Does misuse lead to a disorder? The misuse of prescription tranquilizer and sedative medications and subsequent substance use disorders in a U.S. longitudinal sample

CJ Boyd[1,2,3], **B West**[4], and **SE McCabe**[1,2]

[1]Center for the Study of Drugs, Alcohol, Smoking and Health, School of Nursing, University of Michigan, Ann Arbor, MI, USA, 48109

[2]Institute for Research on Women and Gender, University of Michigan, Ann Arbor, MI, USA, 48109

[3]Addiction Center, Department of Psychiatry, University of Michigan, Ann Arbor, MI, USA, 48109

[4]Institute for Social Research, Survey Research Center, University of Michigan, Ann Arbor, MI, USA, 48106

Abstract

Objectives—We used two waves of National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) data and examined whether the misuse of prescription tranquilizers or sedatives at Wave 1 was associated with either continued misuse, tranquilizer/sedative use disorder, or other substance use disorder (SUD) at Wave 2.

Methods—Prospective data were analyzed from structured diagnostic interviews using the Alcohol Use disorders and Associated Disabilities Interview Schedule: DSM-IV Version (AUDADIS-DSM-IV). A nationally representative sample of 34,653 of U.S. adults, 18 years or older at Wave 1 (2001–2002), were re-interviewed at Wave 2 (2004–2005). After applying the survey weights, the sample represented a population that was 52% female, 71% White, 12% Hispanic, 11% African American, 4% Asian and 2% Native American or other.

Results—An estimated 79% of adults who engaged in tranquilizer or sedative misuse at Wave 1 had stopped using these drugs at Wave 2. Only a small percentage (4.3%) of misusers at Wave 1 had a tranquilizer or sedative use disorder at Wave 2. However, forty-five percent (45.0%) of misusers at Wave 1 had at least one other SUD at Wave 2. Among those in remission from a sedative or tranquilizer use disorder at Wave 1, 4.8% had a tranquilizer or sedative use disorder while 34.7% had at least one other SUD at Wave 2.

Conclusions—Most adults who engaged in the misuse of prescription tranquilizers or sedatives ceased using within 3 years; however, their prior misuse was associated with higher prevalence of having a SUD three years later.

Keywords

Prescription drug misuse; tranquilizer medication misuse; sedative medication misuse; drug use disorders; substance abuse

1. Introduction

There has been an upward trend in the prescribing of tranquilizer and sleep medications in the United States (Comer, Olfson, and Mojtabai, 2010; Fenton, Keyes, Martins, and Hasin, 2010; Fortuna, Robbins, Caiola, Hoynt, and Halterman, 2010; Ford and Lacernza, 2011; Thomas, Conrad, Casler and Goodman, 2006), with a parallel increase in the misuse of these drug classes (Ford and McCutcheon, 2012; Rigg and Ford, 2014; Goodwin and Hasin, 2002). In 2015, the National Survey on Drug Use and Health (NSDUH) estimated that annually 617,000 U.S. adults had used prescribed tranquilizers and 434,000 had used prescribed sedatives; furthermore, 15.4% had misused tranquilizers and 8.1% misused sedatives (Hughes, Williams, Lipari, Bose, Copello and Kroutil, 2016). There were some variations among past-year users (Hughes et al., 2016), with women more likely to use tranquilizers (19.2%) and sedatives (8.8%) when compared to men (12.1% and 5.9%, respectively). Women were also more likely to be dependent on these two drug classes, particularly tranquilizers (Goodwin and Hasin, 2002; Cotto, Davis, Dowling, Elcano, Staton, and Weiss, 2010). While a higher percentage of women over the age of 25 years used tranquilizers compared to younger women (20.1% vs 13.4%), younger women had a higher prevalence of tranquilizer *misuse* [> 25 years = 1.7% misused; 18 to 25 years = 4.9% (Hughes et al., 2016)].

The term 'misuse' as used in the NSDUH is defined somewhat differently than in other studies, including the first two waves of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-I and NESARC-II). Throughout this paper, we use the term *misuse* to describe two different behaviors that are often reported in the literature. These behaviors are independent but may co-occur, and include 1) the use of prescription medications that are not prescribed to the user, and 2) the use of prescription medication in a manner not intended by the prescriber (e.g., using too much, using to get high).

Grant and colleagues (2016) used NESARC data to note the importance of examining specific drug use disorders, because *specific* drugs are often associated with *different* co-morbid factors. Blanco and colleagues (2013) examined the predictors of remission from specific prescription drug use disorders using a cross-section of the NESARC Wave 1 data. They found a significant proportion of respondents with a past prescription drug use disorder, yet about half had remitted approximately five years after the onset of their disorders. Most respondents who remitted from prescription drug use disorders did not develop another substance use disorder (SUD), although approximately 19.8% of sedative misusers and 17.4% of tranquilizer misusers developed a new SUD. One limitation of this

study is that cross-sectional data were used, thereby limiting our understanding of how prescription drug misuse changes over time.

To address the dearth of longtitudinal findings on prescription tranquilizer and sedative misuse, we analyzed data from the NESARC-I and II to answer the following:

1.   Does the misuse of prescription tranquilizers and sedatives at Wave 1 predict continued tranquilizer or sedative misuse at Wave 2?

