



Published in final edited form as:

*Am J Addict.* 2013 ; 22(3): 261–265. doi:10.1111/j.1521-0391.2012.12008.x.

## Frequency and Severity of Comorbid Mood and Anxiety Disorders in Prescription Opioid Dependence

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### Abstract

**Background and Objectives:** Comorbid substance use disorders and mood and anxiety disorders are associated with more severe psychiatric symptoms, social and occupational impairment, and economic burden. To date, the majority of research has focused on comorbidity in illicit drug users, rather than prescription drug users. To address this gap in the literature, the present cross-sectional study investigated the clinical profiles of individuals with prescription opioid dependence with or without comorbid mood and anxiety disorders.

**Methods:** Ninety individuals with prescription opioid use were recruited to participate in the study procedures. All participants completed a structured clinical interview and series of self-report measures.

**Results and Conclusions:** Of the 85 individuals with prescription opioid dependence, 47.1% ( $n = 40$ ) were diagnosed with a comorbid mood or anxiety disorder. The findings showed that individuals with prescription opioid dependence and comorbid mood and anxiety disorders demonstrated significantly more severe alcohol use, psychiatric symptoms, and sleep impairment than individuals without comorbidity.

**Scientific Significance:** The findings highlight the frequency and severity of co-occurring mood and anxiety disorders in individuals with prescription opioid dependence and suggest that integrated interventions are needed to address these growing problems. (*Am J Addict* 2013;22:261–265)

### INTRODUCTION

Comorbidity between substance use disorders and mood and anxiety disorders is common, with one-third to almost half of the general population meeting criteria for comorbidity at some point in their lives.<sup>1–3</sup> Comorbidity is hypothesized to be the product of several potential pathways, including: (1) one disorder directly causes the other disorder (eg, prolonged substance abuse resulting in depressive symptoms), (2) one disorder serves as an

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Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

indirect risk factor for the other disorder (eg, frequent self-medication of social anxiety with substances transitions into a substance use disorder), and (3) two disorders develop from a common source (eg, shared genetic predisposition and/or environmental stressor).<sup>2</sup> In comparison to individuals with one disorder alone, individuals with comorbid disorders often demonstrate a more severe course of illness, including increased social and occupational impairment, disability, and economic burden.<sup>2,4,5</sup> In addition, comorbidity has been shown to be associated with poorer treatment outcome, higher rates of relapse, and re-hospitalization.<sup>4,5</sup>

One area of growing concern is the non-medical use of prescription opioids. Research has shown that an increasing number of individuals use prescription opioids, such as hydrocodone and oxycodone products for non-medical purposes (eg, reduce negative affect and improve sleep) with an average age of onset of misuse at approximately 22 years.<sup>6,7</sup> Over time, individuals using prescription opioids nonmedically may become psychologically and physically dependent on the drug.<sup>8</sup> In fact, research shows that as many as 1.7 million out of 4.7 million individuals using opioids for non-medical reasons meet Diagnostic and Statistical Manual-IV-TR (DSM-IV-TR) criteria for substance dependence.<sup>6</sup>

Although research shows that some individuals with prescription opioid dependence consume opioids in order to cope with emotional distress, there is limited research examining the severity of the emotional distress and frequency of comorbid mood and anxiety disorders in this population.<sup>1</sup> In contrast to this paucity in prescription opioid literature, the high rates of psychiatric comorbidity in non-prescription opioid dependence has been repeatedly investigated.<sup>9</sup> In one of the only studies of prescription opioid dependence, Passik et al.<sup>10</sup> investigated psychiatric comorbidity and pain characteristics in patients entering a drug rehabilitation center. The study identified comorbid opioid abuse/dependence with an additional Axis I disorder in 14.7% of patients and comorbid polysubstance abuse/dependence with an additional Axis I disorder in 45.0% of patients. However, the study did not investigate the influence of comorbidity on the severity of either disorder and relied on patients entering drug rehabilitation, limiting the understanding of this population.

The present study investigated the frequency and severity of comorbid mood and anxiety disorders in individuals with prescription opioid dependence. Specifically, the study examined the influence of comorbidity on symptom presentation (eg, drug use, alcohol use, psychiatric status, depression). In addition, associated symptoms and impairment common in both sets of disorders were investigated, including symptoms implicated in the initiation of opioid use (eg, pain, sleep, and medical status) and indicators of impairment (family/social status and employment status). Based on previous research with other drugs of abuse,<sup>2,4,5,9</sup> we hypothesized that individuals with prescription opioid dependence and comorbid mood and anxiety disorders would evidence greater substance use severity, psychiatric symptoms, and related symptoms (eg, sleep, pain, impairment in social and employment status) than individuals without comorbid mood and anxiety disorders.

