

# The Role of a Prescription in Anxiety Medication Use, Abuse, and Dependence

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**Objective:** Prescriptions for anxiety medications have increased substantially in recent years. Individuals with anxiety disorders are at risk of nonmedical use of these medications, but information about whether this risk is elevated among patients with a prescription for such medications is lacking. The authors compared risk of nonmedical use in individuals in a national sample with and without a prescription for anxiety medication and identified characteristics associated with nonmedical use.

**Method:** Data were drawn from face-to-face surveys of 34,653 adult participants in the National Epidemiologic Survey on Alcohol and Related Conditions. The risk of nonmedical use of prescription anxiety medication and associated drug use disorders was computed for individuals who had or had not ever received a prescription for anxiety medication; among those who had received a prescription, charac-

teristics associated with nonmedical use were analyzed.

**Results:** Prescription of anxiety medication was associated with lifetime and past-year nonmedical use (odds ratios, 1.6 and 1.9, respectively) and lifetime DSM-IV abuse or dependence (odds ratio, 2.6). Among respondents who received a prescription (N=4,294), nonmedical use was associated with male sex, younger age, white race, history of use of illicit drugs, history of other drug use disorders, and history of illegal behaviors.

**Conclusions:** These results indicate that prescription for anxiety medications is associated with nonmedical use of these medications, although the direction of causality cannot be determined in this study. Although anxiety medications have clinical utility, greater clinical attention should be given to the potential for their abuse among patients at particular risk.

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Prescription anxiety medications (including sedatives and tranquilizers) have great clinical efficacy (1, 2) and are widely prescribed (3) in the United States. However, in recent years, the nonmedical use of prescription anxiety medications has increased (4–6). Nonmedical use includes use without a doctor's prescription, or use in greater amounts, more frequently, or longer than prescribed or for a reason other than that recommended by a doctor (4, 5). Nonmedical use of prescription anxiety medication can be dangerous and even fatal (2, 7, 8), as evidenced by an estimated 233,875 nonmedical use-related emergency department visits in 2006 (8). Prescription anxiety medications exhibit stronger reinforcing properties than other prescription psychiatric drugs, and these properties are amplified with nonmedical use (1, 2, 7). Consequently, among nonmedical users of prescription anxiety medications, estimates of drug use disorders secondary to such use are high (4, 5, 9). Thus, the nonmedical use of these agents represents a growing and important public health problem. To develop effective prevention and treatment interventions, an improved understanding of nonmedical use of prescription anxiety medication is necessary, including risk factors.

Previous studies indicate that individuals with anxiety disorders have an elevated risk of nonmedical use of pre-

scription anxiety medications (4). However, whether the risk of nonmedical use is increased by receiving a prescription for anxiety medication is unknown. In addition, little is known about nonmedical use of prescription anxiety medication among individuals who have a prescription, since previous epidemiological studies asked only about nonmedical use "without a prescription" (10, 11) or did not distinguish between nonmedical use with and without a prescription (5). School-based and Internet surveys suggest that many individuals with a prescription for psychiatric medication engage in nonmedical use of their own prescriptions (12, 13; unpublished data, available on request from the first author). Thus, while these medications can be obtained and used nonmedically through street sales and prescription drug sharing, individuals with a prescription for anxiety medication may also have an elevated risk of developing drug use disorders secondary to use of prescription anxiety medication. Consequently, there is a need for epidemiological research to obtain estimates and correlates of nonmedical prescription anxiety medication use, abuse, and dependence among individuals with a prescription for such medications.

We investigated these issues using data from the National Epidemiologic Survey on Alcohol and Related Con-

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ditions (NESARC), sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The NESARC is unique in its sample size, representativeness, and comprehensiveness, allowing for generalizable estimates. In this study, we considered two general questions: 1) Is the prevalence of nonmedical prescription anxiety medication use and associated drug use disorders (i.e., abuse and dependence) higher among individuals with a prescription for an anxiety medication than it is among individuals without a prescription? 2) What behavioral, psychiatric, and family history characteristics are associated with nonmedical use of anxiety medications among individuals with a prescription?

