

Addict Benay. Author manuscript; available in PIVIC 2010 June 1.

Published in final edited form as:

Addict Behav. 2009; 34(6-7): 498-504. doi:10.1016/j.addbeh.2009.01.002.

Gender and Comorbidity Among Individuals with Opioid Use Disorders in the NESARC Study

Christine E. Grella^a, Mitchell P. Karno^a, Umme S. Warda^a, Noosha Niv^a, and Alison A. Moore^{a,b}

^aUCLA Integrated Substance Abuse Programs, Semel Institute for Neuroscience and Human Behavior, Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine at UCLA, University of California, Los Angeles, 1640 S. Sepulveda Blvd., Suite 200, Los Angeles, CA 90025-7535

^bDivision of Geriatric Medicine, David Geffen School of Medicine at UCLA, University of California Los Angeles, BOX 951687, 2339 PVUB, Los Angeles, CA 90095-1687

Abstract

This study examines gender differences in the association of lifetime mental and substance use disorders among individuals with opioid use disorders in the United States. The sample (*N*=578) is from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), which is a representative household survey. Bivariate analyses and logistic regression modeling were conducted. About 70% of the sample had a lifetime non-substance use Axis I disorder; women were about twice as likely as men to have either a mood or anxiety disorder. About half of the sample had a personality disorder, with women more likely to have paranoid disorder and men more likely to have antisocial personality disorder. Individuals with a lifetime mental disorder were about three times more likely than others to be dependent on other substances, independent of gender. The study demonstrated an inverse relationship between lifetime mental and other substance use disorders, with women having significantly higher odds for several of the mental disorders and men having greater odds of other substance use disorders.

Keywords

Heroin; Opioids; Gender differences; Psychiatric comorbidity; NESARC

1. Introduction

Considerable research has established the high prevalence of co-occurring mental disorders among individuals who have substance use disorders. National epidemiological studies in the United States, such as the Epidemiologic Catchment Area (ECA) survey and the National Comorbidity Survey (NCS), have yielded prevalence estimates for the association of comorbid mental and substance use disorders. Although these prior studies have disaggregated estimates for alcohol and drug abuse from dependence, they have not addressed comorbidity of specific mental disorders with specific classes of drug use disorders (Kessler et al., 1994, 1996).

Corresponding author: Christine E. Grella, UCLA Integrated Substance Abuse Programs, 1640 S. Sepulveda Blvd., Suite 200, Los Angeles, CA 90025-7535; phone: (310) 267-5451; fax: (310) 473-7885; email: E-mail: Grella@ucla.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Similarly, clinical research with treatment-based samples, which is likely to sample individuals with more severe drug use disorders than the levels found in the general population, has established the relatively high rates of comorbid mental disorders among substance users in treatment, particularly affective and anxiety disorders.

1.1. Prevalence of Heroin and Other Opioid Use

The present paper focuses on gender differences in comorbidity, including both non-substance use psychiatric disorders and other substance use disorders, among individuals with opioid use disorders in the United States. According to the National Survey on Drug Use and Health (NSDUH) in 2002, there were an estimated 600 000 individuals aged twelve or older in the United States who used heroin in the past year; about one third of these (210 000 individuals) met criteria for past-year dependence or abuse on heroin (Substance Abuse and Mental Health Services Administration [SAMHSA], 2004). Non-medical use of prescription opioids is more prevalent than heroin use, and the number of individuals with opioid use disorders in the United States has increased dramatically in the past 15 years (Compton & Volkow, 2006; Blanco et al., 2007; Cicero, Inciardi, & Munoz, 2005). According to data from NSDUH, approximately 1.5 million persons aged 12 or older met the criteria for past-year abuse of or dependence on prescription pain relievers (SAMHSA, 2004), second only to the rate for abuse or dependence on marijuana (4.3 million). Furthermore, recent research suggests that there is considerable overlap among users of heroin and other opioids (Rosenblum et al., 2007; Darke et al., 2006; Fischer et al., 2005; Fischer et al., 2006 Brands et al., 2004; Grau et al., 2007; Fischer & Rehm, 2007).

Increasingly, heroin use and non-medical use of other opioids is a worldwide problem. A report by the United Nations estimates that among individuals aged 15-64 years in the global population, approximately 15.6 million used opiates or opioids, including 11.1 million of those who used heroin, in 2005-06 (United Nations Office of Drugs and Crime, 2007). Indeed, a prominent researcher has asserted that "opioids make the single largest contribution to illicit drug-related mortality and morbidity worldwide and remain the major clinical problem for drug treatment agencies" (Darke et al., 2007, p. 49). The high rates of mortality and morbidity associated with opioids stem from their high potential for overdose (Coffin et al., 2007; Paulozzi et al., 2006), the risk of infectious diseases associated with injection use, involvement in criminal behaviors and lifestyle, and the poor health, nutrition, and environmental conditions that often accompany their use (Teesson et al., 2006). Moreover, longitudinal research has shown that heroin-dependent individuals are less likely than individuals dependent on cocaine or methamphetamine to reduce or cease their use in the 10 years following initiation of use, suggesting a more protected course of addiction (Hser, Evans, Huang, Brecht, & Li, 2008).

1.2. Gender and Psychiatric and Substance Use Comorbidity Among Heroin/Opioid Users

Prior clinical research has demonstrated that psychiatric disorders are prevalent among individuals who are in treatment for use of heroin or other opioids (Ahmadi et al., 2004; Brooner, King, Kidorf, Schmidt, & Bigelow, 1997; Callaly et al., 2001). There is also a strong association between non-medical use of prescription opioids and other substance use disorders (Huang et al., 2006; McCabe, Cranford, & West, 2008). Moreover, among opioid users in methadone treatment, dependence on other substances has been associated with having other psychiatric disorders (Darke & Ross, 1997).

