Psychiatric Disorders Among Patients Seeking Treatment for Co-Occurring Chronic Pain and Opioid Use Disorder

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ABSTRACT

Objective: Psychiatric comorbidities complicate treatment of patients with chronic pain and opioid use disorder, but the prevalence of specific comorbid psychiatric disorders in this population has not been systematically investigated.

Methods: 170 consecutive participants entering a treatment research program for co-occurring chronic pain and opioid use disorder between March 2009 and July 2013 were evaluated with the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders (SCID-I/P) and the Diagnostic Interview for *DSM-IV* Personality Disorders (DIPD-IV).

Results: The prevalence of any lifetime (and current) comorbid Axis I disorder was 91% (75%); 52% met criteria for lifetime anxiety disorder (48% current), 57% for lifetime mood disorder (48% current), and 78% for lifetime nonopioid substance use disorder (34% current). Common current anxiety diagnoses were posttraumatic stress disorder (21%), generalized anxiety disorder (16%), and panic disorder without agoraphobia (16%). Common current mood diagnoses were major depressive disorder (40%) and dysthymia (11%). A majority of patients had a personality disorder (52%).

Conclusions: High rates and persistence of co-occurring psychiatric disorders, including anxiety or mood disorders, may explain in part the difficulty providers have treating patients with co-occurring opioid use disorder and chronic pain and suggest possible targets for improving treatment.

Trial Registration: ClinicalTrials.gov identifiers: buprenorphine/naloxone treatment (NCT00634803), opioid treatment program–based methadone maintenance treatment (NCT00727675)

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The use of opioid analgesics to treat chronic noncancer pain (ie, pain lasting at least 3 months) has increased 3-fold since the early 1990s and has brought with it an epidemic of nonmedical opioid use, opioid overdose, and opioid use disorder.[1–5] Patients with co-occurring chronic pain and opioid use disorder present considerable management challenges: Unrelieved pain is associated with anxiety and depression, sleep problems, and opioid or other substance misuse, often to self-medicate.[6–9] Clinicians report difficulty managing patients with chronic pain and opioid use disorder because of the perceived high rates of accompanying psychopathology, a dearth of evidence-based treatments for these coexisting conditions, and a paucity of providers who specialize in their treatment.[10–12] Given their expertise in psychiatric assessment and treatment, prescribing adjuvant psychotropic pain medications (eg, antidepressants), and the biopsychosocial model, psychiatrists can perform a pivotal role in the treatment of chronic pain and opioid use disorder.[13–15] However, many may feel ill-equipped to do so; medical schools and psychiatry residency programs in the United States provide limited training on managing chronic pain, especially in the context of an opioid use disorder.[13,16] Increased knowledge about the psychiatric comorbidity of co-occurring opioid use disorder and chronic pain might assist psychiatrists in treating or consulting on this vulnerable patient population.

High rates of psychiatric disorders have been found among patients with chronic pain[17–22] and with opioid use disorder,[23–25] and co-occurring psychopathology in patients with these disorders has important treatment implications.[26,27] Relatively few studies have investigated psychopathology among patients with co-occurring opioid use disorder and chronic pain, however. Elevated levels of anxiety and depression have been reported in surveys of methadone-maintained patients with chronic pain,[6,9,28,29] and 1 small study found high rates of Axis I disorders among 40 patients with chronic pain who were referred from multidisciplinary pain clinics and who also had either opioid abuse (n = 12) or dependence (n = 28).[30] Although anxiety and depression can exacerbate pain in nonaddicted patients with chronic pain,[26,31] the association of pain with anxiety disorders or with mood disorders has not been systematically examined in those with co-occurring opioid use disorder and chronic pain.

