



# Risk factors for incident nonmedical prescription opioid use and abuse and dependence: Results from a longitudinal nationally representative sample

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## ABSTRACT

**Background:** There has been a significant increase in opioid prescriptions and the prevalence of opioid nonmedical use. Nonmedical use may lead to opioid abuse/dependence, a serious public health concern. The aim of this paper was to determine the mental and physical health predictors of incident nonmedical prescription opioid use (NMPOU) and abuse/dependence, and the impact of comorbidity in a longitudinal, nationally representative sample.

**Methods:** Data come from Waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions ( $N=34,653$ ;  $\geq 20$  years old). Mental disorders were assessed using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV edition. Physical conditions were based on self-reports of physician-diagnoses. Multiple logistic regression models examined the associations between mental and physical health predictors at Wave 1 and their association to incident NMPOU and abuse/dependence disorders at Wave 2.

**Results:** After adjusting for sociodemographics, Axis I and II mental disorders and physical conditions, the presence of mental disorders (i.e., mood, personality disorders and substance use disorders), physical conditions (i.e., increasing number of physical conditions, any physical condition, arteriosclerosis or hypertension, cardiovascular disease and arthritis) and sociodemographic factors (i.e., sex and marital status) at Wave 1 positively predicted incident abuse/dependence at Wave 2. Comorbid disorders increased the risk of NMPOU and abuse/dependence.

**Conclusion:** These results suggest the importance of mental and physical comorbidity as a risk for NMPOU and abuse/dependence, emphasizing the need for careful screening practices when prescribing opioids.

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## 1. Introduction

Prescription opioids are a widely used method of analgesia for many chronic pain conditions (Chou et al., 2009). There have been significant increases in the number of opioid prescriptions over the past 10 years (Compton and Volkow, 2006; Leong et al., 2009). The prevalence of nonmedical prescription opioid use (NMPOU) has also increased and become a serious public health concern (Gilson et al., 2004). Further, prescription opioids are linked to drug overdose-related deaths (Centers for Disease Control and Prevention, 2012), which have progressively increased (Paulozzi et al., 2006). Of concern, unanticipated medical and mental disorders were found to be one of the root causes for opioid-related overdose deaths (Webster et al., 2011). NMPOU can manifest as

using opioids without a prescription, or taking opioids in ways or for reasons others than prescribed (Becker et al., 2008), which may lead to opioid abuse or dependence (Becker et al., 2008). Nationally representative data estimates the lifetime prevalence of NMPOU to be 4.7%, with a lifetime prevalence of an opioid use disorder at 1.4%, which likely represents a conservative estimate (Huang et al., 2006).

The association between NMPOU and abuse/dependence and mental disorders has been well documented in the literature. Past research, largely cross-sectional, has demonstrated that having either an Axis I or Axis II mental disorder is associated with an increased likelihood of NMPOU and abuse/dependence disorder (Becker et al., 2008; Fenton et al., 2012; Grant et al., 2004; Huang et al., 2006; Martins et al., 2012, 2009). While robust, very few longitudinal, nationally representative studies exist and no studies adjust for Axis II mental disorders, nor chronic physical conditions.

The examination of physical health correlates of NMPOU and abuse/dependence has been limited. Several studies have demonstrated an association between pain and opioid abuse/dependence

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(Becker et al., 2008; Edlund et al., 2007; Havens et al., 2009; Novak et al., 2009). Conversely, another study found no correlation between pain score and the risk of NMPOU; however, this sample was drawn from a small primary care sample and may not be generalizable to the larger population (Ives et al., 2006). Currently, little is known regarding the role of chronic physical conditions on the incidence of NMPOU and abuse/dependence in the population. This is a significant gap in the literature, as visiting a physician for a chronic physical condition is an access-point for opioid prescriptions and an important point for prevention of abuse. In addition, there is no available information on which physical conditions might be the most important risk factors for NMPOU and abuse/dependence.

To the best of our knowledge, this is the first study that uses a nationally representative sample to longitudinally examine Axis I and II mental disorders and physical conditions that precede incident NMPOU and abuse/dependence. Findings can help inform prescribing practices by increasing awareness and emphasizing appropriate screening for risk factors. Further, we will examine additive effects among the aforementioned variables to look at the dose-response relationship of Axis I and II mental disorders and physical conditions, as the clinical picture indicates that patients with comorbid disorders may be at increased risk of poor outcomes and mortality (Lawrence et al., 2010). We aim to disentangle this relationship and understand the role of comorbidity in driving this relationship.