Further, numerous studies have shown that women opioid users have more pervasive and severe mental health problems compared with men (Chatham et al., 1999; Rutherford et al., 1997; Tetrault et al., 2007). In studies conducted with both treatment and non-treatment samples, women opioid users are more likely than their male counterparts to exhibit high levels of global psychological distress and comorbid mental disorders, primarily mood and anxiety disorders,

although men have higher rates of antisocial personality disorder (Rounsaville et al., 1982; Darke et al., 1992; Darke, Swift, & Hall, 1994; Darke, Hall, & Swift, 1994; Luthar et al., 1996; Peles et al., 2007; Calsyn et al., 1996).

Recent findings from the Australian Treatment Outcome Study (ATOS) have provided more evidence of the high prevalence of mental disorders among opioid users, including both those who were in treatment (methadone/buprenorphine maintenance therapy, detoxification, residential rehabilitation) and not in treatment. Most prevalent are major depression, posttraumatic stress disorder (PTSD), and antisocial personality disorder (Darke et al., 2007). Consistent with prior research, females in ATOS generally had poorer overall mental health status and were more likely to have depression or PTSD, whereas males were more likely to meet criteria for antisocial personality disorder (Ross et al., 2005).

1.3. Present Study

The aim of the present study is to examine whether the association of mental and other substance use disorders among opioid users varies by gender. We examine gender differences in comorbidity among individuals who meet criteria for lifetime abuse or dependence on either heroin or other opioids (i.e., synthetic substances usually available as prescription medications, including oxycodone, hydrocodone, morphine, methadone, hydromorphone, fentanyl, and buprenorphine).

The study uses data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). NESARC represents an advance over prior national epidemiological studies conducted in the U.S. in affording an adequate sample size and more refined diagnostic criteria that permit analyses of subgroups by type of drug use and their association with specific (rather than global) mental disorders. Prior NESARC research has shown that mood and anxiety disorders are more strongly associated with drug use disorders, including opioid use, among women than men (Conway et al., 2006). This study extends the prior research conducted on opioid users in NESARC by examining gender differences in the conjoint effects of other substance use and mental disorders among individuals with lifetime opioid use disorders. The study is guided by two aims: (1) to determine the prevalence of lifetime mental and other substance use disorders among a community-based sample of individuals with opioid use disorders and (2) to determine whether there are differential relationships between mental and other substance use disorders within this sample by gender.

2. Method

2.1. NESARC Study

The 2001-2002 NESARC uses a representative sample of the United States. The study methodology has been described in detail elsewhere (Grant et al., 2003, Grant, Stinson et al., 2004). The target population of the NESARC was the civilian, non-institutional population of the United States, aged 18 and older, residing in households as well as in group quarters (e.g., group homes, halfway houses). Face-to-face interviews were conducted with 43 093 respondents. The overall survey response rate was 81%. African Americans, Hispanics, and young adults (ages 18–24 years) were over-sampled, with data adjusted for over-sampling and household- and person-level non-response. The weighted data were then adjusted to represent the U.S. civilian population based on the 2000 census. The research protocol, including informed-consent procedures, received full ethical review and approval from the U.S. Census Bureau and the U.S. Office of Management and Budget.

2.2. DSM-IV Drug Use Disorders Assessment

The Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV Version (AUDADIS-IV) was used to assess lifetime substance use disorders (Grant & Hasin, 1991). The AUDADIS-IV includes an extensive list of symptom questions that separately operationalizes DSM-IV criteria for abuse and dependence on alcohol, cannabis, cocaine, heroin, opioids other than heroin and methadone (i.e., "painkillers"), stimulants, tranquilizers, sedatives, hallucinogens, inhalants/solvents, and other drugs. Lifetime diagnoses of abuse required the participant to have met at least one of the four criteria defined for abuse in a twelve month-period at any time. Lifetime diagnoses of dependence required at least three of the seven DSM-IV criteria for dependence to be met within the same one-year period. Numerous studies conducted with clinical and general population samples have demonstrated good-to-excellent reliability and validity of the AUDADIS-IV for assessing DSM-IV substance use disorders (Grant et al., 2003; Grant, Stinson et al., 2004).

2.3. DSM-IV Mood, Anxiety, and Personality Disorders Assessment

The AUDADIS-IV was used to generate diagnoses of: (1) mood disorders, including major depression, dysthymia, mania, and hypomania; (2) anxiety disorders, including panic disorder with and without agoraphobia, social phobia, specific phobia, and generalized anxiety disorder; and (3) personality disorders, including paranoid, avoidant, dependent, obsessive-compulsive, schizoid, histrionic, and antisocial.

Lifetime mood and anxiety diagnoses in NESARC are consistent with the DSM-IV criteria for "primary" or independent diagnosis, meaning those mental disorders that are neither substance-induced nor due to a general medical condition (Grant, Stinson et al., 2004). Survey respondents classified with disorders that only were substance-induced and/or due to a general medical condition, as well as depressive episodes entirely accounted for by bereavement, were not included in the analyses presented here.

AUDADIS-IV assessment of DSM-IV personality disorders have been described previously (Grant et al., 2005). Briefly, to receive a diagnosis, respondents needed to endorse the required number of DSM-IV symptoms for the specific personality disorder, with ≥ 1 symptom causing distress or social/occupational impairment. Reliability and validity of AUDADIS-IV assessments are fair to good for mood, anxiety, and personality disorders (Grant et al., 2003; Grant, Stinson et al., 2004).