## METHOD

### Participants

Ninety participants were recruited with prescription opioid dependence to participate in the study. Newspaper and other media advertisements and flyers posted in local health clinics were the primary sources of recruitment. Participants were part of a larger study on the relationship between stress, drug cues, and the hypothalamic–pituitary–adrenal (HPA) axis. General exclusion criteria included: pregnancy or nursing; body mass index  $\geq 39$ ; and major medical (eg, diabetes) or mental health (eg, bipolar disorder) conditions which could affect HPA axis functioning.

All participants completed the Structured Clinical Interview for the DSM-IV (SCID) to assess current prescription opioid dependence and other substance use disorders, and the Mini International Neuropsychiatric Interview (MINI) to assess mood and anxiety disorders (ie, major depressive disorder, generalized anxiety disorder, posttraumatic stress disorder, panic disorder, agoraphobia, social phobia, specific phobia, and obsessive compulsive disorder).<sup>11,12</sup> Eighty-five participants (94.4%) met diagnostic criteria for substance dependence on prescription opioids and were retained in the analyses (five participants were excluded). Forty (47.1%) participants with prescription opioid dependence met DSM-IV-TR for a mood or anxiety disorder. Based on these diagnoses, two diagnostic groups were developed: prescription opioid dependence without comorbid mood and anxiety disorders ( $n = 45$ ), and prescription opioid dependence with comorbid mood and anxiety disorders ( $n = 40$ ).

### Procedures

All procedures were approved by the local institution review board. Written informed consent was obtained before any study procedures were performed. Potential participants were initially screened by telephone and if eligible, invited for a clinical interview and a history and physical examination. The clinical assessment included the SCID, MINI, and the Addiction Severity Index—Lite (ASI),<sup>13</sup> as well as several self-report measures: Inventory of Depressive Symptomatology (IDS),<sup>14</sup> Pittsburgh Sleep Quality Index (PSQI),<sup>15</sup> and the Brief Pain Inventory—Short Form (BPI-SF).<sup>16</sup> The ASI is a semi-structured instrument that assesses seven functional domains related to addictions, including drug use, alcohol use, medical status, psychiatric status, family and social status, employment status, and legal status.<sup>13</sup> The IDS is a 30-item measure designed to assess the severity of depressive symptoms.<sup>14</sup> The PSQI is a 10-item measure that assesses seven domains related to sleep quality, including sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, daytime dysfunction, and overall sleep quality.<sup>15</sup> The BPI-SF is a nine-item measure designed to assess pain intensity and interference.<sup>16</sup> Each of these measures has received repeated support for their psychometric properties in the literature.

### Data Analyses

Group differences in substance-related symptoms (eg, ASI drug use subscale), general psychiatric symptoms (eg, depression and psychiatric status), related symptoms (eg, sleep disturbance and pain), and impairment (eg, ASI medical and employment subscales) were

investigated between the prescription opioid dependent without comorbid mood and anxiety disorders and prescription opioid dependent with comorbid mood and anxiety disorders groups through a series of independent samples *t*-tests. Prior to investigating symptom differences, two variable  $\chi^2$  tests and independent samples *t*-tests were used to investigate group differences on demographic characteristics. Based on these analyses, significant group differences in demographics were entered as covariates for the remainder of the analyses.

## RESULTS

### Sample Characteristics

The average age of participants was 34.9 (SD = 11.8) years and the majority were Caucasian (82.4%; 10.6% African American; 4.7% Native American; 2.4% Hispanic), single (63.5%; 14.1% married; 18.8% divorced), and completed at least some college (54.1%; 35.3% high school graduates; 10.6% less than high school). Approximately half were female (50.6%) and more than half were unemployed (60.0%). No significant group differences were found in any of the demographic categories.

