

# **HHS Public Access**

J Subst Abuse Treat. Author manuscript; available in PMC 2021 July 01.

Published in final edited form as:

Author manuscript

J Subst Abuse Treat. 2020 July ; 114: 108012. doi:10.1016/j.jsat.2020.108012.

## Co-occurring opioid and sedative use disorder: Gender differences in use patterns and psychiatric co-morbidities in the United States

Jennifer D. Ellis, M.A.<sup>1,2</sup>, Brian P. Pittman, M.S.<sup>2</sup>, Sherry A. McKee, PhD<sup>2</sup>

<sup>1</sup>.Department of Psychology, Wayne State University

<sup>2</sup> Department of Psychiatry, Yale University School of Medicine

## Abstract

Non-medical use of both opioids and sedatives increases risk of overdose or accident. The purpose of the present study was to describe rates of co-use, to examine baseline characteristics and psychiatric conditions potentially associated with meeting criteria for co-occurring opioid use disorder and sedative use disorder, and to examine whether these relationships varied by gender. Participants were 330 individuals from the NESARC-III who met criteria for current opioid use disorder. Gender-stratified logistic regression analyses, accounting for the survey design, were used to identify psychiatric conditions associated with meeting criteria for co-occurring sedative use disorder. Results indicated that 16.4% of the sample also met criteria for sedative use disorder. Notably, 55.6% of the sample attained opioids through their own prescription. Of those with cooccurring sedative use disorder, 47.2% attained sedatives through their own prescription. Posttraumatic stress disorder (OR = 3.02, 95% CI = 1.40 - 6.51) and antisocial personality disorder (OR = 2.72, 95% CI = 1.37 - 5.41) were associated with co-occurring sedative use disorder among both men and women with opioid use disorder. Depressive disorders (OR = 2.12, 95% CI = 1.01 - 4.42) and schizotypal personality disorder (OR = 5.78, 95% CI = 2.48 - 13.49) were associated with co-occurring sedative use disorder in women only. Results of the present study highlight the importance of prescription monitoring, further research into gender-informed treatments, and implementation of treatments for substance use and co-occurring symptoms.

## Keywords

opioids; sedatives; gender differences; co-occurring; prescribing

Declarations of interest: None

Corresponding Author: Jennifer Ellis, M.A., One Long Wharf Drive, New Haven, CT, 06519, jennifer.ellis@yale.edu. Author Statement:

**Jennifer D. Ellis:** Conceptualization, formal analysis, writing – original draft, writing – review and editing. **Brian P. Pittman:** Formal analysis, writing – review and editing.

Sherry A. McKee: Conceptualization, writing - review and editing, supervision.

**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 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.

Publisher's Disclaimer: Disclaimer: This publication does not express the views of DMHAS, the State of Connecticut, NIDA, or NIAAA.

## 1. Introduction

Over the past decade, rates of opioid use and opioid overdose have substantially increased (Rudd, Aleshire, Zibbell, & Gladden, 2016). Using opioids in combination with sedative medications, such as benzodiazepines or tranquilizers (Stein et al., 2017; Sun et al., 2017), can increase risk of overdose, as both medications suppress the central nervous system, and the combination of the two increases respiratory depression (Chou et al., 2009). Both medications have a high potential for addiction. And co-use of these medications is common, with some estimates from national data suggesting that 11.3% of those with an opioid use disorder (OUD) also have a sedative/tranquilizer use disorder (Votaw, Witkiewitz, Valeri, Bogunovic, & McHugh, 2019).

Certain psychiatric conditions may increase the risk of using opioids in combination with sedatives. Post-traumatic stress disorder (PTSD; Gressler, Martin, Hudson, & Painter, 2018; Yarborough et al., 2019), anxiety disorders (Gressler et al., 2018; Yarborough et al., 2019), depressive symptoms (Saunders et al., 2012), and bipolar disorder (Bouvier et al., 2018; Yarborough et al., 2019) have all been associated with sedative and/or benzodiazepine use among patients with OUD or those on chronic opioid therapy. However, these studies varied widely with regard to the psychiatric conditions included in the analyses, and with regard to the study population; samples have included patients with chronic pain, veterans, and young adults misusing prescription medication. Additionally, very few studies have examined the full diagnostic criteria for OUD and sedative use disorder. Thus, there remains a need for a comprehensive investigation into psychiatric co-morbidity among those meeting criteria for both opioid and sedative use disorder among a nationally representative sample of individuals with OUD.