2.4. Participants

The sample for this study (N= 578) included all individuals in the 2001-2002 NESARC who met criteria for lifetime abuse or dependence on heroin or other opioids. This sample represented 1.75% of the total (weighted) NESARC general population sample (weighted N = 3.18 M). Among this sample, 104 individuals (13.8% of the weighted study sample) met criteria for abuse or dependence on heroin; about half of these (48.8%) had abuse or dependence on heroin only and the others (51.2%) had abuse and/or dependence on both heroin and other opioids. A majority of the sample (N=521, 93.3% of the weighted study sample) met criteria for abuse or dependence on other opioids. Among these, 47 individuals (7.1% of the weighted study sample) met criteria for abuse and/or dependence on both heroin and other opioids.

The sample comprised 32.6% females (unweighted N=223) and 67.4% males (unweighted N=355). Ages ranged from 18 years to 95 years. The average (S.D.) age was 38.5 (13.5) years for males and 37.9 (13.5) for females. Approximately 78% of the sample were White, 6% were African American, 7% Hispanic, and 9% of other groups (i.e., American Indian, Alaska Native, Asian, Native Hawaiian/Pacific Islander). About half of the sample were married (49%), 21% had been previously married, and 29% had never been married. A greater proportion of males

had never been married (32% vs. 24%, respectively), whereas a greater proportion of females had been previously married (28% vs. 18%, respectively; p < .001). Close to half of the sample had some college education or higher (49%), whereas 19% had less than a high school degree and about one-third (32% were high school graduates. A majority of the sample (77%) were from urban areas, with 35% from the South, 29% from the West, 22% from the Midwest, and 14% from the Northeast.

2.5. Statistical Methods

Cross-tabulations were used to calculate lifetime prevalence estimates for non-substance use psychiatric disorders (i.e., mood, anxiety, and personality) and for other substance use disorders (abuse or dependence) among the study sample by gender. The strength of these associations was assessed in logistic regression models, in which the dependent variable was the diagnosis of mental or other substance use disorders and gender was entered as a dummy variable (women = 1, men = 0). In a final model, the association among substance use and mental disorders was assessed by fitting separate logistic regression models for abuse and dependence on each substance, with comorbidity (for psychiatric disorders) entered as a dummy variable; these models were both unadjusted and adjusted for gender.

All analyses were conducted with SUDAAN Version 9.0, a software program that uses Taylor series linearization to make adjustments for the NESARC's sample design characteristics (Research Triangle Institute, 2005). The significance level for all tests was set at p < .05 (although p-values < .01 and .001 are also reported). Odds ratios (OR) and 95% confidence intervals (CI) are reported. Unweighted N's are reported in the tables; all statistics are weighted.

3. Results

3.1. Mood and Anxiety Disorders Among Individuals with Lifetime Opioid Use Disorders by Gender

Table 1 shows the prevalence of lifetime Axis 1 mood and anxiety disorders by gender and associated OR's derived from the logistic regression models. Altogether, about 70% of the study sample met criteria for at least one Axis I (non-substance use) disorder, 60% had at least one mood disorder, and 39% had at least one anxiety disorder. The most prevalent disorder was major depression, with over half (52%) of the sample meeting criteria for this diagnosis.

Women had twice the odds as men for having a lifetime mood disorder and were approximately twice as likely as men to have each of the specific mood disorders except for hypomanic disorder. Similarly, women had nearly twice the odds of men for having an anxiety disorder, with significantly greater odds of having social phobia, specific phobia, or generalized anxiety disorder. There was no difference between men and women, however, in the odds of having panic disorder, either with or without agoraphobia. Overall, there was no significant gender difference in the likelihood of having any Axis I (non-substance use) disorder.

3.2. Personality Disorders Among Individuals with Lifetime Opioid Use Disorders by Gender

Overall, about half of the sample met criteria for at least one personality disorder (see Table 1). Antisocial personality disorder was the most prevalent, among 30% of the sample. Women had about twice the odds as men for having paranoid personality disorder, but were somewhat more than half as likely as men to have antisocial personality disorder. Overall, there was no gender difference in the likelihood of having at least one of the personality disorders that was assessed.

3.3. Lifetime Other Substance Use Disorders among Individuals with Opioid Use Disorders by Gender

The prevalence rates for lifetime abuse and dependence on specific substances by gender are shown in Table 2. A majority of the sample met criteria for heroin/opioid abuse (73%) and the remainder (27%) met criteria for dependence. The most prevalent substance used (other than opioids) was alcohol, with 63% of the sample meeting criteria for alcohol dependence and 22% for alcohol abuse. Abuse on other substances was more common than dependence, with about half of the sample having a history of marijuana abuse, approximately one third having a history of abuse on cocaine, sedatives, amphetamines, hallucinogens, or tranquilizers; and 11% inhalant abuse. Overall, close to one quarter of the sample (22.6%) met criteria for abuse on another substance and almost 70% met criteria for dependence on another substance (in addition to heroin/other opioids).

Results from the logistic regression models showed that women were less likely than men to meet criteria for abuse on cocaine (OR = 0.34), marijuana (OR = 0.51), sedatives (OR = 0.50), tranquilizers (OR = 0.49), and inhalants (OR = 0.48). Women were also significantly less likely than men to be dependent on alcohol (OR = 0.59).

3.4. Other Substance Use Disorders Among Individuals with Opioid Use Disorders by Comorbidity

The prevalence rates for abuse and dependence on other substances for opioid users with and without any comorbid mental disorder (Axis I or II) are shown in Table 3. Individuals with lifetime Axis I disorders or Axis II disorders were about one third less likely to meet criteria for abuse of heroin or alcohol, although they were more likely to meet criteria for abuse of sedatives (OR = 1.67). In contrast, individuals with a lifetime mental disorder were significantly more likely to meet criteria for dependence on heroin (OR = 2.94), cocaine (2.92), marijuana (OR = 2.16), alcohol (OR = 2.81), sedatives (OR = 2.48), and tranquilizers (OR = 3.77). In the model predicting an aggregate variable of "any other substance disorder" (besides heroin/other opioids), individuals with a lifetime mental disorder were about two-thirds less likely than others to abuse another substance and were over three times more likely to be dependent on another substance.