Consequently, this study evaluated the prevalence of *DSM-IV-TR*[32] Axis I and Axis II disorders and the association between psychiatric disorders and pain intensity or pain interference (ie, decrement in functioning resulting from pain) among patients with co-occurring opioid use disorder and chronic pain entering either of 2 clinical trials combining behavioral interventions and opioid agonist maintenance treatment with buprenorphine/naloxone or methadone. We anticipated that rates of Axis I psychiatric disorders would be even higher among patients with co-occurring opioid use disorder and chronic pain than those previously reported among patients with either condition alone. Finally, we hypothesized that in comparison to patients with neither an anxiety disorder nor a mood disorder, those with an anxiety disorder, a mood

Clinical Points

- This study found high rates of current and lifetime Axis I and Axis II psychiatric disorders in patients with co-occurring chronic pain and opioid dependence.
- This study found that despite the high rates and persistence of current Axis I psychiatric disorders, very few participants had received mental health treatment or a psychiatric medication in the previous month.
- The high rates and persistence of psychiatric disorders and low rates of current mental health treatment among participants with co-occurring chronic pain and opioid use disorder suggest important clinical targets in developing treatments for these co-occurring chronic medical conditions.

disorder, or both would have higher pain intensity and pain interference.

METHODS

Participants

Participants were a consecutive series of 170 adults who completed evaluations for enrollment in a treatment research program for co-occurring chronic pain and opioid dependence in New Haven, Connecticut, between March 2009 and July 2013. Participants were recruited through referrals from providers and intake workers at primary care centers, pain management clinics, and opioid treatment programs; advertisements (eg, radio, Internet, posters in the community); and word-of-mouth. Participants (n = 113) were evaluated for a research protocol involving office-based buprenorphine/naloxone treatment (NCT00634803), while the remaining 57 were assessed for a research protocol involving opioid treatment program–based methadone maintenance treatment (NCT00727675). Participants were administered the diagnostic interviews following medication induction and initial stabilization (generally 1 to 2 weeks following initiation of either buprenorphine/naloxone or methadone). The study received appropriate Institutional Review Board and institutional approval (at Yale University School of Medicine and at APT Foundation). Participants provided voluntary, written informed consent. The study design and conduct complied with the Declaration of Helsinki.

To be eligible for study inclusion, participants needed to (1) be at least 18 years old; (2) be able to read and write in English; (3) experience moderate to severe chronic low back pain (ratings of pain at its worst or peak in the previous week ≥ 4 on a 0 ["no pain"] to 10 ["worst pain imaginable"] numeric rating scale) of at least 6 months' duration and classified as nonspecific in origin according to the guidelines issued by the American College of Physicians (ACP) and the American Pain Society (APS);[33] and (4) meet *DSM-IV-TR* criteria for opioid dependence[32] and joint American Academy of Pain Medicine-American Pain Society-American Society of Addiction Medicine (AAPM-APS-ASAM) criteria for opioid addiction, which require compulsive use, continued use despite harm, or craving.[34] Participants could have multiple sites of pain, but low back pain was required to be a primary pain site. Exclusion criteria included drug treatment in the prior 30 days and current suicide or homicide risk. Participants received a comprehensive evaluation from a study physician prior to admission to ensure study eligibility.

Demographic and Clinical Characteristics

Participants provided information on demographics (age, sex, race, ethnicity, education, employment, marital status) and clinical characteristics (HIV status, primary drug of abuse [heroin, opioid medication, other], outpatient mental health visit in the previous month [yes/no], and whether they had taken prescribed psychiatric medication in the previous month [yes/no]).

Pain Characteristics

Participants provided information on current pain location and genesis and the duration of chronic pain. Participants also completed the Brief Pain Inventory (BPI),[35,36] where they rated 4 facets of pain experienced in the past 7 days (ie, "pain at its worst," "pain at its least," "pain on average," "pain right now") using 0 ("no pain at all") to 10 ("pain as bad as you can imagine") scales, and 7 pain interference items that assessed the extent to which their pain in the last 7 days had interfered with their "general activity," "mood," "walking ability," "normal work (includes both outside the home and housework)," "relations with other people," "sleep," and "enjoyment of life" using 0 ("does not interfere") to 10 ("completely interferes") scales. The mean of the 4 pain intensity ratings was calculated to find the "pain severity score," while the mean of the 7 interference items was calculated to determine the "pain interference score" (both scored on 0 to 10 scales).[37]

Diagnostic Interviews

The Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders, Patient Edition (SCID-I/P)[38] includes modules on current (prior 30 days) and lifetime (either current or past) mood, anxiety, and substance use disorders, while the Diagnostic Interview for *DSM-IV* Personality Disorders (DIPD-IV)[39] collects diagnostic information pertaining to the previous 2 years (ie, current only) on Cluster A (paranoid, schizoid, schizotypal), Cluster B (antisocial, borderline, histrionic, narcissistic), and Cluster C (avoidant, dependent, obsessive-compulsive) personality disorders.

