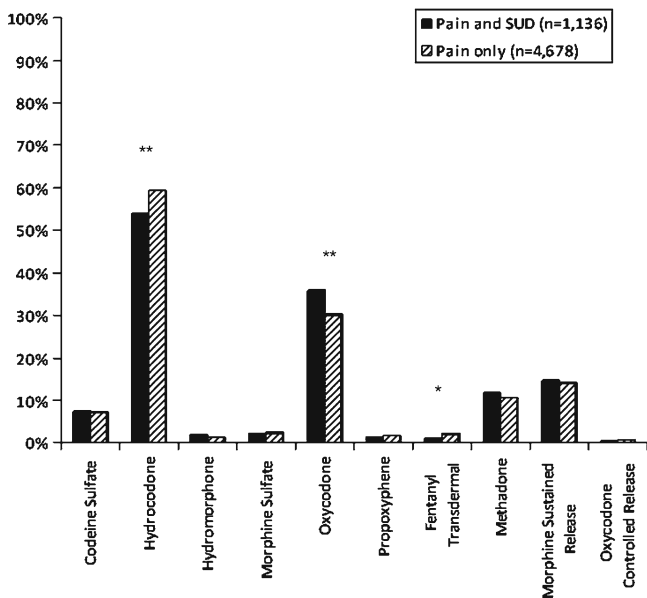


Figure 1. Unadjusted comparison of prescriptions for opioid medications based on Substance Use Disorder (SUD) status. Note. * = $p < 0.05$. ** = $p \leq 0.001$.

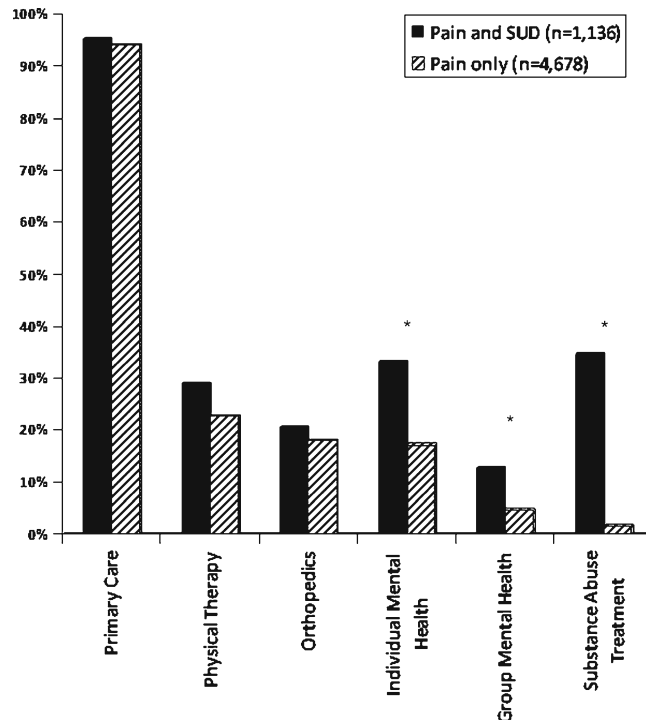


Figure 3. Unadjusted differences in medical utilization based on Substance Use Disorder (SUD) status. Note. This provides dichotomous data comparing whether patient's received any of these services in the 12 months after each patient's index date. * = $p \leq 0.001$.

visits with primary care, physical therapy, or orthopedics.

Logistic regression models were built to evaluate whether patients with SUD were more likely to receive certain aspects of treatment consistent with clinical guidelines for chronic opioid therapy (Table 3). After controlling for VA facility, age, gender, major depression diagnosis, and pain intensity, patients with SUD were more likely to have had a mental health appointment (OR = 1.49, 95% CI = 1.26–1.77) and to have been administered a UDS (OR = 3.53, 95% CI = 3.06–4.06) than patients without SUD.

There was no difference in the likelihood of having more intensive primary care treatment, receiving a long-acting opioid, attending physical therapy, or receiving an antidepressant.