In order to test whether the associations observed among the substance use and mental disorders were affected by gender, we re-ran the logistic regression models predicting each of the categories of substance abuse/dependence, with gender entered as a covariate (see Table 3). Although in most of these models gender was significantly and independently associated with having several of the substance use disorders, the odds for comorbidity were virtually the same as in the unadjusted models, thus demonstrating that the relationship between lifetime mental disorders and other substance use disorders among individuals with opioid use disorders is independent of gender.

4. Discussion

This study demonstrated a high prevalence of lifetime mood, anxiety, and some personality disorders as well as of other substance use disorders among a population-based sample with lifetime heroin/other opioid abuse or dependence. Indeed, our findings showed that approximately 70% met criteria for a lifetime mood or anxiety disorder, about half met criteria for a personality disorder, and approximately 70% had another lifetime substance dependence disorder. The prevalence of the various psychiatric disorders examined was considerably higher among this sample of individuals with heroin/opioid disorders as compared with the general population, as would be expected from prior research (Grant, Stinson et al., 2004; Grant et al., 2005).

With respect to gender differences, the study revealed that the odds of having some of the mental disorders examined among opioid users approximated the odds for men and women in the general population. For example, women in the general population are about twice as likely as men to have major depression or dysthymia (Grant & Weissman, 2007) or generalized anxiety disorder (Vesga-Lopez et al., 2008), which is comparable to the findings in the present study. In contrast, for other disorders, the gender differences were attenuated or heightened, in ways that indicated greater odds of comorbidity for women opioid users relative to men, as compared with the general population. For example, women opioid users were somewhat over half as likely as men to have antisocial personality disorder, compared with about one-third the odds for women compared with men in the general population (Grant, Hasin et al., 2004). Women opioid users had nearly three times the odds of men for having specific phobia, compared with about twice the odds for women versus men in the general population (Stinson et al., 2007). Similarly, women opioid users had nearly twice the odds of men for having paranoid personality disorder as compared with one-third greater odds for women versus men in the general population (Grant, Hasin et al., 2004).

Moreover, our study showed that having a lifetime mental disorder more than doubled the odds of dependence on cocaine, marijuana, alcohol, and sedatives, and increased by the odds of dependence on tranquilizers by nearly four-fold. Although women were about twice as likely as men to have a lifetime mood or anxiety disorder, they were significantly less likely to abuse other substances or to be dependent on alcohol. Hence, the association between lifetime mental disorders and other substance use disorders was independent of gender, even though women overall had significantly higher odds for several of the mental disorders and men had greater odds of having other substance use disorders.

We note that there was a higher prevalence of lifetime mental disorders observed in this study as compared with previous studies that have been conducted with treatment-based samples of opioid users (e.g., Brooner et al., 1997). There may be several reasons for the different prevalence rates observed. First, more recent epidemiological surveys, including NESARC, use improved instrumentation and methods that have yielded higher prevalence rates for psychiatric disorders compared with earlier surveys. This point is discussed in articles by Kessler et al. (1994), with regard to increased prevalence rates of psychiatric disorders from the ECA to the NCS; Kessler et al. (2005), which discusses differences in sampling frames, age ranges, diagnostic systems used to define disorders, and measures used across various population surveys; and Narrow et al. (2002) with regard to controlling for the clinical severity of disorders (e.g., suicidality and level of disability), which may underlie discrepancies across surveys. Second, differences in prevalence rates across studies may stem from differences in populations sampled as well as possible cohort and history effects. However, the study findings are consistent with prior research conducted with both treatment- and population-based samples with regard to the generally higher prevalence of mental disorders among women opioid users, with the exception being the higher prevalence of antisocial personality disorder among men.

4.1. Limitations

Several study limitations should be considered in the interpretation of study findings. The associations among opioid use disorders, mental disorders, and other substance use disorders were assessed for lifetime prevalence; therefore, we cannot discern temporal ordering of the disorders or the degree to which they were concurrent or causally related. For example, it is possible that individuals who were initially prescribed opioids for pain relief may have developed abuse or dependence on these substances, with a greater vulnerability to developing these and other substance use disorders among individuals with pre-existing mental disorders (Sullivan, Edlund, Steffick, & Unützer, 2005).

In addition, as with all retrospective studies, recall of specific symptoms over time may be inaccurate and influenced by the respondent's current mental and physical health status (Anthony, Neumark, & Van Etten, 2000); however, the validity of such data can be enhanced by use of standardized procedures and rigorous staff training and oversight (Del Boca & Noll, 2000), all of which were implemented in the NESARC study. We note that many epidemiological and clinical studies have relied upon data obtained through retrospective reports, which provides a valuable base for estimating prevalence of psychiatric disorders, although any interpretation of study findings should keep these limitations in mind (Turner, 2003).

4.2. Conclusion

Comorbidity of mental disorders among opioid users is of clinical significance because it is associated with poorer psychosocial functioning and health status (Cacciola et al., 2001). Similarly, comorbidity of multiple substance use disorders has been associated with a greater likelihood of suicidal behavior (Borges, Walters, & Kessler, 2000). Moreover, among those in treatment, comorbid mental disorders are associated with poorer outcomes, including lower rates of treatment retention and higher rates of relapse to drug use following treatment (Rounsaville et al., 1986; Compton et al., 2003, Mason et al., 1998). Recent findings from ATOS have shown that although opioid users demonstrate large improvements in their health and social functioning following their admission to treatment, the presence of co-occurring disorders moderates these improvements (Havard et al., 2006; Mills et al., 2007), and many individuals continue to suffer the detrimental effects of psychopathology following treatment. The growing use of opioids, both medically and non-medically, raises concerns about users' vulnerability to developing substance use disorders, particularly among those with a history of mental disorders. The current study provides further evidence of the relatively high prevalence of mental and other substance use disorders among opioid users, the enhanced rates of several mental disorders among women, and the imperative to screen for and provide adequate treatment for mental and other substance use disorders among individuals with a history of opioid abuse or dependence.