Interviewers

The diagnostic interviews were conducted by addiction psychiatry and psychology fellows as well as clinical and counseling psychologists. A standardized training protocol was followed: Research clinicians attended didactic workshops, observed 2 batteries performed by experienced assessors, conducted 2 supervised batteries, and subsequently conducted the diagnostic evaluations independently, receiving ongoing supervision as needed.

Data Analysis

Descriptive statistics were used to calculate demographic characteristics and the prevalence of psychiatric disorders. We performed *t*-tests and χ^2 tests to compare baseline characteristics between patients from the buprenorphine/naloxone and methadone maintenance trials. Subsequent analyses examined the overall sample, using univariate analysis of variance (ANOVA) tests to compare pain severity scores and pain interference scores in patients with (*a*) co-occurring anxiety and mood disorders, (*b*) anxiety or mood disorder (but not both), and (*c*) no anxiety or mood disorders. Separate 2×2 χ^2 tests were performed for participants in the buprenorphine/naloxone and methadone maintenance trials to determine whether the presence of any current or lifetime anxiety, mood, or nonopioid substance use disorder or any current personality disorder was associated with study completion or clinically significant changes in pain severity or pain interference (defined as ≥ 2-point decrease on 0–10 scales from baseline to end of treatment). Chi-square tests were also performed to examine differences between participants whose reported primary drug of abuse was either heroin or prescription opioids on the presence of lifetime and current psychiatric disorders. The Fisher exact test was used in cases where the expected cell frequencies for the χ^2 tests was less than 5. Statistical significance was set at $P < .05$. All statistics were performed on IBM SPSS Statistics Version 19.

RESULTS

Demographic and Clinical Characteristics

The 170 participants ranged in age from 19 to 64 years (mean = 36.0, SD = 10.0); 71% were men, 87% were white, 47% were employed, 87% had greater than or equal to a high school education, 20% were married, and 51% reported opioid medications as their primary drug of abuse (Table 1). The mean ages at onset of chronic pain and opioid dependence were 23.7 and 25.3, respectively. On average, participants in the buprenorphine/naloxone trial, in comparison to those in the methadone maintenance trial, were ($P < .05$) younger (34.6 vs 38.8 years); more likely to be employed (56% vs 28%) and report that opioid medication was their primary drug of abuse (61% vs 30%); and less likely to report that they had been prescribed psychiatric medication in the past month (11% vs 23%).

Table 1. Demographic and Clinical Characteristics of Patients With Chronic Pain and Opioid Dependence[a]

Characteristic	Buprenorphine/ Naloxone (n = 113)	Methadone (n = 57)	Total (N = 170)
Age, mean (SD),[b] y	34.6 (9.3)	38.8 (10.6)	36.0 (10.0)
Sex			
Male	70.8 (80)	71.9 (41)	71.2 (121)
Female	29.2 (33)	28.1 (16)	28.8 (49)
Race			
White	86.7 (98)	87.7 (50)	87.1 (148)
Black	4.4 (5)	5.3 (3)	4.7 (8)
Other	8.9 (10)	7.0 (4)	8.2 (14)
Ethnicity			
Hispanic	9.7 (11)	10.5 (6)	10.0 (17)
Non-Hispanic	90.3 (102)	89.5 (51)	90.0 (153)
Education[c]			
Less than high school	12.5 (14)	14.0 (8)	13.0 (22)
High school graduates	87.5 (98)	86.0 (49)	87.0 (147)
Employment status[d]			
Employed (full time, part time, student)	55.8 (63)	28.1 (16)	46.5 (79)
Unemployed (not employed, retired)	44.2 (50)	71.9 (41)	53.5 (91)
Marital status			
Married	21.2 (24)	17.5 (10)	20.0 (34)
Single/divorced/separated	78.8 (89)	82.5 (47)	80.0 (136)
HIV status			
Positive	1.8 (2)	0.0 (0)	1.2 (2)
Negative	96.5 (109)	96.5 (55)	96.5 (164)
Never tested/uncertain	1.8 (2)	3.5 (2)	2.4 (4)
Primary drug of abuse[d]			
Heroin	38.1 (43)	59.6 (34)	45.3 (77)
Opioid medication	61.1 (69)	29.8 (17)	50.6 (86)
Other	0.9 (1)	10.5 (6)	4.1 (7)
Outpatient mental health visit in prior month[e]	3.5 (4)	3.6 (2)	3.5 (6)
Prescribed psychiatric medication in prior month[d,e]	10.6 (12)	23.2 (13)	14.8 (25)