Furthermore, very few studies have examined whether psychiatric conditions associated with co-occurring OUD and sedative use disorder vary by gender. Nonetheless, sex is an important biological variable (National Institutes of Health, 2015), and examining gender differences in psychiatric correlates of co-occurring opioid and sedative use disorder may help to identify gender-specific pathways to substance use and help inform interventions that are sensitive to sex and gender. For example, Hearon and colleagues (2011) found that anxiety sensitivity was associated with illicit sedative use in women, but not men, in methadone treatment. Similarly, anxiety sensitivity was associated with nonmedical benzodiazepine use among women, but not men undergoing inpatient detoxification from opioids (McHugh et al., 2017). However, a comprehensive analysis of gender differences in the psychiatric comorbidity among individuals with co-occurring opioid and sedative use disorder has not been done.

The purpose of the current study was to 1) explore psychiatric conditions associated with meeting criteria for co-occurring sedative use disorder among a nationally representative sample of individuals with OUD and 2) to examine how these associations varied by gender. A secondary aim of the study was to examine the number of respondents who accessed opioid and sedative medication through their own prescription.

## 2. Materials and Methods

#### 2.1 Participants

The National Epidemiological Survey on Alcohol and Related Conditions-III (NESARC-III) served as the data source for this study. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) conducted the NESARC-III between April 2012 and June 2013. We used multistage cluster sampling to recruit a representative sample of noninstitutionalized adults living in the United States (for more detail, see Grant et al., 2014). Of the 36,309 individuals who participated in the NESARC-III, 330 met criteria for past-year OUD and were considered eligible for the current study.

#### 2.2. Measures

All participants completed the Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5), a valid and reliable in-person, computer-assisted interview that measures DSM-5 criteria for substance use, physical and mental disabilities, and risk factors for substance use and mental health conditions (Hasin et al., 2015; Grant et al., 2015).

**2.2.1. Demographic information**—Participants reported their sex, race, income, and age.

**2.2.2 Substance use disorders**—Participants were dichotomized into two groups: 1) individuals with past-year OUD and 2) individuals who met criteria for OUD in combination with past-year sedative use disorder. Age of first use, duration of heaviest use, and frequency of use (in the past 12 months, and during the participant's heaviest use were also examined). Participants were also asked whether the experiences that they had with opioids and sedatives occurred with or without a prescription.

**2.2.3. Co-occurring psychopathology**—Co-occurring personality disorders (borderline personality disorder, antisocial personality disorder, schizotypal personality disorder), depressive disorders (major depressive disorder, dysthymia), anxiety disorders (agoraphobia, panic disorder, generalized anxiety disorder, social anxiety disorder), bipolar disorder, and PTSD were examined in this study. Feeding and eating disorders (anorexia nervosa, bulimia nervosa, binge eating disorder) were initially considered but were not included in analyses due to low co-morbidity rates among individuals with OUD (Ns < 5).

Agoraphobia, panic disorder, generalized anxiety disorder, and social anxiety disorder were collapsed into a single category, "any anxiety disorder", due to their phenomenological similarity and the limited number of cases for each disorder independently. Similarly, dysthymia and depression were also collapsed into a single category of "depressive disorders" to reduce multiple comparisons.

## 2.3 Data Analysis

First, descriptive information of the study was generated and analyzed in SPSS version 26. Chi-square tests were used to examine gender differences in demographic characteristics and study variables. Next, logistic regression analyses were conducted using PROC

SURVEYLOGISTIC in SAS, version 9.4 (Cary, NC). This procedure allowed us to incorporate the stratification, clustering (i.e., primary sampling unit [PSU]), and unequal weighting of the sampling design. Non-stratified logistic regression analyses were conducted to examine correlates of co-occurring sedative use disorder in both men and women. Additionally, a series of gender-stratified logistic regression analyses were conducted to examine whether each form of psychopathology was associated with meeting co-occurring sedative use disorder (Clayton & Tannenbaum, 2016). Each condition was entered with demographic characteristics (race, age, income) to adjust for potential confounding effects. Power analyses suggested that we were able to detect a small effect at 80% for the non-stratified analyses, and a small to medium effect at 80% power for the gender stratified analyses.

## 3. Results

#### 3.1 Participant characteristics

Across both genders, 16.4% (N= 54) of those with OUD met criteria for co-occurring sedative use disorder. Gender differences in participant characteristics are presented in Table 1. In line with analyses using the full NESARC sample from waves 1 and 2, depressive disorders, anxiety disorders, bipolar disorder, and PTSD were more common in women; antisocial personality disorder was more common in men; and there were no differences in schizotypal personality disorder (Armstrong, Ronzitti, Hoff, & Potenza, 2018; Kachadourian, Pilver, & Potenza, 2014). In a divergence from the full NESARC sample from wave 2 (Hoertel, Peyre, Wall, Limosin, & Blanco, 2014), women with OUD were not more likely to meet criteria for borderline personality disorder than were men with OUD. Men and women did not differ significantly on age at first opioid use, painkiller use frequency during the past year, painkiller use. Among men and women who had ever used sedatives, there were no gender differences for age at first sedative use, or the duration of their heaviest use, or the duration of their heaviest use.