## Method

### Sample

Data for the study came from waves 1 and 2 of the NESARC. The NESARC target population was the noninstitutionalized civilian population age 18 and older residing in households and group quarters. Blacks, Hispanics, and young adults (ages 18–24) were oversampled, with data adjusted for oversampling and household- and person-level nonresponse. The weighted data were then adjusted to represent the U.S. civilian population based on data from the 2000 census. Wave 1 of the study, conducted in 2001 and 2002, has been described elsewhere (14). For wave 2 (15), conducted in 2004 and 2005, interviewers trained by the U.S. Census Bureau reinterviewed all possible eligible respondents from wave 1. Excluding respondents ineligible for the wave 2 interview because they were deceased (N=1,403), deported, mentally or physically impaired (N=781), or on active duty in the armed forces throughout the follow-up period (N=950), the wave 2 response rate was 86.7%, and the cumulative response rate over the two waves was 70.2%. This analysis includes the 34,653 respondents who completed interviews at waves 1 and 2 because the combined interview information from the two waves provided the greatest item coverage of receipt of prescriptions for anxiety medication. All potential NESARC respondents were informed in writing about the nature of the survey, the statistical uses of the survey data, the voluntary aspect of their participation, and the federal laws that provide for the confidentiality of identifiable survey information. Respondents who gave consent were then interviewed. The research protocol, including informed consent procedures, was approved by the Census Bureau's review board and the U.S. Office of Management and Budget.

### Measures

The interview used in the NESARC was the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV) (16). This structured diagnostic interview, designed for lay interviewers, was developed to advance measurement of substance use and mental disorders in large-scale surveys. To generate DSM-IV diagnoses, computer diagnostic programs implemented the DSM-IV criteria for the disorders using the AUDADIS-IV data.

**Receiving a prescription.** Eleven questions on prescribed medication were asked of all respondents who were screened into the diagnostic module for the following disorders at wave 1 or wave 2: general anxiety, specific phobia, social phobia, and panic disorder with and without agoraphobia. Respondents were asked, "Did a doctor EVER prescribe any medicines or drugs" for the symptoms in question, using nontechnical language to describe the symptoms.

**Nonmedical use of prescription anxiety medications.** All respondents were asked whether they used tranquilizers or sedatives "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." At wave 1, such use was assessed in two time frames: current (past 12 months) and prior to the past 12 months. At wave 2, which was 3 years later, such use was also assessed in two time frames: current (past 12 months) and prior to the past 12 months but since wave 1. These were combined to produce lifetime estimates.

**Abuse and dependence.** The AUDADIS-IV contains symptom-related questions that operationalize DSM-IV criteria for drug use disorders, including drug-specific diagnoses for sedatives and for tranquilizers. Consistent with DSM-IV, a past-year AUDADIS-IV diagnosis of prescription sedative or tranquilizer abuse required at least one of the four abuse criteria in the 12-month period preceding the interview and the absence of a lifetime dependence diagnosis. A lifetime AUDADIS-IV diagnosis of dependence on a prescription sedative or tranquilizer was defined as meeting at least three of the seven dependence criteria within a 12-month period. Binary outcome variables were created for lifetime prescription drug abuse and dependence outcomes involving each prescription drug. In this study, nonmedical use of, abuse of, and dependence on tranquilizers and sedatives were combined into one category of nonmedical prescription anxiety medication use and associated drug use disorders.

The reliability and validity of the AUDADIS-IV prescription sedative and tranquilizer use questions (kappa values, 0.46–0.79) and the excellent reliability of associated substance use disorder diagnoses (kappa values, 0.87–0.93) are well documented in numerous psychometric studies, including in clinical (17) and general population samples (18).

### Predictors of Nonmedical Use

**Behavioral.** Among college students, nonmedical use of prescription anxiety medication is highly associated with illicit drug use and intoxicated driving (10). Therefore, we hypothesized that any lifetime illicit drug use (none compared with any use of marijuana, cocaine, inhalants, hallucinogens, heroin, and other illicit drugs) or ever driving under the influence of drugs or alcohol would predict nonmedical use among individuals with a prescription. Additionally, since delinquent behaviors are associated with nonmedical prescription drug use among adolescents (19), we hypothesized that having legal problems related to drugs or alcohol and ever having "made money illegally such as selling stolen property or selling drugs" would be associated with nonmedical use.