2.   Does the misuse of prescription tranquilizers and sedatives at Wave 1 predict a tranquilizer or sedative use disorder or other SUD at Wave 2?

3.   What is the prevalence of drug misuse and SUD recurrence at Wave 2 among respondents in remission from a lifetime diagnosis of tranquilizer or sedative use disorder at Wave 1?

2. Materials and Methods

2.1. Study design

We extracted data for this secondary analysis from the first two waves of the NESARC survey (2001–2002 and 2004–2005). The NESARC used a prospective design with a nationally representative sample. The target population was the non-institutionalized U.S. adult civilian population, and data came from in-person household interviews. The University of Michigan Institutional Review Board exempted this study because it involved secondary analysis of publicly available data.

2.2. Sample

Stratification of the target population and cluster sampling within strata was conducted (Grant, Kaplan, Shepard, and Moore, 2003; Grant and Kaplan, 2005). Survey weights were computed for Wave 2 respondents to account for unequal probabilities of selection, differential non-response rates across subgroups, and post-stratification adjustments. This study involved 34,653 respondents; the Wave 1 response rate was 81%, and the Wave 2 response rate was 86.7%. After applying the survey weights, this sample represented a population that was 52% female, 71% White, 12% Hispanic, 11% African American, 4% Asian and 2% Native American or other. An estimated 15% of the population was 18–25 years of age, 38% was 26–44 years of age, and 47% was 45 years of age or older.

2.3. Measures

Misuse of Tranquilizer and Sedative Medication—Respondents were asked about their lifetime and current (past-year) use of prescription tranquilizer and sedative medications that were *not* prescribed to them by a doctor or used in a manner unintended by the prescriber (e.g., more often than prescribed, longer than prescribed, or for a reason other than prescribed). The stem question for tranquilizer and sedative medications misuse was, "Now I'd like to ask you about your experiences with medicines and other kinds of drugs that you may have used ON YOUR OWN - that is, either WITHOUT a doctor's prescription; in GREATER amounts, MORE OFTEN, or LONGER than prescribed; or for a reason other than a doctor said you should use them. Have you EVER used any of these

medicines or drugs? [For tranquilizers] "Tranquilizer or anti-anxiety drugs, for example Valium, Librium, muscle relaxants, or Xanax" or [For sedatives] "Sedatives, for example, sleeping pills, barbiturates, Seconal, Qualudes or Chloral Hydrate." (A list was read to the respondent, while showing a picture of the medications.)

Drug-Specific Use Disorders (Tranquilizer and Sedative)—The NESARC included the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV), a fully structured diagnostic interview. DSM-IV criteria (American Psychiatric Association, 2000) were operationalized from the AUDADIS-IV because it contained relevant symptoms, including diagnoses for alcohol and 10 specific drug use disorders. An AUDADIS-IV diagnosis of prescription tranquilizer or sedative use disorder required: 1) the presence of an AUDADIS-IV diagnosis of prescription tranquilizer or sedative *dependence* and 2) at least one positive response to four abuse criteria. The test-retest reliability coefficients (kappas) associated with AUDADIS-IV diagnoses of SUDs involving prescription medications have ranged from $\kappa = 0.69$ to 0.96, and the validity of the AUDADIS-IV has been established (Canino et al., 1999; Cottler et al., 1997; Grant, Harford, Dawson, Chou and Pickering, 1995; Grant, et al., 2003; Grant, 1996; Nelson, Rehm, Usen, Grant and Chatterji, 1999; Pull, Saunders, Avreas, Cottler, Grant, and Hasin, et al., 1997).

Other Substance Use Disorder (SUD)—This was determined for any one (or more) of the following disorders using criteria similar to those used to diagnose tranquilizer or sedative disorder (mentioned above): alcohol, amphetamines, cocaine, inhalants, hallucinogen, heroin, opioid, stimulant, and marijuana. Individual drug disorders were aggregated to yield a past-year other SUD variable. Binary outcome variables using Wave 2 data were created for tranquilizer and sedative use disorders, as well as for any other SUD not involving these medications.

Drug Remission—Remission from tranquilizer and sedative disorder at Wave 1 was determined by reported lifetime tranquilizer or sedative use disorder, but *no* past-year tranquilizer or sedative use disorder at Wave 1.

Drug Use Recurrence—Recurrence was determined with data from Waves 1 and 2. Recurrence was defined as drug remission at Wave 1, but either 1) misuse of sedatives or tranquilizers or 2) a sedative or tranquilizer use disorder at Wave 2.

Drug Use Status Groups—This status was based on self-reported prescription tranquilizer and sedative medication misuse at Wave

1. Three mutually exclusive groups were created: 1) No lifetime misuse: Never engaged in misuse of prescription tranquilizer and/or sedative medications.

2. Lifetime misuse only (misuse that was prior-to-past-year): Engaged in lifetime misuse of prescription tranquilizer and/or sedative medications, but reported no misuse in the past 12 months.

3. Current/past-year misuse: Engaged in misuse of prescription tranquilizer and/or sedative medications in the past 12 months.