A total of 55.6% of the full sample (i.e., those with OUD, with and without co-occurring sedative use disorder) attained opioids through their own prescription. Approximately half (47.2%) of the participants with sedative use disorder attained sedatives through their own prescription. Participants with OUD only were more likely to be using opioids with a prescription than participants with co-occurring OUD and sedative use disorder, participants who attained sedatives through their own prescription were significantly more likely to have also attained opioids through their own prescription, relative to participants who did not attain sedatives through their own prescription,  $\chi^2(1, N=53) = 25.81$ , p < .001. A total of 37.7% of those with co-occurring OUD and sedative use disorder had been prescribed both substances.

Demographic characteristics and opioid use patterns among individuals with and without cooccurring sedative use disorder are shown in Table 2. Unequal variance t-tests suggested that individuals with co-occurring sedative use disorder were more likely to begin using

prescription opioids at a younger age. Individuals with co-occurring sedative use disorder were more likely to meet criteria for most other substance use disorders, with the exception of alcohol use disorder. However, the two groups did not differ on opioid use frequency during the past year or during the period of their heaviest use, nor did they differ on the duration (in weeks) of their heaviest opioid use. Additionally, race, age, and income were not significantly related to meeting criteria for co-occurring sedative use disorder.

#### 3.2 Correlates of sedative use disorder

Logistic regression analyses examining psychiatric conditions associated with meeting criteria for sedative use disorder in combination with OUD are presented in Table 3. Across all participants, PTSD, schizotypal personality disorder, and antisocial personality disorder were associated with a greater likelihood of meeting criteria for a co-occurring sedative use disorder, whereas borderline personality disorder, depressive disorders, anxiety disorders, and bipolar disorder were unrelated. In the gender-stratified analysis, PTSD and antisocial personality disorder were associated with a greater likelihood of meeting criteria for a co-occurring sedative use disorder among both men and women. However, schizotypal personality disorder and depressive disorders were associated with a greater likelihood of meeting criteria for a co-occurring sedative use disorder, and bipolar disorder were unrelated. Borderline personality disorder among both men and women. However, schizotypal personality disorder among both men and women, but not among men. Borderline personality disorder, anxiety disorders, and bipolar disorder were unrelated to meeting criteria for a co-occurring sedative use disorder in the gender stratified analysis among both men and women.

## 4. Discussion

Understanding gender differences in psychiatric conditions associated with co-occurring OUD and sedative use disorder is a critical step in preventing overdose and providing appropriate treatment. Use of sedatives is common among individuals with OUD, with some work suggesting that nearly half of those with OUD have engaged in nonmedical sedative/ tranquilizer use in the past year (Votaw et al., 2019); however, individuals who meet full diagnostic criteria for both disorders represent a particularly high risk group with specific treatment needs. Although prevalence rates of co-occurring OUD and sedative use disorder were not different among men and women in the current study, results indicated that pathways to co-use of opioids and sedatives may vary by gender. Specifically, results from the current study indicated that schizotypal personality disorder and depressive disorders increased risk of co-occurring sedative use disorder were associated with co-occurring sedative use disorder were associated with co-occurring sedative use disorder were associated with co-occurring sedative use disorder among women, but not men, with OUD.

The findings from the current study suggest that PTSD may represent a risk factor for cooccurring OUD and sedative use disorder. This finding is consistent with other work (Gressler et al., 2018; Yarborough et al., 2019) and is not entirely surprising, as sedative medications are often prescribed to treat symptoms of PTSD. However, this finding highlights the need for prescribers to assess co-occurring OUD when prescribing sedative medications for treatment of PTSD, as PTSD is a known risk factor for developing OUD (Hassan, Le Foll, Imtiaz, & Rehm, 2017), and both substances have addictive potential.