[a]All values % (n) unless otherwise noted. Some values may not add to 100% due to rounding.
[b]*t*-test, $P < .05$.
[c]Values for education were based on 112 responses in the buprenorphine/naloxone group.
[d]χ^2, $P < .05$.
[e]Values for outpatient mental health visits and prescribed psychiatric medication were based on 56 responses in the methadone group.

Pain Characteristics

The duration of pain ranged from < 1 to 58 years (mean = 13.2, SD = 10.6). Causes of current pain included accident (63%), nerve pain (22%), arthritis (18%), surgery (17%), opioid withdrawal (16%), work (14%), HIV (0.6%), and "other" (12%). Inclusive of low back pain, the number of reported pain sites ranged from 1 to 10 (mean = 3.0, SD = 1.8) and comprised legs (48%), shoulder (29%), feet (21%), neck (20%), hands (17%), head (15%), stomach (14%), knees (14%), arms (13%), hips (9%), pelvis (9%), teeth (2%), face (1%), and "other" (6%). Participants' mean (SD) pain severity and pain interference scores were 5.6 (1.5) and 6.0 (2.3), respectively.

Psychiatric Disorder Prevalence, Persistence, Comorbidity, and Treatment

The prevalence of any lifetime (and current) comorbid Axis I disorder was 91% (75%). As summarized in Table 2, 52% met criteria for lifetime anxiety disorder (48% current), 57% for lifetime mood disorder (48% current), and 78% for lifetime nonopioid substance use disorder (34% current). A majority of patients had an Axis II disorder (52%). As summarized in Table 3, patients whose primary reported drug of abuse was heroin (compared to prescription opioids) were more likely to meet lifetime criteria for any Axis I disorder and any nonopioid substance use disorder as well as any current Axis II disorder.

The proportion of participants who met lifetime criteria for 0, 1, 2, or at least 3 comorbid psychiatric disorders (ie,

Table 2. Psychiatric Diagnoses of Patients (N = 170) With Chronic Pain and Opioid Dependence[a]