Lifetime mood and anxiety disorders—These disorders were determined with the AUDADIS-IV and excluded psychiatric disorders that were due to medical conditions or drug or alcohol induced. Lifetime mood disorder refers to any primary major depressive, bipolar or dysthymic disorder. Lifetime anxiety disorder refers to primary panic, social anxiety, specific phobias and generalized anxiety disorders. Test-retest reliabilities for the AUDADIS-IV mood, anxiety and personality disorders were reported between k=0.40–0.77 (Blanco, et al., 2013; Grant, et al., 2003; Hasin, Carpenter, McCloud, Smith, Grant, 1997; Ruan, Goldstein, Cho, Smith, Saha, Pickering, et al. 2008).

Lifetime prescribed tranquilizer medications—The legally prescribed use of tranquilizers was determined from respondents who screened positive for the following disorders at Wave 1: general anxiety, specific phobia, social phobia, and panic disorders. Respondents first were asked "Did a doctor EVER prescribe any medicines or drugs" for symptoms associated with mood and anxiety disorders. If a respondent responded "yes" they were asked about receiving prescriptions for specific symptoms associated with the anxiety disorders (e.g., quiet nerves or calm down, fear of situations, etc.).

2.4. Statistical analyses

All analytic techniques in the current study were design-based, using the NESARC survey weights to calculate estimates of population parameters and specialized variance estimation techniques to accommodate the complex design features of the sample when estimating standard errors. Details of how the survey weights were calculated to account for unequal probabilities of selection into the Wave 1 sample, differential nonresponse across subgroups at Wave 1, and attrition from Wave 1 to Wave 2 have been reported elsewhere (Grant et al., 2003; Grant and Kaplan, 2005). We computed separate prevalence estimates of our key outcomes for men and women, and performed design-adjusted Rao-Scott tests of the bivariate associations between respondents' misuse status at Wave 1 and reported SUDs at Wave 2. Prevalence estimates for Wave 2 prescription sedative and/or tranquilizer misuse, DSM-IV sedative and/or tranquilizer use disorders, and other SUDs *since the Wave 1 interview* were computed for each of the seven distinct subclasses of respondents defined by Wave 1 prescription sedative and tranquilizer misuse status. Finally, multivariable logistic regression models were fitted to binary Wave 2 outcomes indicating 1) a prescription sedative or tranquilizer use disorder since the last interview, and 2) any other SUD since the last interview. Wave 1 predictors included in each model were age, sex, race, lifetime alcohol use disorder, lifetime mood disorder, lifetime anxiety disorder, and lifetime prescription of medication to treat anxiety symptoms. We used Stata (Version 15.0) to estimate the models outlined above (StataCorp LP, College Station, Texas), and all Stata code used for the analyses is available upon request.

3. Results

We examined whether current (past-year) misuse of prescription tranquilizers or sedatives at Wave 1 predicted misuse at Wave 2, and found that no lifetime misuse at Wave 1 was associated with low probabilities of developing a sedative or tranquilizer use disorder or other SUD by Wave 2 (see Table 1). Based on the Wave 1 NESARC data, an estimated 5.5%

of adults were lifetime misusers of prescription tranquilizer or sedative medications with an estimated mean age at onset of approximately 24.2 years. Most respondents who misused tranquilizer or sedative medications at Wave 1 had stopped misusing by Wave 2; an estimated 79% of adults engaged in misuse of tranquilizers or sedatives at Wave 1 had stopped misusing at Wave 2.

In order to address the question of reccurence of SUDs over time, we examined the percentage of respondents in remission from tranquilizer or sedative use disorder at Wave 1 who reported SUDs at Wave 2. As shown in Table 1, approximately thirty-four percent (34.7%) of respondents who were in remission from a sedative or tranquilizer use disorder at Wave 1 had developed an other SUD at Wave 2. A much smaller percentage of those in remission at Wave 1 had developed a tranquilizer or sedative use disorder at Wave 2 (4.8%). Finally, we found that seeking drug treatment between Waves 1 and 2 was not significantly associated with ceasing misuse of tranquilizers or sedatives (results not shown).

For men at Wave 1, approximately 16.6% of current tranquilizer misusers and 15.4% of current prescription sedative misusers were doing the same at Wave 2. For women at Wave 1, approximately 14.1% of current tranquilizer misusers and 10.8% of current sedative misusers were doing the same at Wave 2.

We found a few sex and age differences in our analyses. Compared to women, men who reported current prescription tranquilizer or sedative misuse at Wave 1 did not differ from women in terms of developing a tranquilizer or sedative use disorder at Wave 2, but had a higher prevalence of developing an other SUD at Wave 2 (men = 53.3% vs. women = 34.4%, $p < 0.01$). Younger men had a higher prevalence of developing an other SUD (i.e., 18–25 years = 67.2%; 26–44 years = 56.3%; > 45 years = 23.6%). Any sex differences were not supported in the multivariable logistic regression analyses, and thus should be considered cautiously.