### Comorbidity

As noted above, 47.1% of participants with prescription opioid dependence met DSM-IV-TR for a mood or anxiety disorder. Panic disorder was the most common comorbid psychiatric disorder (13.9%), followed by generalized anxiety disorder (10.7%), major depressive disorder (9.0%), posttraumatic stress disorder (6.6%), social phobia (6.6%), and obsessive compulsive disorder (4.9%). Specific phobia was diagnosed in less than 1% of the sample. However, diagnostic comorbidity was not limited to mood and anxiety disorders. A significant minority (27.1%) of participants endorsed a comorbid substance use disorder (alcohol, marijuana, cocaine, sedative, or over-the-counter sleeping pills). When compared across groups, participants in the prescription opioid dependence with comorbidity group were more likely to endorse alcohol dependence (22.5%) and sedative dependence (22.5%) than participants in the prescription opioid dependence without comorbidity group (6.7% and 6.7%;  $\chi^2_s = 4.4$ ,  $p_s < .05$ ). No group differences were found in the other substance use disorders.

### Symptom Severity

As presented in Table 1, the two groups (prescription opioid dependence without comorbidity and prescription opioid dependence with comorbidity) were compared on the ASI, IDS, BPI-SF, and PSQI through a series of *t*-tests. The analyses revealed that the prescription opioid dependence with comorbidity group reported more severe symptoms than the prescription opioid dependence without comorbidity group on the ASI Psychiatric subscale as well as the IDS and PSQI ( $t_s > 2.3$ ;  $p_s < .05$ ). The prescription opioid dependence with comorbidity group also endorsed more severe alcohol use severity, as evidenced by significantly higher scores on the ASI alcohol subscale, than the prescription opioid dependence without comorbidity ( $t = 2.3$ ,  $p < .05$ ).

## DISCUSSION

The present study investigated the frequency and severity of comorbid mood and anxiety disorders in individuals with prescription opioid dependence. Comorbid mood and anxiety disorders were diagnosed in nearly half (47.1%) of the sample, with particularly high prevalence rates of panic disorder (13.9%), generalized anxiety disorder (10.7%), and major depressive disorder (9.0%). The overall rate of psychiatric comorbidity (47.1%) was roughly consistent with previous findings in non-prescription opioid users.<sup>9</sup> Interestingly, comorbid mood and anxiety disorders further worsened many of these symptoms in individuals with prescription opioid dependence, including more severe psychiatric symptoms and worse overall quality of sleep. In addition, individuals in the prescription opioid dependence with comorbidity group reported elevated alcohol use compared to the prescription opioid dependence without comorbidity group. Together, these findings highlight the increased symptom severity and impairment associated with comorbid mood and anxiety disorders in individuals with prescription opioid dependence.

Although the present findings are unable to investigate the temporal order of onset of the comorbid disorders, the increased severity of psychiatric symptoms in individuals with mood and anxiety disorders highlights the potential significance of emotional pain in developing dependence to medications designed to target physical pain. In fact, previous research has shown that psychological factors, such as depression, were predictive of prescription opioid abuse in patients with chronic pain.<sup>16</sup> Given these findings, emotional pain and/or the presence of a mood or anxiety disorder should be thoroughly assessed and monitored in patients prescribed opioids in order to prevent or intervene in potential medication misuse behaviors in this at risk population.

The presence of comorbid mood and anxiety disorders was associated with more severe psychiatric symptoms, alcohol use, and sleep impairment in participants with prescription opioid dependence; however, no group differences were observed in overall drug use, pain severity or interference, or employment, family/social, or legal functioning. Although the increased psychiatric symptoms and sleep impairment were expected due to the nature of the group comparison,<sup>9</sup> the other findings require additional consideration. The lack of differences in pain and level of functioning may be explained by a ceiling effect, as the diagnosis of prescription opioid dependence is associated with high levels of pain and the additional comorbidity may have resulted in little additional symptomatology. There are also several possible explanations for the observed group differences in alcohol use, alcohol dependence, and sedative dependence. First, the addition of the comorbid mood or anxiety disorder may result in an increased need to self-medicate, resulting in increased use of alcohol and polysubstance dependence.<sup>2</sup> Alternatively, it is possible that individuals with polysubstance dependence involving alcohol and/or sedatives are more likely to develop comorbid mood and anxiety disorders.<sup>2</sup> The cross-sectional design of the present study limits the understanding of these relationships, suggesting that additional longitudinal research is merited.