DSM-IV Psychiatric Diagnosis	Lifetime	Current
Axis I diagnosis		
Any Axis I disorder[b]	90.6 (154)	75.3 (128)
Anxiety disorder		
Any anxiety disorder	51.8 (88)	48.2 (82)
Posttraumatic stress disorder	23.5 (40)	20.6 (35)
Generalized anxiety disorder	15.9 (27)	15.9 (27)
Panic disorder (without agoraphobia)	15.9 (27)	15.9 (27)
Social phobia	11.2 (19)	9.4 (16)
Specific phobias	5.9 (10)	5.3 (9)
Obsessive-compulsive disorder	7.1 (12)	6.5 (11)
Panic disorder (with agoraphobia)	3.5 (6)	2.9 (5)
Substance-induced anxiety disorder	2.4 (4)	2.4 (4)
Agoraphobia (no history of panic disorder)	1.2 (2)	1.2 (2)
Anxiety disorder, NOS	1.2 (2)	1.2 (2)
Mood disorder		
Any mood disorder	57.1 (97)	48.2 (82)
Major depressive disorder, recurrent	25.3 (43)	19.4 (33)
Major depressive disorder, single	23.5 (40)	20.6 (35)
Dysthymia	10.6 (18)	10.6 (18)
Bipolar disorder	4.7 (8)	4.7 (8)
Substance induced mood disorder	2.4 (4)	1.8 (3)
Depressive disorder, NOS	0.0 (0)	0.0 (0)
Cyclothymia	0.0 (0)	0.0 (0)
Adjustment disorder	0.0 (0)	0.0 (0)
Opioid dependence	100.0 (170)	100.0 (170)
Nonopioid substance use disorder		
Any nonopioid substance use disorder	77.6 (132)	33.5 (57)
Alcohol dependence	37.6 (64)	4.7 (8)
Alcohol abuse	19.4 (33)	3.5 (6)
Cocaine dependence	31.8 (54)	14.1 (24)
Cocaine abuse	11.8 (20)	3.5 (6)
Cannabis dependence	22.9 (39)	10.0 (17)
Cannabis abuse	18.8 (32)	7.6 (13)
Sedative/hypnotic dependence	6.5 (11)	1.8 (3)
Sedative/hypnotic abuse	8.8 (15)	4.7 (8)
Other drug dependence	7.1 (12)	1.2 (2)
Other drug abuse	5.9 (10)	2.4 (4)
Axis II diagnosis[c]		
Any Axis II disorder	N/A	51.8 (88)
Avoidant personality disorder	N/A	18.8 (32)
Antisocial personality disorder	N/A	21.8 (37)
Paranoid personality disorder	N/A	16.5 (28)
Borderline personality disorder	N/A	12.4 (21)
Obsessive-compulsive personality disorder	N/A	11.2 (19)
Dependent personality disorder	N/A	7.6 (13)
Schizoid personality disorder	N/A	8.2 (14)
Axis IV diagnosis		
Financial problems	N/A	59.4 (101)
Problems with primary support group	N/A	51.2 (87)
Occupational problems	N/A	32.4 (55)
Lack of social support	N/A	8.2 (14)
Relationship problems	N/A	11.2 (19)
Unemployment	N/A	13.5 (23)
Problems with access to medical care	N/A	2.9 (5)
Homelessness	N/A	1.8 (3)
Financial stress	N/A	4.1 (7)
Problems with transportation	N/A	1.2 (2)
Work-related problems	N/A	1.8 (3)
Limited social network	N/A	1.8 (3)
Family stress	N/A	0.6 (1)
Housing problems	N/A	1.8 (3)
Axis V diagnosis		
Global Assessment of Functioning score, mean (SD)	N/A	59.4 (4.8)

[a]All values % (n) unless otherwise noted.
[b]Does not include diagnosis of opioid dependence.
[c]For histrionic, schizotypal, and narcissistic personality disorders, the percentages were all 0.
Abbreviations: N/A = not applicable, NOS = not otherwise specified.

any anxiety disorder, any mood disorder, any nonopioid substance use disorder, any Axis II disorder) was as follows: 9%, 20%, 20%, and 51%, respectively, while the proportion who met current criteria were 19%, 22%, 25%, and 34%, respectively. About two-thirds of participants met criteria for current co-occurring anxiety or mood disorders (65%), including 33% who met criteria for both disorders. Participants' mean (SD) ages at onset for anxiety disorders and mood disorders were 16.9 (10.8) and 23.3 (10.3) years, respectively; the mean (SD) durations of current anxiety disorders and current mood disorders were 12.3 (10.7) and 18.2 (12.5) years, respectively. Of participants meeting criteria for a lifetime anxiety disorder, 93% also met criteria for a current anxiety disorder; 84% of patients meeting criteria for a lifetime mood disorder also met criteria for a current mood disorder. In the month prior to baseline, 4% of participants reported attending a mental health appointment, 15% reported that they had taken a prescribed psychiatric medication, and 16% reported either having a mental health visit or taking a prescribed psychiatric medication.