When compared to respondents without a major depressive disorder at Wave 1, respondents with a lifetime major depressive disorder at Wave 1 had a higher prevalence of tranquilizer or sedative misuse (2.5% vs. 1.1%, $p < 0.0001$) and of sedative or tranquilizer use disorder (0.7% vs. 0.1%, $p < 0.0001$) at Wave 2. Significant associations were also found for those with other specific mood and anxiety disorders versus those without these disorders at Wave 1: bipolar (misuse at Wave 2: 3% vs. 1.2%, $p < 0.0001$; use disorder at Wave 2: 1.4% vs. .01%, $p < 0.0001$); dysthyimia (misuse at Wave 2: 3.1% vs. 1.2%, $p < 0.0001$; use disorder at Wave 2: 1.4% vs. 0.2%, $p < 0.0001$); panic (misuse at Wave 2: 2.6% vs. 1.3%, $p < 0.0001$; use disorder at Wave 2: 0.8% vs. 0.2%, $p < 0.0001$); social anxiety (misuse at Wave 2: 2.5% vs. 1.3%, $p < 0.001$, use disorder at Wave 2: 0.9% vs. 0.2%, $p < 0.0001$); and generalized anxiety disorder (misuse at Wave 2: 2.5% vs. 1.3%, $p < 0.001$, use disorder at Wave 2: 1.5% vs. 0.1%, $p < 0.0001$). Among those with a prescription tranquilizer or sedative use disorder at Wave 1, only an estimated 14.1% still had the disorder at Wave 2.

As can be seen in Table 4, among those who reported any current misuse of prescription tranquilizers or sedatives at Wave 1, there were no age-related differences in the odds of developing a tranquilizer or sedative use disorder at Wave 2 (e.g., older respondents were no

more likely to have a tranquilizer or sedative use disorder than younger respondents). However, the odds of developing an other SUD decreased as a function of age. We conducted multivariable logistic regression analyses to determine if there were significant predictors of the development of SUDs at Wave 2, including age, sex, race, lifetime alcohol use disorder, lifetime mood disorder, lifetime anxiety disorder, and lifetime prescribed medication to treat anxiety symptoms. While we did not identify any significant predictors of having a tranquilizer or sedative use disorder at Wave 2, age was a significant predictor for having an other SUD at Wave 2. Emerging adults (ages 18 to 25 years) had nine-fold higher odds (AOR = 9.43, 95% CI = 4.8 – 18.33) of having an other SUD compared to older adults, and middle-age adults (ages 26 to 44) had a four-fold higher odds of having an other SUD at Wave 2 when compared to older adults (AOR = 4.55, 95% CI = 2.6 – 7.7). Further, individuals with a lifetime history of an alcohol use disorder had over five times greater odds of having an other SUD at Wave 2 (AOR = 5.6, 95% CI = 3.4 – 9.5). Several factors did not significantly predict a tranquilizer or sedative use disorder or other SUD at Wave 2, including sex, race, lifetime mood or anxiety disorders and being prescribed medication for anxiety symptoms.

4. Discussion

There is widespread consensus that misuse of scheduled medications is a significant public health problem in the U.S.; however, the extent to which the misuse of tranquilizer and sedative medication leads to tranquilizer and sedative use disorders has not been well established. The purpose of this secondary analysis of NESARC data was to examine the relationship between the misuse of prescription tranquilizers and sedatives at Wave 1 (2001–2002) and the development of tranquilizers or sedatives use disorders or an other SUD three years later, at Wave 2 (2004–2005).

We were also interested in remission and relapse, and determined that about one-fourth of misusers continued their misuse at Wave 2. Indeed, 23.7% of sedative or tranquilizer misusers at Wave 1 were still engaged in misuse at Wave 2; however, _most_ misusers had ceased to misuse these drug classes three years later. These findings are consistent with the study by Blanco and colleagues[12] that used one wave of NESARC data to examine the correlates of remission from prescription drug use disorders.

Most sedative and tranquilizer misusers at Wave 1 _did not_ engage in misuse at Wave 2. And while it is worth noting the significance of these "quit rates," our findings revealed a worrisome trend: Thirty-four percent (34.4%) of women who misused tranquilizers or sedatives at Wave 1 had an other SUD by Wave 2. The same pattern was true and even stronger for men. Among male misusers at Wave 1, 53.0% had developed an other SUD by Wave 2. In our study, almost two-thirds (58.4%) of those with a tranquilizer or sedative use disorder at Wave 1 had developed an other SUD at Wave 2, an indication that alcohol and drugs other than tranquilizers and sedatives led to the SUD. Moreover, we found that individuals with a lifetime history of an alcohol use disorder had over five times greater odds of having an other SUD, and our findings serve as a reminder for clinicians and researchers to screen for a history of a wide range of substances when working with clients with the risk factors for drug abuse.

Like Blanco et al., (2013), we found age differences for tranquilizer and sedative misusers. Emerging adults had the highest prevalence of SUDs at Wave 2, including those 18 to 25 year olds who <u>did not</u> misuse tranquilizers or sedatives at Wave 1. It is these findings that are consistent with Boyd and colleagues' (Boyd, Teter, West, Morales and McCabe, 2009) earlier prescription opioid work and McCabe et al.'s (McCabe, Veliz, Boyd, and Schulenberg, 2017) more recent study using Monitoring the Future (MTF) data. McCabe et al. showed an association between nonmedical use of prescription sedatives and tranquilizers at age 18 and SUD symptoms at age 35. However, the MTF study did not include all of the DSM-IV SUD symptoms, a strength of this current study. Taken together, these age-related findings add support to the findings from researchers who focus on emerging adults and their higher risk for developing SUDs.