In addition, given the high frequency of comorbidity (ie, nearly 50%) and increase in severity of overlapping symptoms (eg, psychiatric symptoms, sleep impairment, alcohol

use), treatment practices should be developed to target comorbid presentations of substance use disorders and mood and anxiety disorders. The majority of the previous literature has focused on sequential treatment models in which the substance dependence is treated first, with treatment of the mood or anxiety disorder deferred until the patient has achieved some length of sustained abstinence (eg, 6 months).<sup>17,18</sup> However, this specific ordering of treatments is based largely on anecdotal concerns that the treatment of mood and anxiety disorders will exacerbate substance use.<sup>18</sup> Due to mounting evidence that high comorbidity between the disorders (as found in the present study), concurrent covariation of symptoms among the comorbid disorders, and patients' perceptions of the interrelations between their comorbid disorders, there has been a shift in the recent literature towards integrated models of treatment, in which both disorders are simultaneously addressed.<sup>18</sup> Preliminary findings for integrated treatments have demonstrated improvements in both sets of symptoms for the comorbid disorders.<sup>19–21</sup> Additional support for integrated treatments has been provided by investigating the temporal course of improvement in symptoms of the comorbid disorders.<sup>22</sup> Together, these findings suggest that additional research is needed to develop, implement, and disseminate integrated treatment approaches for comorbid prescription opioid use disorders and mood and anxiety disorders to address this growing problem.

The present investigation has several limitations. First, as noted above, the findings focus on a single cross-sectional assessment of symptoms of prescription opioid dependence and mood and anxiety disorders. Future research should incorporate additional assessments of these disorders at multiple time points to better understand the relations between the symptoms and how they influence each other over time. Second, the size of the sample did not allow for the investigation of each individual mood or anxiety disorder separately (eg, panic disorder, generalized anxiety disorder, or major depressive disorder). Third, due to the nature of the larger study, a small number of participants with comorbid mood and anxiety disorders may have been excluded due to the initial screening criteria (eg, major medical or mental health conditions which could affect HPA axis functioning).

## CONCLUSIONS

The present study demonstrated that nearly half of individuals with prescription opioid dependence also met diagnostic criteria for a DSM-IV diagnosis of a mood or anxiety disorder. The comorbid presentation of disorders was associated with more severe psychiatric symptoms, alcohol use, and sleep impairment as compared to those without comorbid mood and anxiety disorders. Although cross-sectional design limited the study's ability to investigate the temporal development of the comorbid disorders, the findings highlight the prominence and risk associated with emotional pain in prescription opioid users, and the importance of developing integrated treatments to address these symptoms simultaneously.

## Acknowledgments

This work was partially supported by Mentored Career Development Awards K23 DA021228 (Dr. Back) and K24 DA00435 (Dr. Brady) from the National Institute on Drug Abuse, Bethesda, MD.

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**Table 1.** Descriptive statistics and group differences on the addiction, psychiatric, and related symptoms and impairments

Symptom scale	Opioid dependence without comorbidity ( <i>n</i> = 45)	Opioid dependence with comorbidity ( <i>n</i> = 39)	<i>t</i>	<i>d</i>
Addiction symptoms				
ASI—drug use	.22 (.13)	.22 (.13)	.02	.00
ASI—alcohol use	.08 (.09)	.14 (.14)	2.28*	.51
Psychiatric symptoms				
ASI—psychiatric	.11 (.17)	.23 (.18)	2.97***	.69
IDS—depression	16.40 (11.58)	26.70 (15.44)	2.78***	.75
Related symptoms				
BPI-SF—severity	3.23 (2.78)	3.23 (2.67)	.01	.00
BPI-SF—interference	2.56 (2.80)	2.80 (2.97)	.38	.08
PSQI—overall sleep	2.24 (.80)	2.69 (.98)	2.31*	.50
ASI—medical	.23 (.36)	.19 (.29)	.56	.12
Impairment				
ASI—employment	.47 (.26)	.46 (.43)	.12	.03
ASI—family/social	.21 (.16)	.23 (.20)	.41	.11
ASI—legal	.10 (.18)	.14 (.20)	.91	.21

Opioid dependence columns presented as mean (standard deviation). ASI = Addiction Severity Index 5th Edition; IDS = Inventory of Depressive Symptomatology; PSQI = Pittsburgh Sleep Quality Index; BPI-SF = Brief Pain Inventory—Short Form.

\*  $p < .05$

\*\*  $p < .01$ .