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

Cara Katz[a], **Renée El-Gabalawy**[a,b], **Katherine M. Keyes**[c], **Silvia S. Martins**[c], and **Jitender Sareen**[a,b,*]

[a]University of Manitoba, Department of Psychiatry, Winnipeg, Manitoba, Canada

[b]University of Manitoba, Department of Psychology, Winnipeg, Manitoba, Canada

[c]Columbia University, Department of Epidemiology, 722 West 168th Street, Room 1608, New York, NY 10032, United States

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; ≥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.

*Corresponding author at: PZ-482 Bannatyne Ave, Winnipeg, MB, Canada R3E 3N4, Tel.: +1 204 787 7078. sareen@cc.umanitoba.ca (J. Sareen).

Contributors

Cara Katz contributed to literature search, figures, study design, data analysis and interpretation and writing.
Renee El-Gabalawy contributed to figures, study design, data analysis and interpretation and writing.
Katherine M Keyes contributed to literature search, study design, data interpretation and writing.
Silvia S Martins contributed to study design, data interpretation and writing.
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Conflict of interest

There are no conflicts of interest.

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.

Keywords

Epidemiology; Opiates; Comorbidity; Risk factors; Opioids; NMPOU; Nonmedical prescription opioid use; NESARC

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 then 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 (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; $N = 34,653$; ≥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; wid-owed/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, Axis I and II mental disorders (where applicable), and (3) sociodemographics, Axis I and II mental disorders (where applicable), and "any physical condition." In the case of mental disorder covariates, we included the mental disorder category that was not our independent variable. For example, when Axis II mental disorders were our independent variable, we only included Axis I mental disorders as a covariate. Third, we used logistic regression to examine individual physical conditions at Wave 1 and their association to incident NMPOU and abuse/dependence at Wave 2. In this case we included an unadjusted model and a model adjusting for: (1) sociodemographics, and (2) sociodemographics and Axis I and II mental disorders. Finally, we used logistic regressions to examine the additive effect of disorder categories creating a variable that indicated: (1) Axis I-only (no Axis II or physical condition comorbidity), (2) Axis II-only, (3) Physical condition only (i.e., Axis III), (4) Axis I and II only, (5) Axis I and III only, (6) Axis II and III only, and (7) Axis I, II, and III. These analyses allow us to examine the odds of incident NMPOU and abuse/dependence based on various predictors at Wave 1 through the estimation of odds ratios. We analyzed our data using SUDAAN 10.0.1 (Shah etal., 1995), which employs the Taylor Series Linearization method (Levy and Lemeshow, 1999) for variance estimation to account for the complex sampling design of the NESARC. We applied appropriate weighting and stratification variables to ensure that these data were representative of the US population.

3. Results

Table 1 presents samples sizes and weighted percentages for our independent and dependent variables. Among the sample of 34,653, there were 585 (1.82%) incident non-medical users and 191 (0.63%) incident cases of opioid abuse/dependence at Wave 2.

When examining sociodemographic predictors of opioid abuse/dependence, we found that even in the most stringent model, being younger (AOR1: 0.97 [CI 95% 0.97–0.98] $p \leq 0.001$ and 0.97 [CI 95% 0.95–0.98] $p \leq 0.001$) and never having been married (AOR1: 2.25 [CI 95% 1.81–2.80] $p \leq 0.001$ AOR1: 2.13 [CI 95% 1.37–3.22] $p \leq 0.001$) were significant predictors of incident NMPOU and abuse/dependence, respectively. Males were more likely than females to have NMPOU and abuse/dependence (AOR1, females: 0.82 [CI 95% 0.68–1.00] $p \leq 0.05$ and 0.70 [CI 95% 0.95–0.98] $p \leq 0.05$, respectively). In addition, being of Black, non-Hispanic ethnicity was protective for opioid abuse/dependence, using White, non-Hispanics as the reference group (AOR1 0.56 [CI 95% 0.32–0.96] $p \leq 0.05$).

Upon examination of Axis I and II mental disorders as predictors, after adjusting for sociodemographics, Axis I and II mental disorders and having "any physical condition," all mental disorders, except any anxiety disorder, were significant and positive predictors of incident NMPOU and abuse/dependence (AOR3 range: 1.72–3.02 and 1.70–3.99, respectively). Any substance use disorder had the strongest association with both NMPOU and abuse/dependence (AOR3: 3.02 [CI 95% 1.83–5.00] and 3.99 [CI 95% 2.13–7.50] $p \leq 0.001$, respectively).

Table 2 indicates that in the most stringent model, after adjusting for both sociodemographics and Axis I and II mental disorders, only cardiovascular disease was

predictive of incident NMPOU, whereas all chronic physical conditions except gastrointestinal disease significantly predicted incident opioid abuse/dependence in the most stringent model. Hepatic disease could not be examined due to limited statistical power. Cardiovascular disease had the strongest association with opioid abuse/dependence (AOR2: 2.22 [CI 95% 1.01–4.89] $p \leq 0.05$). In addition, having "any physical condition" and increasing numbers of physical conditions were both significantly associated with increased odds of incident opioid abuse/dependence.