In contrast to the findings regarding PTSD and antisocial personality disorder, depressive disorders and schizotypal personality disorder may represent gender-specific risk factors for co-occurring opioid and sedative use disorders. Results could be reflective of gender differences in expressions and functioning of depressive disorders and schizotypal personality disorder. For example, women with major depressive disorder report more intense and frequent depressed mood and sleep disturbance, whereas men with depression are more likely than women to report impulse control problems (Cavanagh, Wilson, Kavanagh, & Caputi, 2017). Similarly, women with schizotypal personality disorder are more likely to report social anxiety and odd beliefs than men (Bora & Arabaci, 2009), whereas men with schizotypal personality disorder are more likely to show negative or disorganized symptoms (Bora & Arabaci, 2009; Fonseca-Pedro, Paino, Lemos-Giráldez, Sierra-Baigrie, Muñiz, 2011). Additionally, research has shown that childhood physical abuse is predictive of schizotypal personality disorder development in women, but not men (Toutountzidis, Gale, Irvine, Sharma, & Laws, 2018) and the association between childhood physical and sexual abuse with depression is stronger in women than in men (Gallo, Munhoz, de Mola, & Murray, 2018). Given that women are more likely to present with affective symptoms, it is possible that women with schizotypal personality disorder and depressive disorders are more likely than men to co-use opioids and sedatives for selfmedication of aversive emotional states and as a result of trauma.

Treatments that address both substance use and co-occurring psychopathology may be particularly important when treating women with co-occurring opioid use and sedative use disorders. However, while research has focused on treatment of co-occurring depression and substance use disorders (Hides, Samet, & Lubman, 2010; Pedrelli et al., 2011; Riper et al., 2014), less is known about the treatment of schizotypal personality disorder and co-occurring substance use. Thus, the latter remains an important area for future study, particularly given the relatively high prevalence rate of schizotypal personality disorder observed in the current study, and the association between schizotypal personality disorder and co-occurring OUD and sedative use disorder in women. Additionally, given that gender-specific pathways to substance use emerged in this study, future interventions should explore the moderating effects of gender on intervention effectiveness, and develop and evaluate treatments informed by gender.

Notably, a significant proportion of participants who were prescribed sedatives were also prescribed opioids in our sample. Given the rates of co-use in the current sample, physicians should consider the risk for dependence when prescribing opioids and/or sedatives. Additionally, physicians should consider that patients may be getting medications from multiple providers. Fortunately, as of September 2019, all but two U.S. states have implemented some form of a prescription drug monitoring program (PDMP) that can be used to check a patient's prescriptions from other providers (CDC, 2019). While some physicians may be prescribing sedatives and opioids concomitantly (Hwang et al., 2016), PDMPs may be a helpful resource for those who would be concerned about co-use of sedatives and opioids. Regardless of whether a patient presents with overt symptoms of opioid or sedative use disorder, physicians should provide psychoeducation to patients about the dangers of mixing substances, as patients may not recognize that mixing substances poses risks for overdose.

The results of this study should be interpreted in the context of the high comorbidity rates between substance use disorders (Grant et al., 2015; Saha et al., 2016), as well as among psychiatric disorders (e.g., Kessler, Chiu, Demler, & Walters, 2005; Pulay et al. 2009). Individuals with co-occurring sedative use disorder were much more likely to meet criteria for other substance use disorders, suggesting that individuals with sedative use disorder may have a more severe clinical profile and may be at a higher risk for polysubstance use generally than those with OUD only. More work is needed, however, to understand how to best address the needs of patients with highly complex clinical presentations and needs.

There are a number of additional limitations associated with the current study. First, our sample size was relatively small, and only a small proportion of respondents met criteria for a sedative use disorder. While we were powered to detect small to medium effects in the gender stratified analyses, the results should be considered in the context of possible Type II error. Additionally, this study was cross-sectional. Thus, it was not possible to determine directionality of associations, and further work is need to examine whether co-occurring OUD and sedative use disorder among women with schizotypal personality disorder or depressive symptoms is explained by these women's desire to cope with negative emotion. Additionally, the NESARC-III does not assess daily use patterns of opioids and sedatives; therefore, it is unclear whether participants purposefully used these substances at the same time to achieve a specific effect, or if they used each substance heavily throughout the day, but not concurrently. Assessing patterns of use, as well as motivations for use patterns, may be a relevant area for future study. It is interesting to note that the women with OUD were significantly older than the men with OUD in our sample, despite similar ages of OUD onset. We controlled for age in our analyses; this may represent another limitation of the current study. Finally, while the NESARC-III asks participants whether they used a prescribed medication, fine-grained information about prescribing practices was not available for this study. Further investigation into prescribing practices of sedative medication may be a relevant area for future study.

#### 4.1 Conclusion

Despite these limitations, the current study provides further evidence that PTSD and antisocial personality disorders are risk factors for co-occurring OUD and sedative use disorder among both men and women. Additionally, the current study provides preliminary evidence that schizotypal personality disorder and depressive disorders are risk factors for co-occurring OUD and sedative use disorder in women. Further research into genderspecific pathways to co-occurring opioid and sedative use, and overdose risk broadly, is warranted.