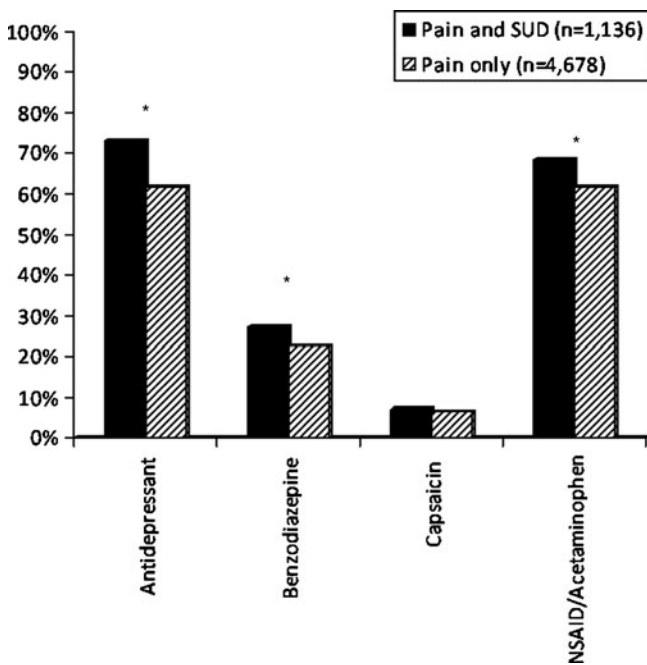


Figure 2. Unadjusted comparison of prescriptions for other medications based on Substance Use Disorder (SUD) status. Note. This evaluates prescriptions for certain medications at the time of each patient's index date. * = $p \leq 0.001$.

DISCUSSION

This study provides information on overall adherence to clinical recommendations for managing patients on chronic opioid therapy, with a focus on patients with SUD. Overall, we found mixed results between guideline recommendations and clinical practice. In the total sample of patients prescribed chronic opioid therapy, in the 12 months after the index date, 26% received a long-acting opioid, 24% were administered a UDS, and 29% received physical therapy. Conversely, two-thirds of patients were seen by their primary care provider four or more times in the 12 month period and 86% with a depressive disorder received an antidepressant medication. Whether adherence to clinical guidelines is associated with improvements in pain severity and function remains to be tested.

Twenty percent of CNCP patients who were prescribed chronic opioid therapy had a SUD diagnosis, which may be an underestimate as SUDs are often under-recognized in clinical settings. Results indicate that providers should consistently screen CNCP patients for SUD comorbidity. Two guideline concordant recommendations occurred at higher rates among patients with SUD. Patients with SUD were 1.5 times more likely to participate in a mental health session and 3.5 times more likely to be given a UDS. These data are

Table 3. Likelihood of Receiving Guideline-Concordant Care Based on Substance Use Disorder (SUD) Status (n=5,814)

	Pain and SUD (n=1136)	Pain Only (n=4678)	Odds Ratio (95% confidence interval)
More Intensive Treatment in Primary Care			1.08 (0.94 – 1.23)
Number of patients with ≥ 4 visits/year (%)	720 (63.4%)	2853 (61.0%)	
Average number of appointments (SD), range	5.7 (4.6), 0-45	5.4 (4.7), 0-66	
Long-acting Opioid			0.94 (0.81 – 1.09)
Number of patients who received any (%)	306 (26.9%)	1216 (26.0%)	
Physical Therapy			1.08 (0.94 – 1.25)
Number of patients who received any (%)	348 (30.6%)	1336 (28.6%)	
Average number of appointments (SD), range	0.9 (2.1), 0-23	0.8 (2.4), 0-43	
Urine Drug Screen			3.53 (3.06 – 4.06)
Number of patients who received any (%)	534 (47.0%)	859 (18.4%)	
Average number of administrations (SD), range	2.2 (4.7), 0-54	0.6 (1.8), 0-34	
Mental Health Visit*			1.49 (1.26 – 1.77)
Number of patients who received any (%)	337 (29.7%)	803 (17.2%)	
Average number of appointments (SD), range	2.5 (6.2), 0-60	1.7 (5.4), 0-118	
Antidepressant Medication+			1.26 (0.96 – 1.67)
Number of patients who received any (%)	554 (88.2%)	1583 (85.8%)	

Note. The Odds Ratios tested whether patients with a SUD were more likely to receive certain medical services. Analyses controlled for the effects of VA facility, age, gender, average pain score, and major depressive disorder diagnosis. * = For the variable mental health visit, this included only patients who were diagnosed with an axis I psychiatric disorder (n=3,374). + = For antidepressant use, this included only patients who were diagnosed with major depressive disorder or dysthymia (n=2,472)

important, as psychological interventions have consistently strong outcome data in treating pain and improving function³³, including studies of patients with pain and SUD³⁴, and regular UDS monitoring is central for the provision of safe treatment with opioids and improves the detection of aberrant medication use.³⁵ However, only half of CNCP patients with SUD received at least one UDS and 35% received substance abuse treatment, suggesting that additional steps are needed to increase guideline adherence. In addition, despite patients with SUD being at higher risk, there was no significant difference in the likelihood of receiving more intensive treatment in primary care, receiving a long-acting opioid, participating in physical therapy, or receiving a prescription for an antidepressant medication. Patients with SUD were also more likely to have a concurrent prescription for benzodiazepine medications, which may increase risk of overdose and death. A number of approaches may need to be used to increase adherence to treatment guidelines, including better system support to assist providers.