Acknowledgments

This work was supported by the National Institute on Drug Abuse grants DA020944 (PI: M. Karno) and DA15390 (PI: Grella). We gratefully acknowledge the support of Elizabeth Teshome and Kris Langabeer in manuscript preparation.

References

- Ahmadi J, Majdi B, Mahdavi S, Mohagheghzadeh M. Mood disorders in opioid-dependent patients. Journal of Affective Disorders 2004;82(1):139–142. [PubMed: 15465588]
- Anthony, J.; Neumark, Y.; Van Etten, M. Do I do what I say?: A perspective on self-report methods in drug dependence epidemiology. In: Stone, A.; Turkkan, J.; Bachrach, C., editors. The science of self-report: Implications for research and practice. Hillsdale, NJ: Lawrence Earlbaum Associates; 2000. p. 175-198.
- Blanco C, Alderson D, Ogburn E, Grant BF, Nunes EV, Hatzenbuehler ML, et al. Changes in the prevalence of non-medical prescription drug use and drug use disorders in the United States: 1991-1992 and 2001-2002. Drug and Alcohol Dependence 2007;90:252–260. [PubMed: 17513069]
- Borges G, Walters EE, Kessler RC. Associations of substance use, abuse, and dependence with subsequent suicidal behaviour. American Journal of Epidemiology 2000;151:781–789. [PubMed: 10965975]
- Brands B, Blake J, Sproule B, Gourlay D, Busto U. Prescription opioid abuse in patients presenting for methadone maintenance treatment. Drug and Alcohol Dependence 2004;73:199–207. [PubMed: 14725960]

Brooner RK, King VL, Kidorf M, Schmidt CW, Bigelow GE. Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. Archives of General Psychiatry 1997;54(1):71–80. [PubMed: 9006403]

- Cacciola JS, Alterman AI, Rutherford MJ, McKay JR, Mulvaney FD. The relationship of psychiatric comorbidity to treatment outcomes in methadone maintained patients. Drug and Alcohol Dependence 2001;61:271–280. [PubMed: 11164691]
- Callaly T, Trauer T, Munro L, Whelan G. Prevalence of psychiatric disorder in a methadone maintenance population. Australian and New Zealand Journal of Psychiatry 2001;35:601–605. [PubMed: 11551274]
- Calsyn DA, Fleming C, Wells EA, Saxon AJ. Personality disorder subtypes among opiate addicts in methadone maintenance. Psychology of Addictive Behaviors 1996;10(1):3–8.
- Chatham LR, Hiller ML, Rowan-Szal GA, Joe GW, Simpson DD. Gender differences at admission and follow-up in a sample of methadone maintenance clients. Substance Use & Misuse 1999;34(8):1137–1165. [PubMed: 10359226]
- Cicero TJ, Inciardi JA, Munoz A. Trends in abuse of Oxycontin and other opioid analgesics in the United States: 2002-2004. Journal of Pain 2005;6(10):662–672. [PubMed: 16202959]
- Coffin PO, Tracy M, Bucciarelli A, Ompad D, Vlahov D, Galea S. Identifying injection drug users at risk of nonfatal overdose. Academic Emergency Medicine 2007;14(7):616–623. [PubMed: 17554010]
- Compton WM, Cottler LB, Jacobs JL, Ben-Abdallah A, Spitznagel ED. The role of psychiatric disorders in predicting drug dependence treatment outcomes. American Journal of Psychiatry 2003;160(5): 890–895. [PubMed: 12727692]
- Compton WM, Volkow ND. Major increases in opioid analgesic abuse in the United States: Concerns and strategies. Drug and Alcohol Dependence 2006;81:103–107. [PubMed: 16023304]
- Conway KP, Compton W, Stinson FS, Grant BF. Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Journal of Clinical Psychiatry 2006;67(2):247–257. [PubMed: 16566620]
- Darke S, Hall WD, Swift W. Prevalence, symptoms and correlates of antisocial personality disorder among methadone maintenance clients. Drug and Alcohol Dependence 1994;34(3):253–257. [PubMed: 8033764]
- Darke S, Ross J. Polydrug dependence and psychiatric comorbidity among heroin injectors. Drug and Alcohol Dependence 1997;48:135–141. [PubMed: 9363413]
- Darke S, Ross J, Teesson M. The Australian treatment outcome study (ATOS): What have we learnt about treatment for heroin dependence? Drug and Alcohol Review 2007;26:49–54. [PubMed: 17364836]
- Darke S, Swift W, Hall W. Prevalence, severity and correlates of psychological morbidity among methadone maintenance clients. Addiction 1994;89(2):211–217. [PubMed: 8173487]
- Darke S, Williamson A, Ross J, Teesson M. Reductions in heroin use are not associated with increases in other drug use: 2-year findings from the Australian treatment outcome study. Drug and Alcohol Dependence 2006;84(2):201–205. [PubMed: 16580792]
- Darke S, Wodak A, Hall W, Heather N, Ward J. Prevalence and predictors of psychopathology among opioid users. British Journal of Addiction 1992;87:771–776. [PubMed: 1591528]
- Del Boca FK, Noll JA. Truth or consequences: The validity of self-report data in health services research on addictions. Addiction 2000;95:S347–S360. [PubMed: 11132362]
- Fischer B, Rehm J. Illicit opioid use in the 21st century: Witnessing a paradigm shift? Addiction 2007;102 (4):499–501. [PubMed: 17362281]
- Fischer B, Rehm J, Brissette S, Brochu S, Bruneau J, el-Guebaly N, et al. Illicit opioid use in Canada: Comparing social, health, and drug use characteristics of untreated users in five cities (OPICAN Study). Journal of Urban Health 2005;82(2):250–266. [PubMed: 15872194]
- Fischer B, Rehm J, Patra J, Firestone-Cruz M. Changes in illicit opioid use across Canada. Canadian Medical Association Journal 2006;175(11):1385–1387. [PubMed: 17116905]
- Grant BF, Dawson DA, Stinson FS, Chou PS, Kay W, Pickering R. The alcohol use disorder and associated disabilities interview schedule-IV (AUDADIS-IV): Reliability of alcohol consumption,

tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. Drug and Alcohol Dependence 2003;71:7–16. [PubMed: 12821201]

- Grant, BF.; Hasin, DS. The Alcohol Use Disorders and Associated Disabilities Interview Schedule. Rockville, MD: National Institute of Alcohol Abuse and Alcoholism; 1991.
- Grant BF, Hasin DS, Stinson FS, Dawson DA, Chou SP, Ruan WJ, et al. Prevalence, correlates, and disability of personality disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Journal of Clinical Psychiatry 2004;65:948–958. [PubMed: 15291684]
- Grant BF, Stinson FS, Dawson DA, Chou P, Dufour MC, Compton W, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the national epidemiologic survey on alcohol and related conditions. Archives of General Psychiatry 2004;61(8): 807–816. [PubMed: 15289279]
- Grant BF, Stinson FS, Dawson DA, Chou SP, Ruan WJ. Co-occurrence of DSM-IV personality disorders in the United States: Results from the national epidemiologic survey on alcohol and related conditions. Comprehensive Psychiatry 2005;46(1):1–5. [PubMed: 15714187]
- Grant, BF.; Weissman, MM. Gender and the prevalence of psychiatric disorders. In: Narrow, WE.; First, MB.; Sirovatk, M.; Regier, DA., editors. Age and gender considerations in psychiatric diagnosis: A research agenda for DSM-V. Arlington, VA: American Psychiatric Association; 2007. p. 31-45.
- Grau LE, Dasgupta N, Harvey AP, Irwin K, Givens A, Kinzly ML, et al. Illicit use of opioids: Is OxyContin[®] a "gateway drug"? American Journal on Addictions 2007;16:166–173. [PubMed: 17612819]
- Havard A, Teesson M, Darke S, Ross J. Depression among heroin users: 12-month outcomes from the Australian treatment outcome study. Journal of Substance Abuse Treatment 2006;30:355–362. [PubMed: 16716851]
- Hser YI, Evans E, Huang D, Brecht ML, Li L. Comparing the dynamic course of heroin, cocaine, and methamphetamine use over 10 years. Addictive Behaviors 2008;33:1581–1589. [PubMed: 18790574]
- Huang B, Dawson DA, Stinson FS, Hasin DS, Ruan WJ, Saha TD, et al. Prevalence, correlates, and comorbidity of nonmedical prescription drug use and drug use disorders in the United States: Results of the national epidemiologic survey on alcohol and related conditions. Journal of Clinical Psychiatry 2006;67:1062–1073. [PubMed: 16889449]
- Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and ageof-onset distributions of DSM-IV disorders in the National Comorbidity survey replication. Archives of General Psychiatry 2005;62:593–602. [PubMed: 15939837]
- Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III--R psychiatric disorders in the United States: Results from the National Comorbidity Study. Archives of General Psychiatry 1994;51(1):8–19. [PubMed: 8279933]
- Kessler RC, Nelson CB, McGonagle KA, Edlund MJ, Frank RG, Leaf PJ. The epidemiology of cooccurring addictive and mental disorders: Implications for prevention and service utilization. American Journal of Orthopsychiatry 1996;66:17–31. [PubMed: 8720638]
- Luthar SS, Cushing G, Rounsaville BJ. Gender differences among opioid abusers: Pathways to disorder and profiles of psychopathology. Drug and Alcohol Dependence 1996;43(3):179–190. [PubMed: 9023074]
- Mason BJ, Kocsis JH, Melia D, Khuri ET, Sweeney J, Wells A, et al. Psychiatric comorbidity in methadone maintained patients. Journal of Addictive Diseases 1998;17(3):75–89. [PubMed: 9789161]
- McCabe SE, Cranford JA, West BT. Trends in prescription drug abuse and dependence, co-occurrence with other substance use disorders, and treatment utilization: Results from two national surveys. Addictive Behaviors 2008;33:1297–1305. [PubMed: 18632211]
- Mills KL, Teesson M, Ross J, Darke S. The impact of post-traumatic stress disorder on treatment outcomes for heroin dependence. Addiction 2007;102:447–454. [PubMed: 17298653]
- Narrow WE, Rae DS, Robins LN, Regier DA. Revised prevalence estimates of mental disorders in the United States: Using a clinical significance criterion to reconcile 2 surveys' estimates. Archives of General Psychiatry 2002;59:115–123. [PubMed: 11825131]

Paulozzi LJ, Budnitz DS, Xi Y. Increasing deaths from opioid analgesics in the United States. Pharmacoepidemiology and Drug Safety 2006;15(9):618–627. [PubMed: 16862602]