## Acknowledgments:

Funding/support: This work was funded in part by P01AA027473 (SAM), and U54AA027989 (SAM), the State of Connecticut, Department of Mental Health and Addiction Services (DMHAS). The National Epidemiologic Survey on Alcohol and Related Conditions Wave III (NESARC-III) was sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), with supplemental support from NIDA. Support is acknowledged from the intramural program, NIAAA, National Institutes of Health.

Role of the sponsor: Sponsors and funders of the NESARC-III and specific funders of this study had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and the decision to submit the manuscript for publication.

## References

- Armstrong JL, Ronzitti S, Hoff RA, & Potenza MN (2018). Gender moderates the relationship between stressful life events and psychopathology: Findings from a national study. Journal of psychiatric research, 107, 34–41. [PubMed: 30316084]
- Bora E, & Baysan Arabaci L (2009). Effect of age and gender on schizotypal personality traits in the normal population. Psychiatry and Clinical Neurosciences, 63(5), 663–669. [PubMed: 19674380]
- Bouvier BA, Waye KM, Elston B, Hadland SE, Green TC, & Marshall BD (2018). Prevalence and correlates of benzodiazepine use and misuse among young adults who use prescription opioids nonmedically. Drug and Alcohol Dependence, 183, 73–77. [PubMed: 29241103]
- Cavanagh A, Wilson CJ, Kavanagh DJ, & Caputi P (2017). Differences in the expression of symptoms in men versus women with depression: a systematic review and meta-analysis. Harvard Review of Psychiatry, 25(1), 29–38. [PubMed: 28059934]
- Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. (9, 2019). Opioid Overdose: State information. Retrieved from https://www.cdc.gov/drugoverdose/ states/index.html
- Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, ... & Gilson AM (2009). Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. The Journal of Pain, 10(2), 113–130.Clayton & Tannenbaum, 2016 [PubMed: 19187889]
- Fonseca-Pedrero E, Paino M, Lemos-Giráldez S, Sierra-Baigrie S, & Muñiz J (2011). Measurement invariance of the Schizotypal Personality Questionnaire-Brief across gender and age. Psychiatry Research, 190(2–3), 309–315. [PubMed: 21663975]
- Gallo EAG, Munhoz TN, de Mola CL, & Murray J (2018). Gender differences in the effects of childhood maltreatment on adult depression and anxiety: a systematic review and meta-analysis. Child Abuse & Neglect, 79, 107–114. [PubMed: 29428878]
- Grant B, Amsbary M, Chu A, Sigman R, Kali J, Sugawana Y, Jiao R, Goldstein R, Jung J, Zhang H (2014) Source and Accuracy Statement: National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARCIII). National Institute on Alcohol Abuse and Alcoholism, Rockville, MD.
- Grant BF, Goldstein RB, Smith SM, Jung J, Zhang H, Chou SP, ... & Aivadyan C (2015). The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5): reliability of substance use and psychiatric disorder modules in a general population sample. Drug and Alcohol Dependence, 148, 27–33. [PubMed: 25595052]
- Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, ... & Hasin DS (2015). Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry, 72(8), 757–766. [PubMed: 26039070]
- Gressler LE, Martin BC, Hudson TJ, & Painter JT (2018). Relationship between concomitant benzodiazepine-opioid use and adverse outcomes among US veterans. Pain, 159(3), 451–459. [PubMed: 29189516]
- Hasin DS, Greenstein E, Aivadyan C, Stohl M, Aharonovich E, Saha T, ... & Grant BF (2015). The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5): procedural validity of substance use disorders modules through clinical re-appraisal in a general population sample. Drug and Alcohol Dependence, 148, 40–46. [PubMed: 25604321]
- Hassan AN, Le Foll B, Imtiaz S, & Rehm J (2017). The effect of post-traumatic stress disorder on the risk of developing prescription opioid use disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions III. Drug and Alcohol Dependence, 179, 260–266. [PubMed: 28818717]
- Hearon BA, Calkins AW, Halperin DM, Kathryn McHugh R, Murray HW, & Otto MW (2011). Anxiety sensitivity and illicit sedative use among opiate-dependent women and men. The American Journal of Drug and Alcohol Abuse, 37(1), 43–47. [PubMed: 21090958]