**Psychiatric.** Population-based studies indicate an association between nonmedical use of prescription anxiety medication and mood, anxiety, personality, alcohol, and drug use disorders (4). Therefore, we hypothesized that any personality disorder or any lifetime mood, anxiety, alcohol, or drug use disorder would predict nonmedical use of prescription anxiety medication among individuals with a prescription. The AUDADIS-IV questions operationalize DSM-IV criteria for all psychiatric disorders. The advantages of AUDADIS diagnoses over other survey instruments have been reviewed elsewhere (14, 20, 21). The fair to excellent reliability and validity of the AUDADIS-IV criteria and diagnoses for alcohol and drug use disorders (kappa values, 0.53–0.84), mood and anxiety disorders (kappa values, 0.40–0.73) (22), and personality disorders (kappa values, 0.40–0.71) are well documented in numerous psychometric studies (17, 18, 23), in clinical reappraisals by psychiatrists (24), in clinical and general population samples (25), and in several countries as part of the World Health Organization and National Institutes of Health International Study on Reliability and Validity (26).

**TABLE 1. Nonmedical Use of Prescription Anxiety Medication and Drug Use Disorders Among Individuals With and Without a Prescription**

Anxiety Medication Characteristic	Analysis <sup>a</sup>											
	Total Sample (N=34,653)		Received a Prescription (N=4,294)		Never Received a Prescription (N=30,359)		Controlling for Sociodemographic Variables		Controlling for Sociodemographic Variables and Anxiety Disorders		Controlling for Sociodemographic Variables and Anxiety Severity	
	%	SE	%	SE	%	SE	Odds Ratio <sup>b</sup>	95% CI	Odds Ratio <sup>c</sup>	95% CI	Odds Ratio <sup>d</sup>	95% CI
Nonmedical use												
Lifetime (N=2,432)	7.4	0.2	16.0	0.7	6.3	0.2	2.98*	2.61–3.39	2.13*	1.84–2.46	1.61*	1.36–1.91
Past year (N=593)	1.9	0.1	4.6	0.4	1.5	0.1	3.36*	2.62–4.31	2.42*	1.86–3.16	1.94*	1.40–2.69
Lifetime drug use disorders												
Abuse (N=425)	1.3	0.1	3.8	0.4	1.0	0.1	4.53*	3.38–6.06	3.28*	2.33–4.62	2.54*	1.73–3.73
Dependence (N=164)	0.5	0.1	2.3	0.3	0.3	0.0	8.66*	5.62–13.34	4.82*	2.83–8.22	3.24*	1.85–5.67
Abuse or dependence (N=589)	1.9	0.1	6.0	0.5	1.3	0.1	5.42*	4.22–6.97	3.70*	2.74–4.99	2.60*	1.88–3.60

<sup>a</sup> Individuals with a prescription for anxiety medication compared with those without a prescription.

<sup>b</sup> Adjusted for age, sex, race, and education.

<sup>c</sup> Adjusted for age, sex, race, education, and any lifetime anxiety disorder (panic disorder, social phobia, specific phobia, or generalized anxiety disorder).

<sup>d</sup> Adjusted for age, sex, race, education, and severity of any anxiety disorder.

\* $p < 0.05$ .

**Family history.** A family history of psychopathology is associated with substance use (27, 28), and a family history of alcohol or drug problems is associated with nonmedical use of prescription drugs (5). Therefore, we predicted that a family history of depression and alcohol, drug, or behavioral problems would predict nonmedical use. Family history was assessed by reading descriptions of observable manifestations of each disorder (29) designed to address sensitivity issues in family history information (30, 31) and then asking about relatives by category. We considered psychiatric disorders only among parents and siblings, since these have the best validity and good to excellent test-retest reliability (29).