We found that sex, race, and a history of mood or anxiety disorders did not significantly predict the onset of a specific drug or substance use disorder at Wave 2. Although we discovered no race differences, we found that a higher percentage of men reported a SUD at Wave 2, compared to women. Of note, more rigorous, multivariable statistical analyses failed to reveal sex differences and limit our conclusions. There may be different longitudinal patterns for sub-populations of users and individual drug-specific disorders that differ from an aggregate of all substance use disorders.

4.1. Strengths and limitations

This investigation is one of the few national and prospective studies to examine lifetime and current tranquilizer and sedative misuse, as well as the prevalence of recurrence from a prior tranquilizer or sedative use disorder. The relatively large NESARC longitudinal sample allowed for the calculation of prevalence estimates and allowed us to examine the role that lifetime and current misuse plays in the development of SUDs. It cannot be overstated that our ability to examine tranquilizer and sedative misuse over time, in a large two-wave national sample, is a strength of this study.

Despite these strengths, there are some limitations. Our results cannot be generalized to populations outside of the United States and risk groups (Compton, Dawson, Duffy and Grant, 2010) such as incarcerated, homeless, or transient individuals. These subgroups were not included in the NESARC target population, and this may lead to underestimates of tranquilizer and sedative misuse. Further, the subpopulation samples were relatively small (producing large standard errors), and this constrains interpretations. This study involved secondary analysis, and not all of the NESARC questions were ideal for our purposes. The NESARC question pertaining to prescription drug misuse is a complex question that includes multiple and very different behaviors in one question (e.g., used without a doctor's knowledge, used to get high, etc.) leading to an overly broad operational definition of misuse. Additionally, the prevalence estimates of misuse were probably underestimated because the NESARC did not list some commonly misused sedatives (e.g., zolpidem) and tranquilizers (e.g., clonazepam) as examples, and it was conducted over a decade ago (Hughes et al., 2016). Finally, the longitudinal NESARC included only DSM-IV criteria for our use, and moreover, detailed data on the medical use of specific tranquilizer and sedative medications was not available.

4.2. Conclusion

It appears that the misuse of prescription tranquilizers and sedatives is a harbinger of other substance use. This conclusion is consistent with those of Blanco et al. (2013) and Stinson et al., (2005) based on their cross-sectional NESARC Wave 1 studies. Our conclusions extend prior findings and reinforce the idea that alcohol and drug treatment services should be well-integrated when treating individuals with tranquilizer or sedative use disorders.

Acknowledgments

References

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4. Arlington, VA: APA Press; 2000.

Blanco C, Secades-Villa R, Garcia-Rodriquez O, Labrador-Mendez M, Wang S, Schwartz RP. Probability and predictors of remission from life-time prescription drug use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Journal of Psychiatric Research. 2013; 47:42–49. [PubMed: 22985744]

Boyd CJ, Teter CJ, West B, Morales M, McCabe SE. Non-medical use of prescription analgesics: A three-year national longitudinal study. Journal of Addictive Diseases. 2009; 28:232–242. [PubMed: 20155592]

Canino GJ, Bravo M, Ramfrez R, Febo V, Fernandez R, Hasin D. The Spanish alcohol use disorder and associated disabilities interview schedule (AUDADIS): Reliability and concordance with clinical diagnoses in a Hispanic population. Journal of Studies on Alcohol. 1999; 60:790–799. [PubMed: 10606491]

Comer JS, Olfson M, Mojtabai R. National trends in child and adolescent psychotropic polypharmacy in office-based practice, 1996–2007. Journal of the American Academy of Child and Adolescent Psychiatry. 2010; 49:1001–1010. [PubMed: 20855045]

Compton WM, Dawson D, Duffy SQ, Grant BF. The effect of inmate populations on estimates of DSM-IV alcohol and drug use disorders in the United States. American Journal of Psychiatry. 2010; 167:473–4.

Cottler LB, Grant BF, Blaine J, Mavreas V, Pull CB, Hasin D, et al. Concordance of DSM-IV alcohol and drug use disorder criteria and diagnoses as measured by AUDADIS-ADR, CIDI, and SCAN. Drug and Alcohol Dependence. 1997; 47:195–205. [PubMed: 9306045]

Cotto JH, Davis E, Dowling GJ, Elcano JC, Staton AB, Weiss SR. Gender effects on drug use, abuse, and dependence: A Special analysis of results from the National Survey on Drug Use and Health. Gender Medicine. 2010; 7:402–413. [PubMed: 21056867]

Fenton MC, Keyes KM, Martins SS, Hasin DS. The role of a prescription in anxiety medication use, abuse, and dependence. American Journal of Psychiatry. 2010; 167:1247–1253. [PubMed: 20595413]

Fortuna RJ, Robbins BW, Caiola E, Joynt M, Halterman JS. Prescribing of controlled medications to adolescents and young adults in the United States. Pediatrics. 2010; 126:1108–1116. [PubMed: 21115581]

Ford JA, Lacerenza C. The relationship between source of diversion and prescription drug misuse, abuse and dependence. Substance Use & Misuse. 2011; 46:819–827. [PubMed: 21174499]

Ford JA, McCutcheon J. The misuse of Ambien among adolescents: Prevalence and correlates in a national sample. Addictive Behaviors. 2012; 37:1389–1394. [PubMed: 22795592]