- Peles E, Schreiber S, Naumovskya Y, Adelson M. Depression in methadone maintenance treatment patients: Rate and risk factors. Journal of Affective Disorders 2007;99:213–220. [PubMed: 17055063]
- Research Triangle Institute. Software for Survey Data Analysis (SUDAAN), Version 9.0. Research Triangle Institute; Research Triangle Park, NC: 2005.
- Rosenblum A, Parrino M, Schnoll SH, Fong C, Maxwell C, Cleland CM, et al. Prescription opioid abuse among enrollees into methadone maintenance treatment. Drug and Alcohol Dependence 2007;90(1): 64–71. [PubMed: 17386981]
- Ross J, Teesson M, Darke S, Lynskey M, Ali R, Ritter A, et al. The characteristics of heroin users entering treatment: Findings from the Australian Treatment Outcome Study (ATOS). Drug and Alcohol Review 2005;24:411–418. [PubMed: 16298835]
- Rounsaville BJ, Kosten TR, Weissman MM, Kleber HD. Prognostic significance of psychopathology in treated opiate addicts: A 2.5-year follow-up study. Archives of General Psychiatry 1986;43(8):739–745. [PubMed: 3729668]
- Rounsaville BJ, Weissman MM, Kleber H, Wilber C. Heterogeneity of psychiatric diagnosis in treated opiate addicts. Archives of General Psychiatry 1982;39(2):161–166. [PubMed: 7065830]
- Rutherford MJ, Cacciola JS, Alterman AI, Cook TG. Social competence in opiate-addicted individuals: Gender differences, relationship to psychiatric diagnoses, and treatment response. Addictive Behaviors 1997;22(3):419–425. [PubMed: 9183511]
- Stinson FS, Dawson DA, Patricia Chou S, Smith S, Goldstein RB, June Ruan W, Grant BF. The epidemiology of DSM-IV specific phobia in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychological Medicine 2007;37(7):1047–1059. [PubMed: 17335637]
- Substance Abuse and Mental Health Services Administration, Office of Applied Studies. The NSDUH Report: Nonmedical use of prescription pain relievers. Rockville, MD; May 21. 2004 Retrieved July 23, 2007 from http://www.oas.samhsa.gov/2k4/pain/pain.cfm
- Sullivan MD, Edlund MJ, Steffick D, Unützer J. Regular use of prescribed opioids: Association with common psychiatric disorders. Pain 2005;119(13):95–103. [PubMed: 16298066]
- Teesson M, Ross J, Darke S, Lynskey M, Ali R, Ritter A, et al. One year outcomes for heroin dependence: Findings from the Australian Treatment Outcome Study (ATOS). Drug and Alcohol Dependence 2006;83(2):174–180. [PubMed: 16343809]
- Tetrault JM, Desai RA, Becker WC, Fiellin DA, Concato J, Sullivan LE. Gender and non-medical use of prescription opioids: Results from a national US survey. Addiction 2007;103(2):258–268. [PubMed: 18042194]
- Turner RJ. The pursuit of socially modifiable contingencies in mental health. Journal of Health and Social Behavior 2003;44:1–17. [PubMed: 12751307]
- United Nations, Office of Drugs and Crime. World drug report. 2007. Retrieved December 14, 2007 from http://www.unodc.org/unodc/en/data-and-analysis/WDR-2007.html
- Vesga-López O, Schneier FR, Wang S, Heimberg RG, Liu SM, Hasin DS, et al. Gender Differences in Generalized Anxiety Disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Journal of Clinical Psychiatry 2008;69:1606–1616. [PubMed: 19192444]

	Men (%) (N = 355)	Women (%) (N = 223)	Total (%) (N = 578)	Odds Ratio ^b (95% confidence interval)
Any mood or anxiety disorder	68.5	73.8	70.3	1.30 (0.84, 2.00)
Any mood disorder	54.1	71.2	59.7	2.10 (1.35, 3.26)**
Major depression	45.7	63.5	51.5	2.07 (1.38, 3.12)**
Dysthymia	15.3	25.3	18.6	1.88 (1.20, 2.93)**
Manic disorder	16.7	27.1	20.1	1.86 (1.17, 2.94)*
Hypomanic disorder	9.0	10.9	9.6	1.24 (0.61, 2.50)
Any anxiety disorder	33.6	50.1	39.0	1.98 (1.35, 2.92)***
Panic disorder w/o agoraphobia	13.2	18.3	14.9	1.46 (0.88, 2.45)
Panic disorder w/ agoraphobia	4.1	6.6	4.9	1.65 (0.63, 4.33)
Social phobia	9.3	19.8	12.7	2.42 (1.36, 4.30)**
Specific phobia	12.9	30.1	18.5	2.91 (1.69, 5.02)***
Generalized anxiety disorder	9.7	17.7	12.3	2.01 (1.13, 3.56)*
Any personality disorder	49.2	50.7	49.7	1.06 (0.74, 1.52)
Paranoid	12.9	22.2	15.9	1.93 (1.17, 3.21)*
Avoidant	9.5	12.4	10.4	1.35 (0.71, 2.57)
Dependent	3.0	2.3	2.8	0.77 (0.25, 2.37)
Obsessive compulsive	16.0	23.0	18.3	1.56 (0.95, 2.57)
Schizoid	11.5	12.8	11.9	1.13 (0.61, 2.11)
Histrionic	9.8	8.5	9.4	0.86 (0.42, 1.76)
Antisocial	34.1	22.4	30.3	0.56 (0.36, 0.87)*

^{*}p < .05,

^{**} p < .01,

^{***} p < .001

^aN's are unweighted; statistics are weighted.