Anxiety and Mood Disorders, Pain Severity, Pain Interference

Among participants with current co-occurring anxiety and mood disorders, either a current anxiety or mood disorder (but not both), or no current anxiety or mood disorders, there were no significant differences found in pain severity score (5.7 vs 5.7 vs 5.5, respectively) ($F = 0.53$; $df = 2, 167$; $P = .58$) or pain interference score (6.3 vs 6.0 vs 5.7, respectively) ($F = 1.14$; $df = 2, 167$; $P = .32$). Treatment retention and clinically significant changes in pain severity or pain interference were not significantly associated with the presence of current or lifetime psychiatric disorders (P values ranged from .12 to 1.00 and .06 to 1.00, respectively, for participants in the buprenorphine/naloxone and methadone maintenance trials).

DISCUSSION

This study found a very high prevalence of *DSM-IV-TR* Axis I and Axis II disorders among patients seeking treatment for co-occurring opioid use disorder and chronic pain. Most participants (81%) met current criteria for at least 1—and the majority (59%) for at least 2—of the following psychiatric comorbidities: anxiety disorder, mood disorder, nonopioid substance use disorder, or personality disorder. Notably, a high proportion of participants with lifetime psychiatric disorders also met current diagnostic criteria. Despite the high prevalence and persistence of psychopathology, few participants had received either mental health treatment (3.5%) or a psychiatric medication in the previous month (14.8%). Contrary to findings among patients with chronic pain but without co-occurring opioid use disorder,[26,31] in this study, the presence of an anxiety disorder, mood disorder, or both was not associated with higher pain severity or pain interference scores.

Table 3. Comparison of Psychiatric Diagnoses in Patients With Chronic Pain and Opioid Dependence by Self-Reported Primary Drug of Abuse[a]

	Lifetime				Current			
DSM-IV Psychiatric Diagnosis	Heroin, %	Rx Opioid, %	χ^2	*P*	Heroin, %	Rx Opioid, %	χ^2	*P*
Axis I diagnosis								
Any Axis I disorder[b]	97.4	84.9	7.620	**.005**	80.5	68.6	3.015	.059
Anxiety disorder								
Any anxiety disorder	53.2	50.0	0.171	.399	53.2	43.0	1.702	.126
Posttraumatic stress disorder	27.3	22.1	0.589	.279	27.3	16.3	2.912	.065
Generalized anxiety disorder	16.9	12.8	0.542	.303	16.9	12.8	0.542	.303
Panic disorder (without agoraphobia)	14.3	17.4	0.302	.370	14.3	17.4	0.302	.370
Social phobia	14.3	9.3	0.980	.228	11.7	8.1	0.578	.309
Specific phobias	5.2	5.8	0.030[c]	1.000	5.2	4.7	0.026[c]	1.000
Obsessive-compulsive disorder	9.1	5.8	0.640	.308	7.8	5.8	0.253	.423
Panic disorder (with agoraphobia)	3.9	3.5	0.019[c]	1.000	3.9	2.3	0.337[c]	.668
Substance induced anxiety disorder	2.6	1.2	0.463[c]	.603	2.6	1.2	0.463[c]	.603
Agoraphobia (no history of panic disorder)	1.3	1.2	0.006[c]	1.000	1.3	1.2	0.006[c]	1.000
Anxiety disorder, NOS	2.6	0.0	2.262[c]	.222	2.6	0.0	2.262[c]	.222
Mood disorder								
Any mood disorder	59.7	53.5	0.646	.259	48.1	46.5	0.039	.484
Major depressive disorder, recurrent	35.1	16.3	7.615	**.005**	26.0	12.8	4.584	**.026**
Major depressive disorder, single	16.9	30.2	3.978	**.034**	14.3	26.7	3.820	**.038**
Dysthymia	6.5	12.8	1.820	.139	6.5	12.8	1.820	.139
Bipolar disorder	3.9	4.7	0.056[c]	1.000	3.9	4.7	0.056[c]	1.000
Substance-induced mood disorder	2.6	2.3	0.013[c]	1.000	2.6	1.2	0.463[c]	.603
Depressive disorder, NOS	0.0	0.0	N/A	N/A	0.0	0.0	N/A	N/A
Cyclothymia	0.0	0.0	N/A	N/A	0.0	0.0	N/A	N/A
Adjustment disorder	0.0	0.0	N/A	N/A	0.0	0.0	N/A	N/A
Opioid dependence	100.0	100.0	N/A	N/A	100.0	100.0	N/A	N/A
Nonopioid substance use disorder								
Any nonopioid substance use disorder	88.3	69.8	8.285	**.003**	39.0	27.9	2.241	.092
Alcohol dependence	45.5	31.4	3.407	**.046**	6.5	2.3	1.717[c]	.257
Alcohol abuse	16.9	22.1	0.699	.262	2.6	4.7	0.483[c]	.685
Cocaine dependence	41.6	23.3	6.264	**.010**	18.2	11.6	1.390	.169
Cocaine abuse	15.6	8.1	2.187	.109	5.2	2.3	0.943[c]	.423
Cannabis dependence	27.3	17.4	2.282	.093	10.4	8.1	0.246	.410
Cannabis abuse	23.4	16.3	1.297	.173	9.1	7.0	0.247	.416
Sedative/Hypnotic dependence	10.4	2.3	4.588[c]	**.048**	2.6	0.0	2.262[c]	.222
Sedative/Hypnotic abuse	9.1	9.3	0.002	.590	5.2	4.7	0.026[c]	1.000
Other drug dependence	7.8	5.8	0.253	.423	1.3	1.2	0.006[c]	1.000
Other drug abuse	9.1	3.5	2.214[c]	.193	2.6	2.3	0.013[c]	1.000
Axis II diagnosis[d]								
Any Axis II disorder	N/A	N/A	N/A	N/A	61.0	44.2	4.624	**.023**
Antisocial personality disorder	N/A	N/A	N/A	N/A	26.0	18.6	1.282	.173
Paranoid personality disorder	N/A	N/A	N/A	N/A	20.8	12.8	1.876	.123
Avoidant personality disorder	N/A	N/A	N/A	N/A	18.2	18.6	0.005	.554
Obsessive-compulsive personality disorder	N/A	N/A	N/A	N/A	14.3	8.1	1.562	.159
Borderline personality disorder	N/A	N/A	N/A	N/A	11.7	12.8	0.046	.511
Schizoid personality disorder	N/A	N/A	N/A	N/A	10.4	5.8	1.159	.216
Dependent personality disorder	N/A	N/A	N/A	N/A	5.2	9.3	1.005	.243