Goodwin RD, Hasin DS. Sedative use and misuse in the United States. Addiction. 2002; 97:555–562. [PubMed: 12033656]

Grant BF, Saha TD, Ruan WJ, Goldstein RB, Chou R, Jung J, et al. Epidemiology of DSM-5 Drug Use Disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. JAMA Psychiatry. 2016; 73:39–47. [PubMed: 26580136]

Grant BF, Harford TC, Dawson DA, Chou PS, Pickering R. The alcohol use disorder and associated disabilities schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. Drug and Alcohol Dependence. 1995; 39:37–44. [PubMed: 7587973]

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. DSM-IV, DSM-III-R and ICD-10 alcohol and drug abuse/harmful use and dependence, United States, 1992: A nosological comparison. Alcohol: Clinical and Experimental Research. 1996; 20:1481–1488.

Grant, BF., Kaplan, K., Shepard, K., Moore, T. Source and accuracy statement for wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). National Institute on Alcohol Abuse and Alcoholism; Bethesda, MD: 2003.

Grant, BF., Kaplan, KD. Source and accuracy statement for the wave 2 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). National Institute on Alcohol Abuse and Alcoholism; Rockville, MD: 2005.

Hasin D, Carpenter KM, McCloud S, Smith M, Grant BF. The alcohol use disorder and associated disabilities interview schedule (AUDADIS): reliability of alcohol and drug modules in a clinical sample. Drug and Alcohol Dependence. 1997; 44:133–141. [PubMed: 9088785]

Hughes, A., Williams, MR., Lipari, RN., Bose, J., Copello, EAP., Kroutil, LA. [accessed August 20, 2017] Prescription drug use and misuse in the United States: Results from the 2015 National Survey on Drug Use and Health. NSDUH Data Review. 2016 Sep. Available online at: http://www.samhsa.gov/data/

McCabe SE, Veliz P, Boyd CJ, Schulenberg JE. Medical and nonmedical use of prescription sedatives and anxiolytics: Adolescents' use and substance use disorder symptoms in adulthood. Addictive Behaviors. 2017; 65:296–301. [PubMed: 27569697]

National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). [accessed June 9, 2008] Wave 1 and Wave 2 (NIH NIAAA – NESARC website). Available online at: http://www.nesarc.niaaa.nih.gov/

Nelson CB, Rehm J, Usten B, Grant BF, Chatterji S. Factor structure for DSM-IV substance use disorder criteria endorsed by alcohol, cannabis, cocaine and opiate users: results from the world health organization reliability and validity study. Addiction. 1999; 94:843–855. [PubMed: 10665074]

Pull CB, Saunders JB, Mavreas V, Cottler LB, Grant BF, Hasin DS, et al. Concordance between ICD-10 alcohol and drug use disorder criteria and diagnoses as measured by the AUDADIS-ADR, CIDI, and SCAN: Results of a cross-national study. Drug and Alcohol Dependence. 1997; 47:207–216. [PubMed: 9306046]

Rigg KK, Ford JA. The misuse of benzodiazepines among adolescents: Psychosocial risk factors in a national sample. Drug and Alcohol Dependence. 2014; 137:137–142. [PubMed: 24582910]

Ruan W, Goldstein RB, Cho SP, Smith SM, Saha TD, Pickering RP, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV); reliability of new psychiatric diagnostic modules and risk factors in a general population sample. Drug and Alcohol Dependence. 2008; 92:27–36. [PubMed: 17706375]

Stinson FS, Grant BF, Dawson DA, Ruan WJ, Huang B, Saha T. Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Drug and Alcohol Dependence. 2005; 80:105–116. [PubMed: 16157233]

Thomas CP, Conrad P, Casler R, Goodman E. Trends in the use of psychotropic medications among adolescents, 1994 to 2001. Psychiatric Services. 2006; 57:63–69. [PubMed: 16399964]

Highlights

- Most prescription sedative or tranquilizer (ST) misuse ceased within 3 years.

- Over one-third of ST misusers had a substance use disorder (SUD) 3 years later.

- Most adults with a ST use disorder had a SUD 3 years later.

- About one-third of adults in remission from a ST use disorder had a SUD in 3 years.

Table 1

Prevalence estimates of misuse of prescription tranquilizers, sedatives and substance disorders over time

