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# Factors predicting development of opioid use disorders among individuals who receive an initial opioid prescription: Mathematical modeling using a database of commercially-insured individuals



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#### ABSTRACT

*Background*: Prescription drug abuse in the United States and elsewhere in the world is increasing at an alarming rate with non-medical opioid use, in particular, increasing to epidemic proportions over the past two decades. It is imperative to identify individuals most likely to develop opioid abuse or dependence to inform large-scale, targeted prevention efforts.

Methods: The present investigation utilized a large commercial insurance claims database to identify demographic, mental health, physical health, and healthcare service utilization variables that differentiate persons who receive an opioid abuse or dependence diagnosis within two years of filling an opioid prescription (OUDs) from those who do not receive such a diagnosis within the same time frame (non-OUDs).

Results: When compared to non-OUDs, OUDs were more likely to: (1) be male (59.9% vs. 44.2% for non-OUDs) and younger (M = 37.9 vs. 47.7); (2) have a prescription history of more opioids (1.7 vs. 1.2), and more days supply of opioids (M = 272.5, vs. M = 33.2; (3) have prescriptions filled at more pharmacies (M = 3.3 per year vs. M = 1.3); (4) have greater rates of psychiatric disorders; (5) utilize more medical and psychiatric services; and (6) be prescribed more concomitant medications. A predictive model incorporating these findings was 79.5% concordant with actual OUDs in the data set.

Conclusions: Understanding correlates of OUD development can help to predict risk and inform prevention efforts.

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#### 1. Introduction

North America comprises the world's largest drug market and evidences the highest drug-related mortality rate in the world (International Narcotics Control Board, 2012). Within the United States the problem of prescription drug misuse and opioid misuse (broadly defined as using the medication in a manner different than prescribed) in particular, has reached epidemic proportions. Pain relievers were the most commonly misused drug in the psychotherapeutics category from 2002 to 2011 (Substance Abuse and

Mental Health Services Administration (SAMHSA), 2012) and from 2004 to 2011, the number of medical emergencies involving opioids increased by 183% (SAMHSA, 2013).

Abuse of prescription drugs is a significant public health problem, associated with high costs both to the health care system and to the individuals who use them. From an economic perspective, it is estimated that opioid misusers' medical care costs are eight times greater than those of non-misusers (White et al., 2005). Mortality due to prescription drug use is a significant cause of death in the United States, accounting for 36% of all poisoning deaths in 2007, a number that tripled from 1999 to 2007 (Warner et al., 2011). It is estimated that 0.04% of individuals receiving a prescription opioid have a fatal overdose, with the odds of mortality higher among those receiving an opioid for pain (Bohnert et al., 2011).

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Identifying patients who misuse these substances is often difficult, since clinicians must disentangle legitimate pain management needs from possible abuse. When opioid abuse or dependence develops, patients' medical treatment is complicated by tolerance, withdrawal, or potential overdose. Little is known about factors that may place individuals at risk for the development of prescription drug use disorders. As a recent editorial indicates, these individuals may differ significantly from those who are typically studied in substance use disorder research; specifically, many at risk for opioid use disorders may not have a history of illicit drug use prior to developing a problem with opioids (Darke, 2011). Since the rates of prescribing opioids, state by state, are linked to mortality due to overdose, it is clear that a prescription of an opioid places individuals at risk for eventual misuse (Paulozzi et al., 2011).

#### 1.1. Prediction of misuse of opioids/opioid use disorders

Researchers have attempted to identify factors that may predict later drug abuse and dependence. Earlier age of nonmedical use of prescription drugs, earlier initiation of alcohol use, family history of alcoholism, and polydrug abuse are predictive of greater risk for developing prescription drug abuse or dependence (McCabe et al., 2007). Previous research has found that there are particular demographic variables that place individuals at higher risk for the development of a diagnosis of opioid abuse and dependence. Specifically, individuals who are younger (Edlund et al., 2007, 2010) and male (Edlund et al., 2007) were more likely to develop abuse and dependence. Additionally, receiving a larger number of days' supply of prescription opioids was a predictor of an opioid use disorder diagnosis (Edlund et al., 2007), as was having a higher average daily dose (Edlund et al., 2010).