## 2. Methods

### 2.1. Sample

Data come from Waves 1 (2001–2002) and 2 (2004–2005) of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC;  $N = 34,653$ ;  $\geq 20$  years of age); a longitudinal, nationally representative survey conducted by the National Institute on Alcohol Abuse and Alcoholism. The target population of the NESARC is civilian, non-institutionalized individuals 18 years and older at Wave 1 in the United States, including the District of Columbia, Alaska and Hawaii. The data were weighted to reflect the national civilian population based on the 2000 census. All eligible respondents were re-interviewed at Wave 2, which excluded those who were deceased, deported, physically or mentally ill, or on active military duty at follow-up. Of those eligible to participate in Wave 2, 86.7% completed interviews, totaling a cumulative response rate of 70.2% for both waves. Ethical approval or research protocol, including informed consent, was approved by the Census Bureau's review board and the US Office of Management and Budget. Face-to-face interviews were conducted by trained lay interviewers of the US Census Bureau who had at least five years experience. More detailed methodology can be found elsewhere (Grant et al., 2003).

### 2.2. Measures

**2.2.1. Sociodemographic variables.** The sociodemographic variables assessed were age (continuous), sex, race/ethnicity (White, non-Hispanic; Black, non-Hispanic; other; Hispanic, any race), education (less than high school; high school or equivalent; some college or more), marital status (married/common law; widowed/separated/divorced; never married) and past-year household income (\$0–\$19,999; \$20,000–\$34,999; \$40,000–\$59,999; \$60,000+).

**2.2.2. Mental disorders.** Axis I and II Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) mental disorders were assessed using the Alcohol Use Disorder and Associated Disability Interview Schedule (AUDADIS-IV), a structured diagnostic interview for use by trained-lay interviewers and clinicians. The

AUDADIS-IV has been shown to have a good-to-excellent reliability for drug use disorders and substance abuse (Chatterji et al., 1997; Grant et al., 2003; Hasin et al., 1997), good-to-excellent reliability for alcohol consumption, tobacco use and major depression, fair-to-good for selected DSM-IV Axis I and II mental disorders, and good-to-excellent for the dimensional symptom scales of DSM-IV Axis I and II mental disorders (Grant et al., 2003). Axis I mental disorders include Waves 1 and 2 past-year mood disorders (i.e., major depression, dysthymia, mania, and hypomania), anxiety disorders (i.e., panic disorder with and without agoraphobia, social phobia, specific phobia, and generalized anxiety disorder), and substance use disorders (i.e., alcohol abuse and dependence, nicotine dependence, and drug abuse and dependence including opioid abuse/dependence). Axis II mental disorders include lifetime antisocial, dependent, obsessive compulsive, paranoid, schizotypal, avoidant, or histrionic personality disorders.

**2.2.3. Non-medical prescription opioid use (NMPOU).** We categorized NMPOU based on yes/no answer to having ever misused an opioid prescription. Non-medical use was defined as “without a prescription, in greater amounts, more often, or longer than prescribed, or for a reason other than a doctor said you should use them”. Non-medical incident use at Wave 2 excluded those who met criteria for Wave 1-lifetime NMPOU or Wave 2-lifetime abuse and/or dependence. Incidence was defined as new onset cases of NMPOU (since last interview) at Wave 2, among those with no history of lifetime NMPOU or abuse/dependence at Wave 2.

**2.2.4. Opioid abuse/dependence.** Those who answered yes to the NMPOU screening question were asked subsequent questions, assessed by the AUDADIS-IV, to determine if they met abuse/dependence criteria. Those who met criteria for lifetime abuse/dependence at Wave 1 were excluded from analyses to gain the true incident population.

**2.2.5. Physical conditions (Axis III).** The NESARC assessed 11 physical conditions at Wave 1, which were self-reported physical conditions based on physician diagnoses. Broad physical condition variables were created by combining individual physical conditions into categories with similar clinical presentations, which were also based on prior research (El-Gabalawy et al., 2010). We assessed the following physical conditions: (1) arteriosclerosis or hypertension, (2) hepatic disease (i.e., cirrhosis of the liver, liver disease), (3) cardiovascular disease (i.e., angina pectoris, tachycardia, myocardial infarction, heart disease), (4) gastrointestinal disease (i.e., stomach ulcer, gastritis) and (5) arthritis. We also created an “any physical condition” variable, which included those who endorsed at least one condition. Finally, we created a number of physical conditions variable, which ranged from zero to nine.

### 2.3. Analytic strategy

We derived weighted prevalence rates for all of the primary variables. We also conducted cross-tabulations, which provided the prevalence rates of the relationships of the variables assessed at Wave 1 and incident NMPOU and abuse/dependence. First, we used logistic regression to examine the relationship between sociodemographics at Wave 1 and their association to incident opioid NMPOU and abuse/dependence as an outcome variable at Wave 2. We examined this association in an unadjusted model, as well as a model adjusting for Axis I and II mental disorders. Second, we used logistic regressions to examine mental disorder variables at Wave 1 and their association to incident NMPOU and abuse/dependence at Wave 2. In this analysis we included an unadjusted model and models adjusting for: (1) sociodemographics, (2) sociodemographics,

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