- Hides L, Samet S, & Lubman DI (2010). Cognitive behaviour therapy (CBT) for the treatment of cooccurring depression and substance use: Current evidence and directions for future research. Drug and Alcohol Review, 29(5), 508–517. [PubMed: 20887574]
- Hoertel N, Peyre H, Wall MM, Limosin F, & Blanco C (2014). Examining sex differences in DSM-IV borderline personality disorder symptom expression using Item Response Theory (IRT). Journal of Psychiatric Research, 59, 213–219. [PubMed: 25258339]
- Hwang CS, Kang EM, Kornegay CJ, Staffa JA, Jones CM, & McAninch JK (2016). Trends in the concomitant prescribing of opioids and benzodiazepines, 2002–2014. American Journal of Preventive Medicine, 51(2), 151–160. [PubMed: 27079639]
- Kachadourian LK, Pilver CE, & Potenza MN (2014). Trauma, PTSD, and binge and hazardous drinking among women and men: findings from a national study. Journal of Psychiatric Research, 55, 35–43. [PubMed: 24838049]
- Kessler RC, Chiu WT, Demler O, & Walters EE (2005). Prevalence, severity, and comorbidity of 12month DSM-IV disorders in the National Comorbidity Survey Replication. Archives of general psychiatry, 62(6), 617–627. [PubMed: 15939839]
- McHugh RK, Votaw VR, Bogunovic O, Karakula SL, Griffin ML, & Weiss RD (2017). Anxiety sensitivity and nonmedical benzodiazepine use among adults with opioid use disorder. Addictive Behaviors, 65, 283–288. [PubMed: 27575980]
- NIH Office of Research on Women's Health. https://orwh.od.nih.gov/sex-gender. Accessed January 31, 2020.
- Pedrelli P, Iovieno N, Vitali M, Tedeschini E, Bentley KH, & Papakostas GI (2011). Treatment of major depressive disorder and dysthymic disorder with antidepressants in patients with comorbid opiate use disorders enrolled in methadone maintenance therapy: a meta-analysis. Journal of Clinical Psychopharmacology, 31(5), 582–586. [PubMed: 21869696]
- Pulay AJ, Stinson FS, Dawson DA, Goldstein RB, Chou SP, Huang B, ... & Hasin DS (2009). Prevalence, correlates, disability, and comorbidity of DSM-IV schizotypal personality disorder: results from the wave 2 national epidemiologic survey on alcohol and related conditions. Primary care companion to the Journal of clinical psychiatry, 11(2), 53–67.
- Riper H, Andersson G, Hunter SB, de Wit J, Berking M, & Cuijpers P (2014). Treatment of comorbid alcohol use disorders and depression with cognitive-behavioural therapy and motivational interviewing: A meta-analysis. Addiction, 109(3), 394–406. [PubMed: 24304463]
- Rudd RA, Aleshire N, Zibbell JE, & Matthew Gladden R (2016). Increases in drug and opioid overdose deaths—United States, 2000–2014. American Journal of Transplantation, 16(4), 1323– 1327.
- SAS Institute. (2015). Base SAS 9.4 procedures guide. SAS Institute.
- Saha TD, Kerridge BT, Goldstein RB, Chou SP, Zhang H, Jung J, ... & Hasin DS (2016). Nonmedical prescription opioid use and DSM-5 nonmedical prescription opioid use disorder in the United States. The Journal of Clinical Psychiatry, 77(6), 772–780. [PubMed: 27337416]
- Saunders KW, Von Korff M, Campbell CI, Banta-Green CJ, Sullivan MD, Merrill JO, & Weisner C (2012). Concurrent use of alcohol and sedatives among persons prescribed chronic opioid therapy: prevalence and risk factors. The Journal of Pain, 13(3), 266–275. [PubMed: 22285611]
- Stein BD, Mendelsohn J, Gordon AJ, et al. (2017). Opioid analgesic and benzodiazepine prescribing among Medicaid-enrollees with opioid use disorders: The influence of provider communities. Journal of Addictive Diseases, 36(1), 14–22. [PubMed: 27449904]
- Sun EC, Dixit A, Humphreys K, Darnall BD, Baker LC, Mackey S. (2017). Association between concurrent use of prescription opioids and benzodiazepines and overdose: Retrospective analysis. BMJ Open, 356, 760–767.
- Toutountzidis D, Gale TM, Irvine K, Sharma S, & Laws KR (2018). Sex differences in the association between childhood adversities and schizotypal personality traits. Psychiatry Research, 269, 31–37. [PubMed: 30145298]
- Votaw VR, Witkiewitz K, Valeri L, Bogunovic O, & McHugh RK (2019). Nonmedical prescription sedative/tranquilizer use in alcohol and opioid use disorders. Addictive Behaviors, 88, 48–55. [PubMed: 30142484]

Yarborough BJH, Stumbo SP, Stoneburner A, Smith N, Dobscha SK, Deyo RA, & Morasco BJ (2019). Correlates of benzodiazepine use and adverse outcomes among patients with chronic pain prescribed long-term opioid therapy. Pain Medicine, 20(6), 1148–1155. [PubMed: 30204893]

## Highlights:

- 16.4% of those with an opioid use disorder (OUD) met criteria for sedative use disorder (SUD)
- Antisocial PD and PTSD were associated with co-occurring SUD in both men and women
- Depressive symptoms and schizotypal PD were associated with co-occurring SUD in women
- 37.7% of those with both OUD and SUD had been prescribed both substances.