### Statistical Analysis

Weighted means, frequencies, and cross-tabulations were computed. To estimate the association between receiving a prescription for an anxiety medication and nonmedical use, abuse, and dependence, adjusted odds ratios were derived from multiple logistic regressions controlling for age, sex, race, and education, which are associated with nonmedical prescription drug use (4, 5). The possibility of confounding from anxiety disorder diagnoses was ruled out in additional models that controlled for any lifetime anxiety disorder (including panic, social phobia, specific phobia, and generalized anxiety). Further potential confounding from the severity of anxiety disorders was assessed with the addition of a severity indicator covariate consisting of a multilevel categorical variable measuring the number of DSM-IV anxiety disorder symptoms. To assess whether these associations are specific to nonmedical prescription anxiety medication use or general to all substance use, we repeated the analysis described above for respondents who had never used illegal drugs (marijuana, cocaine, hallucinogens, and heroin), comparing those who had ever received prescription anxiety medication and those who had not. Lastly, odds ratios measuring predictors of lifetime nonmedical prescription anxiety medication use among individuals with a prescription were computed. For each predictor, two odds ratios were computed, the first adjusting for age, sex, race, and education and the second controlling for these characteristics as well as axis I and II comorbidity and behavioral and family history variables. Since this study focused on the odds that respondents who reported nonmedical use had a prescription and on the risk

factors among those who had a prescription, we did not examine predictors of nonmedical use among respondents who had never received a prescription for anxiety medication. Analyses were carried out using SUDAAN (Research Triangle Institute, Research Triangle Park, N.C.), which adjusts for characteristics of complex sample surveys.

## Results

### Nonmedical Use, Abuse, and Dependence

In the overall sample, 11.8% of respondents had received prescriptions for anxiety medication. As shown in Table 1, 16.0% of that subgroup reported lifetime nonmedical use and 4.6% reported abuse or dependence on these drugs. Compared with those who had never received a prescription for anxiety medication, those with a prescription had significantly higher odds of lifetime and past-year nonmedical use (odds ratios, 2.98 and 3.36, respectively) and lifetime DSM-IV diagnoses of abuse (odds ratio=4.53) and dependence (odds ratio=8.66), controlling for sociodemographic characteristics only. Adding any anxiety disorder into the models did not affect significance but reduced the magnitude of associations, especially for dependence (odds ratio=4.82). Adding anxiety disorder severity further reduced the magnitude of associations, although all associations remained significant.

Among respondents who had never used illegal drugs (N=27,024), adjusting for sociodemographic characteristics and anxiety disorder severity revealed significant associations between having a prescription and lifetime (odds ratio=1.70; 95% confidence interval [CI]=1.22–2.36) and past-year (odds ratio=1.69; 95% CI=1.01–2.82) nonmedical use. These associations were of similar magnitude to those observed for the overall sample. Strikingly, the association for abuse or dependence on prescription

**TABLE 2. Behavioral, Psychiatric, and Family History Predictors of Lifetime Nonmedical Use of Prescription Anxiety Medications (N=657) Among Respondents With a Prescription (N=4,294)**

Characteristic	Analysis <sup>a</sup>			
	Controlling for Sociodemographic Variables		Controlling for All Sociodemographic, Behavioral, and Psychiatric Variables	
	Odds Ratio <sup>b</sup>	95% CI	Odds Ratio <sup>c</sup>	95% CI
<b>Lifetime behavioral characteristics</b>				
Number of illegal drugs used				
2 or more (N=648)	16.59*	12.60–21.84	2.88*	1.82–4.57
1 (N=769)	3.80*	2.86–5.03	1.51	1.00–2.30
0 (N=2,877) (reference)	1.00		1.00	
Drove under influence of				
Alcohol (N=1,075)	3.49*	2.81–4.33	1.07	0.75–1.53
Drugs (N=641)	11.23*	8.51–14.81	1.35	0.87–2.10
Legal problems from				
Alcohol (N=429)	4.15*	3.12–5.51	1.10	0.76–1.61
Drugs (N=205)	7.01*	4.84–10.16	1.33	0.83–2.12
Sold drugs or stolen property (N=219)	9.53*	6.47–14.02	1.64*	1.03–2.61
<b>Lifetime psychiatric characteristics</b>				
Any anxiety disorder (N=3,039)	1.46*	1.14–1.87	1.15	0.87–1.53
Any mood disorder (N=2,834)	2.13*	1.67–2.72	1.16	0.88–1.54
Any alcohol use disorder (N=1,815)	3.90*	3.10–4.90	1.26	0.87–1.81
Any drug use disorder (N=896)	15.71*	12.07–20.45	5.22*	3.10–8.82
Any personality disorder (N=2,007)	2.57*	2.06–3.20	1.52*	1.13–2.03
<b>Family history<sup>d</sup></b>				
Alcohol problems (N=1,998)	1.64*	1.30–2.05	0.97	0.72–1.31
Drug problems (N=938)	2.03*	1.59–2.58	1.17	0.83–1.65
Behavioral problems (N=1,148)	1.46*	1.17–1.83	0.73	0.54–1.01
Depression (N=2,150)	1.40*	1.13–1.74	0.80	0.60–1.07