Misuse of prescription sedatives and tranquilizers at Wave 1	Misuse of prescription tranquilizers/sedatives in past 3 years (at Wave 2: 2004–2005)			Substance use disorders in past 3 years (at Wave 2: 2004–2005)			
	Misuse prescription sedative in past 3 years % (SE)	Misuse prescription tranquilizer in past 3 years % (SE)	Misuse prescription sedative OR tranquilizer in past 3 years % (SE)	Prescription sedative use disorder in past 3 years % (SE)	Prescription tranquilizer use disorder in past 3 years % (SE)	Prescription sedative OR tranquilizer use disorder in past 3 years % (SE)	Other substance use disorder in past 3 years % (SE)
Misuse of prescription sedatives							
No lifetime misuse	1.47% (0.08%)	1.25% (0.08%)	2.23% (0.10%)	0.18% (0.03%)	0.29% (0.05%)	0.39% (0.05%)	12.48% (0.32%)
Prior-to-past-year misuse only	6.58% (1.01%)	7.10% (1.09%)	10.19% (1.29%)	0.98% (0.43%)	1.82% (0.64%)	1.87% (0.65%)	29.67% (2.19%)
Current misuse (past-year)	19.68% (2.32%)	11.51% (1.71%)	22.97% (2.42%)	3.54% (1.16%)	3.28% (1.12%)	5.36% (1.34%)	40.86% (2.88%)
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
Misuse of prescription tranquilizers							
No lifetime use	1.54% (0.08%)	1.17% (0.08%)	2.25% (0.10%)	0.18% (0.03%)	0.27% (0.05%)	0.38% (0.05%)	12.36% (0.32%)
Prior-to-past-year misuse only	6.95% (0.97%)	8.42% (1.1%)	10.97% (1.20%)	1.42% (0.50%)	2.64% (0.63%)	3.14% (0.70%)	35.04% (2.37%)
Current misuse (past-year)	19.55% (3.16%)	20.77% (3.04%)	28.85% (3.51%)	3.44% (1.48%)	4.25% (1.45%)	5.08% (1.59%)	53.72% (3.72%)
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
Misuse of prescription sedatives or tranquilizers							
No lifetime misuse	1.36% (0.08%)	1.07% (0.07%)	2.04% (0.10%)	0.15% (0.03%)	0.25% (0.04%)	0.34% (0.05%)	12.07% (0.32%)
Prior-to-past year misuse only	6.27% (0.82%)	7.13% (0.92%)	9.80% (1.00%)	1.27% (0.43%)	2.19% (0.58%)	2.52% (0.61%)	29.75% (2.03%)
Current misuse (past-year)	18.17% (1.98%)	14.47% (1.70%)	23.74% (2.17%)	2.95% (0.84%)	2.90% (0.82%)	4.28% (0.94%)	44.96% (2.49%)
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
Sedative or tranquilizer use disorder							
No lifetime use disorder	1.69% (0.09%)	1.40% (0.08%)	2.52% (0.11%)	0.19% (0.03%)	0.30% (0.05%)	0.41% (0.05%)	12.98% (0.33%)
Prior-to-past-year disorder only	9.50% (1.92%)	9.40% (2.05%)	13.35% (2.29%)	2.62% (1.20%)	4.25% (1.55%)	4.83% (1.62%)	33.73% (3.05%)
Current use disorder (past-year)	28.13% (5.89%)	18.43% (4.94%)	34.17% (6.12%)	7.79% (3.31%)	9.69% (3.55%)	14.07% (4.29%)	53.49% (7.36%)
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$

Note: p-values are for Rao-Scott F-tests.

Table 2

Males: Prevalence estimates of misuse of prescription sedatives and tranquilizers and substance disorders over time

Age and misuse of prescription tranquilizers and sedatives at Wave 1 (2001–02)	Misuse of prescription tranquilizers/sedatives in past 3 years (at Wave 2: 2004–2005)			Substance use disorders in past 3 years (at Wave 2: 2004–2005)	
	Misuse prescription sedatives (S) in past 3 years % (SE)	Misuse prescription tranquilizers (T) in past 3 years % (SE)	Misuse prescription S or T in past 3 years % (SE)	Prescription ST use disorder in past 3 years % (SE)	Other substance use disorder in past 3 years % (SE)
Total					
No lifetime misuse	1.53% (0.13%)	1.07% (0.12%)	2.09% (0.15%)	0.32% (0.06%)	17.61% (0.46%)
Prior-to-past-year misuse only	5.92% (0.97%)	7.69% (1.32%)	10.18% (1.35%)	2.69% (0.86%)	35.24% (2.87%)
Current misuse (past year)	20.59% (2.76%)	17.26% (2.74%)	25.81% (3.07%)	3.88% (1.38%)	53.02% (3.57%)
	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001
18–25 years					
No lifetime misuse	3.12% (0.51%)	2.37% (0.43%)	4.31% (0.59%)	0.73% (0.28%)	33.74% (1.52%)
Prior-to-past-year misuse only	10.60% (3.93%)	15.89% (6.58%)	22.38% (6.54%)	7.17% (3.44%)	64.84% (7.11%)
Current misuse (past year)	23.12% (4.98%)	21.44% (5.23%)	28.97% (5.83%)	1.10% (1.10%)	67.27% (5.37%)
	P < 0.0001	P < 0.0001	P < 0.0001	P = 0.0001	P < 0.0001
26–44 years					
No lifetime misuse	1.82% (0.23%)	1.22% (0.21%)	2.36% (0.27%)	0.41% (0.11%)	19.24% (0.81%)
Prior-to-past-year misuse only	7.07% (1.53%)	7.78% (1.80%)	10.25% (1.97%)	1.12% (0.65%)	33.60% (3.55%)
Current misuse (past-year)	20.28% (4.47%)	15.00% (3.80%)	24.93% (4.83%)	7.89% (3.46%)	56.32% (6.36%)
	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001
45 years and older					
No lifetime misuse	0.76% (0.12%)	0.52% (0.10%)	1.14% (0.15%)	0.11% (0.04%)	11.04% (0.44%)
Prior-to-past-year misuse only	3.10% (1.15%)	4.97% (1.82%)	6.21% (1.87%)	3.08% (1.71%)	27.68% (3.75%)
Current misuse (past-year)	16.63% (4.70%)	13.16% (4.32%)	21.52% (5.01%)	3.10% (2.21%)	23.63% (5.01%)
	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001

Note: p-values are for Rao-Scott F-tests.