[a]Primary drug of abuse was either heroin or Rx (prescription) opioids. Bolded *P* values were significant at $P < .05$. For chi-square tests, $df = 1$.
[b]Does not include diagnosis of opioid dependence.
[c]Fisher exact test used due to insufficient cell size.
[d]For histrionic, schizotypal, and narcissistic personality disorders, the percentages were all 0.
Abbreviations: N/A = not applicable, NOS = not otherwise specified.

To put the findings of the current study in context, the prevalence of current anxiety disorders (48%) among study participants was higher than found in prior studies* of patients with opioid dependence (5%–17%)[23,24] or in studies of patients with chronic pain (11%–25%).[19–21] (Because of differences in study methodology, we did not make direct statistical comparisons between the current and prior studies.) Similarly, the prevalence of current mood disorders (48%) among study patients was higher than that found in studies of patients with opioid dependence (4%–24%)[23–25] and at the higher end of the range of those reported in studies of patients with chronic pain (34%–56%).[18,40] The prevalence of current nonopioid substance use disorders (34%) was in the range found in previous studies of patients with opioid use disorders (40%–68%)[24,25,41] but substantially higher than the estimated rates of substance use disorders reported in studies of patients with chronic pain (11%–19%).[20–22,42] The prevalence of personality disorders (52%) was also in the range reported in prior studies of patients with opioid use disorders (35%–57%)[23–25,43] or chronic pain (41%–69%).[18,20–22,44,45] Our findings are consistent with a previous investigation of a group of 40 patients with

*In these comparisons, we looked at studies using either *DSM-III-R*, *DSM-IV*, or *DSM-IV-TR* diagnostic criteria for the SCID (Axis I/Axis II) and DIPD (Axis II) to determine diagnostic prevalence.

co-occurring opioid use disorders and chronic pain, which reported numerically even higher rates of lifetime anxiety (93%) and mood disorders (85%) than those found in this study.[30]

