



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



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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.

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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, 45% (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.

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 Lacerza, 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

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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 (National Epidemiologic Survey on Alcohol and Related Conditions, 2008) 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 et al. (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 et al. (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 longitudinal 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

2.3.1. 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.)

2.3.2. 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, Kaplan, et al., 2003; Grant, 1996; Nelson, Rehm, Usen, Grant and Chatterji, 1999; Pull, Saunders, Avreas, Cottler, Grant, and Hasin, et al., 1997).

2.3.3. 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.

2.3.4. 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.

2.3.5. 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.

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