Table 3

Females: Prevalence estimates of misuse of prescription sedatives and tranquilizers and substance disorders over time

Age and misuse of prescription tranquilizers and sedatives at Wave 1 (2001–02)	Misuse of prescription tranquilizers/sedatives in past 3 years (at Wave 2: 2004–2005)			Substance use disorders since in past 3 years (at Wave 2: 2004–2005)	
	Misuse prescription sedatives (S) in past 3 years % (SE)	Misuse prescription tranquilizers (T) in past 3 years % (SE)	Misuse prescription S or T in past 3 years % (SE)	Prescription ST use disorder in past 3 years % (SE)	Other substance use disorder in past 3 years % (SE)
Total					
No lifetime misuse	1.21% (0.10%)	1.08% (0.09%)	1.99% (0.12%)	0.36% (0.06%)	7.12% (0.30%)
Prior-to-past-year misuse only	6.82% (1.44%)	6.24% (1.26%)	9.19% (1.60%)	2.24% (0.87%)	21.13% (1.94%)
Current misuse (past year)	14.99% (2.70%)	10.81% (1.99%)	21.02% (3.00%)	4.82% (1.32%)	34.40% (3.58%)
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
18–25 years					
No lifetime misuse	2.44% (0.38%)	2.48% (0.43%)	4.26% (0.54%)	1.04% (0.29%)	17.56% (1.14%)
Prior-to-past-year misuse only	11.37% (4.76%)	12.86% (4.93%)	15.25% (5.19%)	6.66% (4.18%)	31.54% (6.41%)
Current misuse (past year)	10.13% (4.39%)	11.77% (4.48%)	19.16% (5.67%)	3.15% (2.29%)	59.55% (6.76%)
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P = 0.0035$	$P < 0.0001$
26–44 years					
No lifetime misuse	1.34% (0.18%)	1.11% (0.15%)	2.13% (0.21%)	0.34% (0.09%)	9.11% (0.49%)
Prior-to-past-year misuse only	6.93% (2.27%)	6.05% (1.72%)	9.90% (2.54%)	1.70% (0.93%)	24.82% (2.89%)
Current misuse (past-year)	18.77% (4.46%)	12.35% (3.06%)	25.53% (4.82%)	4.23% (1.76%)	41.42% (5.07%)
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
45 years and older					
No lifetime misuse	0.78% (0.11%)	0.66% (0.08%)	1.25% (0.13%)	0.17% (0.05%)	2.70% (0.22%)
Prior-to-past-year misuse only	4.58% (1.60%)	3.50% (1.47%)	5.37% (1.68%)	1.04% (0.85%)	10.91% (2.28%)
Current misuse (past-year)	14.22% (4.25%)	8.26% (2.77%)	17.10% (4.55%)	6.80% (2.77%)	6.86% (2.78%)
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$

Note: p-values are for Rao-Scott F-tests.

Table 4

Wave 1 predictors of prescription tranquilizer or sedative disorder and other substance use disorders at Wave 2 among the sub-sample that reported any past-year misuse of prescription tranquilizers or sedatives Wave 1 (n = 563), and any substance use disorder at Wave 2 among the overall sample (n = 34,643).

	Sub-sample that reported any past-year misuse of prescription tranquilizers or sedatives at Wave 1 (n = 563)	
In 2001–2002 Wave 1	In 2004–05 (Wave 2) Any Tranquilizer or Sedative Use Disorder in Past 3 Years AOR (95% CI)	In 2004–05 (Wave 2) Other Substance Use Disorder in Past 3 Years AOR (95% CI)
Age		
45 years and older	--	--
26–44 years old	1.09 (0.38 – 3.14)	4.55 (2.68 – 7.74)***
18–25 years old	0.31 (0.07 – 1.45)	9.43 (4.86 – 18.33)***
Sex		
Female	--	--
Male	1.02 (0.37 – 2.77)	1.34 (0.80 – 2.24)
Race		
Black	--	--
White	0.83 (0.21 – 3.29)	1.29 (0.54 – 3.11)
Hispanic	2.82 (0.55 – 14.65)	1.08 (0.32 – 3.65)
Other (includes Asian and American Indian)	1.74 (0.15 – 20.40)	2.20 (0.60 – 8.00)
Lifetime Alcohol Use Disorder		
No	--	--
Yes	1.02 (0.37 – 2.81)	5.69 (3.40 – 9.51)***
Lifetime Mood Disorder		
No	--	--
Yes	1.68 (0.62 – 4.56)	0.90 (0.53 – 1.54)
Lifetime Anxiety Disorder		
No	--	--
Yes	1.52 (0.59 – 3.93)	1.31 (0.75 – 2.30)
Lifetime Prescribed Medicines for Anxiety Symptoms		
No	--	--
Yes	1.14 (0.29 – 4.55)	1.37 (0.64 – 2.92)

Notes: AOR = Adjusted odds ratio. CI = Confidence Interval. -- = Reference group.