This study is among the first to document higher rates of any lifetime Axis I disorder, any lifetime nonopioid substance use disorder, and any current Axis II disorder among patients with co-occurring chronic pain and opioid dependence reporting heroin (compared to prescription opioids) as their primary drug of abuse, and this finding merits further investigation. While patients with an anxiety and/or mood disorder had numerically higher pain intensity and interference than their counterparts without these disorders, group differences did not reach the level of statistical significance but may have done so with a larger sample size. However, it is also possible that the presence of an opioid (or nonopioid substance) use disorder attenuates the relationship previously reported between pain intensity or interference and the presence of anxiety or mood disorders among individuals with chronic pain.[26,31] One striking finding in this study was the high rate of nonopioid substance-related disorders; the extent to which the order of onset of chronic pain and opioid use disorder is associated with the prevalence of psychopathology, including nonopioid substance use disorders, is currently unclear and should be further investigated.

Another important finding of the current study is the high persistence of lifetime anxiety or mood disorders into the present: 93% of patients meeting criteria for a lifetime anxiety disorder also met criteria for a current anxiety disorder, and 84% of patients meeting criteria for a lifetime mood disorder met criteria for a current mood disorder. The high prevalence of current psychiatric comorbidity at treatment entry, as well as the persistence of these disorders, as indicated by the prolonged average duration of anxiety disorders (more than 12 years) and mood disorders (more than 18 years), may explain in part the clinical management problems experienced by providers treating these patients.[10,11] The findings suggest targets for potential pharmacologic or psychosocial treatments (eg, duloxetine and other antidepressant medications[46] and cognitive-behavioral therapy[47–49] have demonstrated efficacy in treating anxiety disorders, mood disorders, and chronic pain). It is notable, however, that neither lifetime nor current psychiatric disorders in the buprenorphine/naloxone or methadone maintenance trials were associated with study completion or clinically significant changes in pain severity or pain interference. This supports the conceptualization of these patients as persons with multiple interrelated morbidities who may benefit from the development and evaluation of integrated patient-centered interventions targeting chronic pain, opioid dependence, and other psychopathology.

Considering the high level of psychiatric comorbidity, it is noteworthy that a minority of participants (16%) reported prior-month receipt of a psychiatric medication or a mental health treatment episode. This low treatment rate may be related to multiple factors, including (*a*) failure of health care professionals to identify and treat psychiatric disorders in this patient group, (*b*) appropriate concerns about the use of benzodiazepines to treat anxiety disorders in this population, (*c*) lack of access to psychiatrists or psychologists with expertise in treating co-occurring opioid use disorder and chronic pain in addition to other psychiatric disorders, (*d*) logistical barriers (eg, financial cost), and (*e*) patient-level factors (eg, lack of awareness of having a potentially treatable psychiatric disorder rather than simply experiencing symptoms of anxiety or depression related to chronic pain or opioid use disorder).

Several potential study limitations are worth noting. We did not collect data on the reliability of the study diagnoses (eg, test-retest, interrater), but use of doctoral-level experienced clinicians as interviewers mitigates this concern. We used *DSM-IV-TR*[32] (and not *DSM-5*[50]) diagnoses. Given the importance of the construct of craving in both *DSM-5* criteria for opioid use disorder[50] and joint AAPM-APS-ASAM criteria for opioid addiction,[34] future research might benefit from a more detailed assessment of opioid craving.[51,52] The extent to which anxiety disorders and mood disorders among participants were primary, or a function of chronic pain or substance use, is unclear. Since participants were seeking treatment for co-occurring chronic pain and opioid dependence, it is unclear whether findings generalize to non–treatment-seeking individuals with these coexisting conditions.

Among patients seeking treatment for opioid use disorder and co-occurring chronic pain, the high rates of current and lifetime Axis I and Axis II disorders, the apparent absence of remission of anxiety disorders and mood disorders, and the low rates of current mental health treatment are salient. Overall, our findings suggest that effective treatments for co-occurring chronic pain and opioid dependence may need to address co-occurring psychiatric disorders, especially given their apparent chronicity, and that strategies for improving access to psychiatric and mental health services for these patients are needed.

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