#### Table 1.

Demographic characteristics, opioid and sedative use patterns, and psychiatric diagnosis of participants with past 12-month OUD by gender.

	Men (N = 154) % or M (SD)	Women (N = 176) % or M (SD)	<i>X</i> <sup>2</sup>	t	p-value
Race			0.19	-	.910
Caucasian	59.7%	57.4%			
African American	22.1%	22.3%			
Other	18.2%	19.3%			
Age	40.5 (14.3)	44.5 (16.3)	-	-2.34	.020*
Family Income <sup>1</sup>	7.9 (4.5)	7.8 (4.4)	-	0.31	.757
Age of first opioid use	26.4 (13.1)	28.8 (14.9)	-	-1.54	.126
Age of first sedative use <sup><math>2</math></sup>	24.0 (12.1)	23.9 (10.1)	-	0.04	.966
Duration (weeks) of heaviest opioid use	261.7 (433.8)	235.3 (385.9)	-	0.58	.559
Duration (weeks) of heaviest sedative use $^2$	40.1 (81.3)	47.7 (95.4)	-	-0.77	.442
Frequency of opioid use at heaviest use $^{3}$	2.2 (1.9)	2.3 (1.9)	-	-0.19	.849
Frequency of sedative use at heaviest use $^{2,3}$	4.0 (3.0)	3.5 (3.0)	-	1.12	.266
Frequency of opioid use in past 12 months $^{\mathcal{3}}$	3.4 (2.7)	3.3 (2.5)	-	0.29	.770
Frequency of sedative use in past 12 months <sup><math>2,3</math></sup>	4.2 (2.7)	3.8 (2.9)	-	0.88	.382
Substance use			0.43	-	.512
Opioid use disorder only	85.1%	82.4%			
Opioid use disorder with co-occurring sedative use disorder	14.9%	17.6%			
Mode of sedative use among those with sedative use disorder $4$			2.50	-	.114
Using with a prescription	34.8%	56.7%			
Using without a prescription	65.2%	43.3%			
Mode of opioid use			1.58	-	.208
Using with a prescription	51.9%	58.9%			
Using without a prescription	48.1%	41.1%			
Borderline personality disorder	44.8%	50.6%	1.09	-	.296
Antisocial personality disorder	32.5%	15.9%	12.48	-	<.001
Schizotypal personality disorder	29.9%	30.7%	0.03	-	.873
Posttraumatic stress disorder	14.9%	29.0%	9.31	-	.002*
Depressive disorders	26.6%	38.6%	5.36	-	.021 *
Anxiety disorders	22.1%	38.6%	10.55	-	.001 *
Bipolar disorder	13.0%	10.2%	0.61	-	.433

\* Denotes a *p*-value less than .05.

I. Income was coded into 21 continuous income range categories by the NESARC-III ranging from (1 = Less than \$5000 to 21 = Over \$200,000).

 $^{\mbox{2.}}$  Includes individuals reporting any sedative use who responded to this question.

<sup>3</sup>. Frequency of use was coded into 10 categories (1=Daily, 2 = Nearly every day, 3 = 3 to 4 times per week, 4 = 1 to 2 times per week, 5 = 2 to 3 times per month, 6 = once per month, 7 = 7 to 11 times in the last year, 8 = 3 to 6 times in the last year, 9 = 2 times in the last year, 10=Once in the last year) by the NESARC-III, and treated continuously in this analysis

 $^{\it 4.}$  Includes individuals with sedative use disorder who responded to this question.

Author Manuscript

#### Table 2.

Demographic characteristics, opioid and sedative use patterns, and psychiatric diagnosis of participants with past 12-month OUD by sedative use disorder.