<sup>a</sup> Lifetime nonmedical prescription anxiety medication users (N=590) compared with all others (N=3,704).

<sup>b</sup> Adjusted for age, sex, race, and education.

<sup>c</sup> Adjusted for age, sex, race, and education; axis I and II disorders; and all behavioral and family history variables included in the table.

<sup>d</sup> Parents and siblings.

\*p<0.05.

anxiety medication in this subsample was almost twice that of the overall sample (odds ratio=5.31; 95% CI=2.24–12.62). Controlling for sociodemographic characteristics and any anxiety disorder revealed similar associations, such as for lifetime nonmedical use (odds ratio=1.96; 95% CI=1.48–2.61) and abuse or dependence (odds ratio=5.63; 95% CI=2.43–13.07).

**Predictors of Nonmedical Use Among Those With a Prescription**

Among respondents with a prescription for anxiety medication (Table 2), adjusting for age, sex, race, and education, nonmedical use was significantly higher among men (odds ratio=1.68; 95% CI=1.34–2.12) and significantly lower among blacks compared with whites (odds ratio=0.55; 95% CI=0.38–0.79) and among respondents age 30 and older compared with those 18–29 years of age (odds ratio=0.37; 95% CI=0.29–0.47). Adjusting for sociodemographic variables, all behavioral (odds ratios, 3.49–16.59) psychiatric (odds ratios, 2.13–15.71), and family history (odds ratios, 1.40–2.03) variables significantly predicted nonmedical use among individuals with a prescription. When also adjusting for all the behavioral, psychiatric, and family history variables, having used more

than one illegal drug (odds ratio=2.88), ever selling drugs or stolen property (odds ratio=1.64), and meeting criteria for any drug use (odds ratio=5.22) or personality (odds ratio=1.52) disorder remained significant predictors of non-medical use.

**Discussion**

To our knowledge, this is the first study to examine the prevalence of nonmedical prescription drug use among individuals with and without a prescription, using a nationally representative sample. We found that 16.0% of respondents with a prescription for anxiety medication reported nonmedical use, compared with 6.3% among individuals without a prescription. Likewise, 6.0% of individuals with a prescription reported a drug use disorder secondary to prescription anxiety medication, compared with only 1.9% among individuals without a prescription. Our findings support the hypothesis that individuals with a prescription for anxiety medication are at significantly elevated risk of nonmedical use (1, 4, 5). Notably, we found that this phenomenon cannot be fully accounted for by anxiety disorder diagnoses, anxiety disorder severity, or co-occurring drug use.

Our findings are consistent with non-population-based surveys that reveal high rates of nonmedical prescription medication use among individuals with a prescription (12, 13; unpublished data, available on request from the first author). No estimates of prescription drug use disorders due to nonmedical use among individuals with a prescription have been published previously. However, around 70% of respondents with a prescription in our sample met criteria for at least one lifetime anxiety disorder diagnosis, and previous population-based (4, 5) and clinical (32) studies have indicated an association between anxiety disorders and drug use disorders secondary to nonmedical use of prescription drugs. Since anxiety medications have significant therapeutic value, research establishing the causes of nonmedical use, abuse, and dependence among those with a prescription is needed.