bWomen = 1, Men = 0

Grella et al. Page 13

	Men (%) (N = 355)	Women (%) (N = 223)	Total (%) (N = 578)	Odds Ratio ^b (95% confidence interval)
Heroin/other opioids				
Abuse	75.6	67.5	73.0	0.67 (0.43, 1.04)
Dependence	24.4	32.5	27.0	1.49 (0.96, 2.31)
Cocaine				
Abuse	37.6	17.0	30.9	0.34 (0.20, 0.58)***
Dependence	17.4	20.5	18.4	1.22 (0.73, 2.03)
Marijuana				
Abuse	56.2	39.3	50.7	0.51 (0.33, 0.78)**
Dependence	19.4	19.9	19.6	1.03 (0.62, 1.72)
Alcohol				
Abuse	22.6	20.4	21.8	0.88 (0.55, 1.41)
Dependence	67.1	54.5	63.0	0.59 (0.40, 0.86)**
Sedatives				
Abuse	37.7	23.3	33.0	0.50 (0.30, 0.85)*
Dependence	9.1	12.9	10.3	1.48 (0.77, 2.87)
Amphetamine				
Abuse	35.9	28.0	33.3	0.70 (0.45, 1.08)
Dependence	13.3	18.5	15.0	1.47 (0.80, 2.72)
Hallucinogen				
Abuse	37.4	27.5	34.2	0.63 (0.40, 1.01)
Dependence	9.0	9.5	9.1	1.06 (0.51, 2.20)
Tranquilizers				
Abuse	37.7	22.7	32.9	0.49 (0.30, 0.78)**
Dependence	8.7	12.4	9.9	1.49 (0.80, 2.81)
Inhalants				
Abuse	13.0	6.7	10.9	0.48 (0.24, 0.95)*
Dependence	1.7	2.1	1.9	1.22 (0.30, 4.99)
Any other substance C				
Abuse	23.1	21.6	22.6	0.92(0.60, 1.41)
Dependence	72.4	62.3	69.1	0.63(0.43, 0.91)*

^{*}p < .05,

^{**} p < .01,

p < .001;

^aN's are unweighted; statistics are weighted;

bWomen = 1, Men = 0;

 $^{^{\}it c}$ any of the above substances, in addition to heroin/other opioids

NIH-PA Author Manuscript NIH-PA Author Manuscript NIH-PA Author Manuscript

	Comorbid (%) $(N = 413)$	Non-Comorbid (%) $(N = 165)$	Total (%) $(N = 578)$	Odds Ratio ^b (95% confidence interval)	Odds Ratios Adjusted for Gender ^d (95% confidence interval)
Heroin/other opioids					
Abuse	67.7	86.0	73.0	0.34 (0.19, 0.60)	$0.35 (0.20, 0.61)^{***}$
Dependence	32.3	14.0	27.0	2.94 (1.68, 5.16)	2.90 (1.64, 5.12)
Cocaine					
Abuse	30.8	31.0	30.9	0.99 (0.59, 1.67)	1.05 (0.61, 1.78)
Dependence	22.3	8.9	18.4	2.92 (1.53, 5.57)**	2.90 (1.52, 5.53)**
Marijuana					
Abuse	50.5	51.0	50.7	0.98 (0.62, 1.54)	1.02 (0.64, 1.62)
Dependence	22.7	11.9	19.6	2.16 (1.06, 4.43)*	$2.16 (1.06, 4.41)^*$
Alcohol					
Abuse	16.3	35.6	21.8	$0.35 (0.21, 0.59)^{***}$	$0.35 (0.21 \ 0.59)^{***}$
Dependence	70.1	45.5	63.0	2.81 (1.73, 4.54)	2.97 (1.81, 4.85)
Sedative					
Abuse	36.1	25.3	33.0	1.67 (1.05, 2.64)*	1.75 (1.10, 2.79)*
Dependence	12.3	5.4	10.3	2.48 (1.10, 5.61)*	2.43 (1.08, 5.51)*
Amphetamine					
Abuse	34.1	31.6	33.3	1.12 (0.70, 1.79)	1.14 (0.71, 1.84)
Dependence	17.0	10.1	15.0	1.83 (0.76, 4.41)	1.80 (0.75, 4.34)
Hallucinogen					
Abuse	36.2	29.3	34.2	1.37 (0.88, 2.13)	1.41 (0.90, 2.21)
Dependence	10.8	5.1	9.1	2.27 (0.60, 8.55)	2.26 (0.61, 8.47)
Tranquilizers					
Abuse	34.7	28.2	32.9	1.36 (0.81, 2.28)	1.42 (0.84, 2.39)
Dependence	12.4	3.6	6.6	3.77 (1.48, 9.62)	3.70 (1.44, 9.49) **
Inhalants					
Abuse	11.5	9.5	10.9	1.24 (0.64, 2.39)	1.28 (0.66, 2.48)
Dependence	2.1	1.2	1.9	1.87 (0.37, 9.38)	1.85 (0.35, 9.80)
Any other substance ^c					

_
_
T
×
7
_
12
\subseteq
Author
0
$\vec{\neg}$
\leq
Man
=
=
\subseteq
S
uscrip
\exists
0
\rightleftarrows

NIH-PA Author Manuscript

NIH-PA Author Manuscript

I	
Odds Ratios Adjusted for Gender ^d (95% confidence interval)	0.32 (0.19, 0.53) *** 3.41 (2.12, 5.50) ***
Odds Ratio ^b (95% confidence interval)	0.32 (0.19, 0.53) *** 3.24 (2.03, 5.18) ***
Total $(\%)$ $(N = 578)$	22.6
Non-Comorbid (%) $(N = 165)$	38.1
Comorbid (%) $(N = 413)$	16.3

** p < .01,

Dependence

 $a_{\rm N}$'s are unweighted; statistics are weighted

 $^{\it C}$ any of the above substances, in addition to heroin/other opioids bComorbid = 1, Non-comorbid = 0

 $d_{\rm W}$ omen have a lower likelihood than men of dependence on alcohol and abuse on amphetamines, tranquilizers, cocaine, inhalants, marijuana, all p < .05