The best methods for treating CNCP among patients with comorbid SUD are unclear. Unfortunately, SUD patients are often excluded from clinical trials, resulting in little empirical data available regarding treatment options.⁹ Recent uncontrolled treatment studies indicate that more intensive, and integrated, treatment options may help to reduce pain and improve functioning among CNCP patients with comorbid SUD.^{36,37} These resources are often beyond the scope of usual practice in primary care, but could be an option for referral.

The results from this study have additional implications for clinical practice. Recent treatment guidelines suggest the presence of SUD is not a contraindication to opioid therapy, though it is recommended that patients with a SUD receive more intensive treatment and monitoring⁶ and participate in substance abuse treatment.⁷ One recent study showed that CNCP patients with a history of SUD are 70% less likely to have clinically significant improvements in pain-related function when receiving usual pain care.³⁸ However, in this prior study, patients with a SUD history had improvements in pain-related function similar to patients without SUD when receive-

ing more intensive and multidisciplinary treatment.³⁸ Given this information as well as current findings showing that patients with SUD did not obtain more intensive care, it is likely that CNCP patients with comorbid SUD are at risk for sub-optimal pain treatment outcomes.

Consistent with prior research, CNCP patients with a SUD diagnosis were more likely to have comorbid psychiatric diagnoses^{38,39}, highlighting the need to integrate pain care and mental health services.⁴⁰ In contrast to previous findings, patients with SUD were not prescribed higher opioid doses¹⁷, despite statistically significant differences in pain scores. Patients with SUD may have decreased pain thresholds, suggesting the need for higher doses to achieve a similar response.^{41,42}

Analyses for this study were based on treatment recommendations, which are often based on expert panels and not empirical data. There are other limitations from this study. All data were obtained from electronic medical records as part of standard care. Diagnoses were not confirmed with clinical interviews. The primary study variable was a past-year SUD diagnosis. This is not necessarily consistent with having a current SUD, as a diagnosis may have been given, but the actual substance use may be in remission. Furthermore, 9% of patients in the pain only group subsequently received a SUD diagnosis in the 12 months after the index date. We chose to leave these participants in the pain only group because we made an *a priori* decision to measure SUD up to the time of the index date. The overall findings from this study, and resulting implications, would not have been substantially influenced if we were to include these patients in the SUD group.

Given our reliance on electronic medical record data, we could not compare differences in pain-related function between the groups. Some patients may have had pain for years prior to this study, and potentially received some interventions in the past (e.g., physical therapy, mental health), but this would not be included in the current analyses. Although we controlled for differences in practice variation based on facility, medical care for CNCP may differ elsewhere. Other aspects of research methodology may limit generalizability. All patients

were veterans, the majority of whom were male, and results may not generalize to non-veterans or women. Additionally, patients with mild pain were excluded, and the results may be limited to those with moderate to severe pain.

Results from this study provide data on overall adherence to clinical guidelines for opioid therapy and compare adherence based on SUD status. Prior research has documented the increased rates of opioid use for the treatment of CNCP among patients with SUD and psychiatric disorders.^{17,43} We have extended this research by detailing the use of medical services to treat pain among patients with CNCP and a past-year SUD diagnosis. These findings indicate that while several elements of care may be different (referral for mental health services, UDS), overall patients with CNCP and SUD receive pain care in a manner that does not differ from patients without a SUD. Further research is needed to assess the impact of improved adherence on clinical outcomes.

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Conflict of Interest: None disclosed.

Corresponding Author: Benjamin J. Morasco, PhD; Mental Health and Clinical Neurosciences Division, Portland VA Medical Center (R&D99), and Department of Psychiatry, Oregon Health & Science University, 3710 SW US Veterans Hospital Road, Portland, OR 97239, USA (e-mail: benjamin.morasco@va.gov).

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