Among individuals with a prescription, behavioral characteristics associated with nonmedical use included illicit drug use, driving while intoxicated, and substance-related criminal activity. Our findings correspond with characteristics associated with college nonmedical prescription anxiety medication users (10). These behavioral characteristics are components of some psychiatric disorders, particularly substance use disorders, which may explain why most substance-related behavioral characteristics lost significance when the analyses controlled for psychiatric disorders. It is especially noteworthy that illicit drug use and selling drugs or stolen property remained significant predictors of nonmedical use even when the analyses controlled for psychiatric characteristics.

Among individuals with a prescription, all psychiatric disorders were significant predictors of nonmedical prescription anxiety medication use in the first set of models. This finding is consistent with previous reports of a high prevalence of psychiatric disorders among nonmedical prescription anxiety medication users in the general population (4, 5, 9). However, adjusting for all sociodemographic, behavioral, and psychiatric characteristics, significant associations were observed only for any drug use disorder and any personality disorder. This suggests that drug use and personality disorders exert a unique effect on nonmedical prescription anxiety medication use, while the effect of other psychiatric characteristics may be due to shared underlying factors. Our results should not be interpreted as indicating a need to withhold potentially important medications from patients. Rather, the findings suggest the need for greater attention to the recognition and management of comorbid psychiatric conditions, particularly personality and drug use disorders, by health care workers involved in pharmacological treatment of anxiety disorders, such as by screening for other substance use disorders before prescribing anxiety medication and monitoring for nonmedical use of prescribed anxiety medication throughout the course of treatment. Prescribers may also consider including an adjunct psychotherapeutic component to their anxiety disorder treatment to

identify, treat, and prevent the development of problems with nonmedical use.

Our study had several limitations. First, all survey questions may have been subject to recall, self-report, and social desirability bias. Second, since only information on lifetime prescription was available, the prescription anxiety medication used nonmedically may not have been the anxiety medication for which respondents had received a prescription; future studies should include questions specific enough to ascertain this information. Third, to maximize statistical power, our definition of nonmedical use was broad, including one-time nonmedical use. However, excluding respondents who engaged in nonmedical anxiety medication use only once within any single year did not change the significance or strength of the association between having a prescription and lifetime nonmedical use. This indicates that our result did not derive from these respondents only. Additionally, the survey questions on nonmedical use did not cover dangerous nonmedical use behaviors (e.g., intranasal administration and coadministration with other psychoactive substances) while using prescription anxiety medication for the appropriate medical reason. Also, anxiety disorders are occasionally treated with medications other than anti-anxiety drugs (33), which may have introduced error into our measure of prescription anxiety medication use, although other medications are prescribed on such a limited basis that this is unlikely to change the results. Additionally, some anti-anxiety medications may have been prescribed for major depression (34), potentially biasing the associations observed in this study toward the null, yielding conservative results. Furthermore, while the gateway questions that screened respondents into the treatment questions were broad, the prescription questions were not asked of all respondents, potentially introducing misclassification bias. However, this possibility is reduced because prescription of medication for any anxiety disorder was assessed in 11 different questions in the wave 1 and 2 interviews, and two-thirds of the sample (67.1%) were asked at least one of these questions.

The study also has several notable strengths. It is the first attempt to consider the nonmedical use of prescription anxiety medication among individuals with a prescription. The sample was large and produced nationally representative findings. Data from two time points were included. And, finally, we were able to examine an important question for which data were previously unavailable.

Research on nonmedical prescription anxiety medication use among psychiatric patients does not detract from the great clinical utility of prescription anxiety medication (1, 2). Development of interventions targeting nonmedical use among patients with a prescription must take care not to reduce prescription of these drugs for patients who need and will benefit from them. Appropriate development of interventions will require an understanding of the characteristics predisposing to nonmedical use among

patients with a prescription. The information we provide here on sociodemographic, behavioral, and psychiatric characteristics associated with nonmedical use of anxiety medication among individuals with a prescription can be used in the design of such interventions.

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