In addition to demographic and other markers, behaviorally-based criteria have been successfully used to identify problematic cases of prescription drug misuse (Smith et al., 2010). In a recent study, clinical expert raters identified key indicators of misuse, including interpersonal problems, arrest history, multiple opioid use, use for no identifiable reason, and comorbid other substance misuse, and used these indicators along with known indicators of misuse to improve accuracy in identifying misuse. This study indicates that multiple sources of data, particularly those regarding different domains of functioning, may best identify those at risk for opioid abuse and dependence.

#### 1.2. Prescription drug use and mental health disorders

Previous studies have also linked problematic use of prescription drugs and mental health diagnoses. Nonmedical use of opioids has been associated with panic, depressive, social phobic or agoraphobic symptoms, and the overall number of psychiatric symptoms endorsed (Becker et al., 2007a,b). Development of opioid abuse and dependence has also been associated with non-opioid substance use and mental health disorders (Edlund et al., 2007, 2010). Recent prospective research has indicated that non-medical use of prescription medications, including opioids, places individuals at risk for unipolar depressive, bipolar, and anxiety disorders (Schepis and Hakes, 2011). The converse relationship may also be true: other mental health conditions may predispose individuals to misuse opioids. In a recent review of the known factors predicting opioid misuse, the authors caution that although many mental health diagnoses may be risk factors for opioid misuse, these conditions are likely to be concealed due to stigma, and some individuals may choose to take prescription opioids to treat undiagnosed co-occurring disorders rather than the appropriate psychiatric medication (Pergolizzi et al., 2012).

#### 1.3. Purpose of this study

This study seeks to identify demographic and healthcare related variables that predict the development of opioid abuse or dependence, utilizing data obtained from the Thomson Reuters MarketScan Commercial Claims and Encounters (CCAE) database, which contains information about commercially insured and Medicare eligible patients. The use of a large sample, physician-diagnosed disorders, and comprehensive demographic and health care utilization data enable detailed analysis of individuals at risk for the development for opioid abuse or dependence. First, individuals diagnosed with opioid use disorders will be compared with those who are not given opioid use diagnoses on a variety of domains. Second, the use of mathematical modeling techniques will aid in identifying people who are at risk for the development of opioid abuse or dependence.

#### 2. Methods and analytic strategy

Patients within the CCAE database who had at least one opioid prescription claim between January 1, 2000 and December 31, 2008 were identified. Patients were included if they maintained continuous insurance eligibility for 6 months prior to, and 2 years beyond, this initial prescription claim (N = 2,841,793). Individuals who subsequently received an ICD-9 CM diagnosis ( $304.0 \times$  or  $305.5 \times$ ) of opioid abuse or dependence were classified as those with opioid use disorders, hereafter referred to as OUDs, (n = 2913), and individuals who did not receive a subsequent opioid abuse or dependence diagnosis were classified as those without opioid use disorders, hereafter referred to as non-OUDs (n = 2,838,880).

Of the OUDs, 266 received a diagnosis of opioid abuse, and the remaining 2647 received a diagnosis of opioid dependence. Abuse and dependence cases were therefore grouped together for the purpose of analyses from this point for the following reasons: (1) over 90% of the cases fell into the more serious category of dependence, (2) an abuse diagnosis is often a precursor to dependence, and (3) the clinical distinction between abuse and dependence is less important than the presence or absence of an addictive condition. Furthermore, the distinction between abuse and dependence has been eliminated in the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013), and replaced with opioid use disorders.

The first set of planned comparisons involved conducting either *t*-tests (for continuous variables) or chi-square analyses (for categorical data) to test for statistically significant differences between cases and controls on a variety of variables present in the database. These analyses also served the purpose of identifying variables of interest for the mathematical modeling to be conducted in the next step. With regard to mental health diagnoses and co-occurring substance use disorders, the predictor variables were not time-dependent (i.e., any lifetime diagnosis was counted as positive in the use of these predictor variables).

Once the variables that statistically discriminated cases from controls were identified, significant interactions between these variables were identified using CHAID (Chi-Square Automatic Interaction Detection) analyses. The goal of a CHAID analysis is to find homogeneous clusters of a response variable where clusters are defined by the levels in a set of predictor variables. Particular emphasis is placed on the interaction of the predictor variables. The algorithm splits the population according to levels in the predictor variable, which make the responses within the resultant groups as similar as possible and the average between groups as different as possible (Biggs et al., 1991; Kass, 1980).

Significant interactions detected through CHAID were reviewed by the research team and included in the subsequent logistic

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