	Opioid use disorder only (N = 276) % or M (SD)	Co-occurring sedative use disorder $(N = 54)$ % or M (SD)	X <sup>2</sup>	ť	p-value
Race			5.03	-	.081
Caucasian	55.8%	72.2%			
African American	24.3%	14.8%			
Other	19.9%	13.0%			
Age	43.3 (15.5)	39.1 (15.2)	-	1.84	.069
Family Income <sup>2</sup>	8.0 (4.5)	7.3 (4.4)	-	1.10	.275
Age of first opioid use	28.3 (14.5)	24.6 (11.3)	-	2.09	.039*
Duration (weeks) of heaviest opioid use	236.8 (398.4)	302.4 (456.2)	-	-0.98	.328
Frequency of opioid use at heaviest use $^{3}$	2.3 (2.0)	2.0 (1.6)	-	1.33	.186
Frequency of opioid use in past 12 months <sup><math>3</math></sup>	3.4 (2.6)	3.0 (2.2)	-	1.20	.234
Mode of opioid use			3.83	-	.050*
Using with a prescription	58.0%	43.4%			
Using without a prescription	42.0%	56.6%			
Past year tobacco use disorder	56.9%	72.2%	4.41	-	.036*
Past year alcohol use disorder	40.2%	53.7%	3.36	-	.067
Past year cannabis use disorder	18.8%	35.2%	7.15	-	.008*
Past year cocaine use disorder	4.0%	22.2%	23.17	-	<.001*
Past year hallucinogen use disorder	1.1%	9.3%	12.75	-	<.001*
Past year stimulant use disorder	4.0%	25.9%	31.05	-	<.001*
Past year club drug use disorder	1.8%	11.1%	12.12	-	<.001*
Past year inhalant/solvent use disorder	0.4%	3.7%	5.60	-	.018*
Borderline personality disorder	44.2%	66.7%	9.13	-	.003*
Antisocial personality disorder	21.0%	37.0%	6.42	-	.011*
Schizotypal personality disorder	26.8%	48.1%	9.74	-	.002*
Posttraumatic stress disorder	19.2%	38.9%	10.06	-	.002*
Depressive disorders	31.9%	38.9%	1.00	-	.317
Anxiety disorders	28.6%	42.6%	4.13	-	.042*
Bipolar disorder	10.5%	16.7%	1.68	-	.195

\* Denotes a *p*-value less than .05.

1. Due to uneven sample sizes, unequal variance t-tests were used to compare individuals with and without co-occurring sedative use disorder

 $^{2}$ . Income was coded into 21 continuous income range categories by the NESARC-III ranging from (1 = Less than \$5000 to 21 = Over \$200,000).

<sup>3</sup>. Frequency of use was coded into 10 categories (1=Daily, 2 = Nearly every day, 3 = 3 to 4 times per week, 4 = 1 to 2 times per week, 5 = 2 to 3 times per month, 6 = once per month, 7 = 7 to 11 times in the last year, 8 = 3 to 6 times in the last year, 9 = 2 times in the last year, 10=Once in the last year) by the NESARC-III, and treated continuously in this analysis

#### Table 3.

Associations between psychopathology and co-occurring sedative use disorder in women and men with OUD.

Variable	Maximum Likelihood Estimate	SE	t(63)	OR (95%CI)
Overall (N = 303)				
Borderline personality disorder	0.58	0.40	1.47	1.79 (0.81 – 3.96)
Antisocial personality disorder	1.00	0.34	2.90	2.72 (1.37 - 5.41)
Schizotypal personality disorder	1.24	0.40	3.12	3.47 (1.56 – 7.68)
Posttraumatic stress disorder	1.10	0.38	2.87	3.02 (1.40 - 6.51)
Depressive disorders	0.23	0.43	0.53	1.26 (0.53 – 2.98)
Anxiety disorders	0.48	0.44	1.08	1.62 (0.67 – 3.92)
Bipolar disorder	0.05	0.48	0.10	1.05 (0.41 – 2.72)
Women (N = $176$ )				
Borderline personality disorder	0.44	0.46	0.94	1.55 (0.61 – 3.96)
Antisocial personality disorder	1.18	0.58	2.02	3.25 (1.00 - 10.55
Schizotypal personality disorder	1.75	0.42	4.19	5.78 (2.48 - 13.49
Posttraumatic stress disorder	1.15	0.46	2.49	3.17 (1.24 - 8.08)
Depressive disorders	0.75	0.36	2.06	2.12 (1.01 – 4.42
Anxiety disorders	0.36	0.35	1.03	1.44 (0.70 – 2.94
Bipolar disorder	0.47	0.48	0.99	1.60 (0.61 – 4.19)
<i>Men</i> (N = 154)				
Borderline personality disorder	0.88	0.53	1.66	2.42 (0.82 - 7.16
Antisocial personality disorder	1.24	0.44	2.83	3.46 (1.41 - 8.47
Schizotypal personality disorder	0.81	0.50	1.62	2.25 (0.81 - 6.21
Posttraumatic stress disorder	1.82	0.66	2.77	6.23 (1.62 – 23.94
Depressive disorders	-0.35	0.69	-0.51	0.70 (0.17 – 2.87)
Anxiety disorders	0.51	0.66	0.77	1.66 (0.43 - 6.39)
Bipolar disorder	0.08	0.74	0.11	1.08 (0.24 - 4.86

\* Denotes a p-value less than .05. All models were adjusted for age, race, and income.

Author Manuscript