The additive analysis (Table 3) demonstrates an additive effect of Axis I, II, and III in predicting incident opioid abuse/dependence, as compared to having no disorder (AOR1 range: 2.31–17.89), even after adjusting for sociodemographics. This effect is similar in predicting incident NMPOU (AOR1 range: 1.54–3.11), with the exception of Axis III disorders alone, which do not have a significant effect on predicting incident NMPOU; however, in combination with Axis I and/or Axis II mental disorders, does have a significant effect. These results emphasize that not only are Axis I, II, and III disorders/conditions individually important risk factors for opioid abuse/dependence, but also the comorbidity of mental disorders and chronic physical conditions.

As a post hoc analysis, we examined both age and sex as individual potential moderators by interacting age and sex with each independent variable in the analysis of physical condition predictors and in the additive analysis, predicting incident opioid abuse/dependence. None of the interactions were significant therefore we did not stratify.

4. Discussion

To the best of our knowledge, this is the first study that demonstrates in a population-based national sample that several chronic physical conditions (i.e., arteriosclerosis or hypertension, cardiovascular disease, arthritis, and any assessed medical condition) are associated with the onset of opioid abuse/dependence even after controlling for sociodemographic factors and Axis I and II mental disorders. Further, we found that increasing numbers of physical conditions are associated with increased risk of opioid abuse/dependence after controlling for the aforementioned confounding variables. Finally and importantly, the additive analysis is novel in that it emphasizes a dose-response relationship of Axis I and II disorders and physical conditions in preceding incident prescription opioid abuse/dependence.

Our results suggest that physical conditions are generally not significantly and positively associated with NMPOU (which excludes those who met lifetime opioid abuse/dependence) when controlling for sociodemographic variables and Axis I and II mental disorders. However, these same physical conditions were significant risk factors for opioid abuse/dependence after controlling for these variables. Although no direct comparisons were made between NMPOU and opioid abuse/dependence, these results may indicate that physical conditions among those with NMPOU may act as a significant risk factor that pushes NMPOU into the more severe opioid abuse/dependence category. This relationship may be direct or mediated by other variables such as increased access to opioids through prescriptions. To shed light on these findings, it is important to first understand driving

factors behind NMPOU, which are most likely complex and multifactorial. We note that opioid abuse/dependence does not simply indicate the development of medical tolerance alone, but indicates a trend of chronic and pathological use that often creates a pattern of systematic and disabling impairment. Our results indicate the relationship between NMPOU and opioid abuse/dependence is important, yet still unclear. For example, some users may be engaging in NMPOU for the purpose of self-medication, whereas others may engage in NMPOU for the purpose of recreational use (Martins et al., 2012; McCabe et al., 2009, 2007). If self-medication in NMPOU is strongly linked to opioid abuse/dependence, it is possible that increased access to opioids through suffering from a medical condition may help explain the findings. Although the physical condition itself may not warrant the prescription of opioids, this condition may predispose the individual to increased levels of pain, prompting them to seek medical help. The literature indicates that there may be a very low threshold for prescribing opioids in our current culture because of intolerance for any pain (Lembke, 2012). Further, among recreational users, previous literature has shown that misuse was more often initiated on the basis of pain, which subsequently led to recreational misuse, and that misuse of an opioid prescription for simple recreational purposes was less likely (Cicero et al., 2008a).

Mental disorders were also a significant risk factor for both NMPOU and abuse/dependence even after controlling for other mental disorders and physical conditions. In addition, the additive analysis shows that comorbidity is a risk factor for both NMPOU and abuse/dependence. These findings are in line with a significant body of prior research (Becker et al., 2008; Fenton et al., 2012; Grant et al., 2004; Huang et al., 2006; Martins et al., 2012, 2009), which has demonstrated that mental disorders are risk factors for NMPOU and abuse/dependence. Unique to this study, physical conditions were not individually and significantly associated with NMPOU; however, when combined with comorbid mental disorders, these relationships became significant. In terms of opioid abuse/dependence, Axis I and II mental disorders and physical conditions individually were significantly and positively associated with abuse/dependence; however, the effect was stronger when comorbidity was present. Of concern, one study found that patients with both chronic pain and mental disorders are more likely to receive opioid prescriptions, and in higher dosages, than those with chronic pain alone (Seal et al., 2012). As previously indicated, the exact mechanisms of these relationships are unknown but the findings warrant attention and follow-up research. These findings may have implications for screening procedures, not only to detect mental health comorbidity, but also to specifically inquire about the nature of one’s pain and how one is coping with it.

The current findings shed light on the complex issue of opioid prescription, but also raise additional questions. While the present study did not collect information on where an individual obtained opioids, some studies indicate that 60% of abused opioids are obtained either directly or indirectly through a physician’s prescription (Lembke, 2012); however, data are highly variable with respect to common sources of opioid medications (Boyer and Wines, 2008; Carise et al., 2007; Cicero et al., 2008b; Inciardi et al., 2009; Volkow et al., 2011). With a large proportion of individuals receiving their opioid prescriptions from physicians, understanding how to risk-stratify becomes an important clinical tool for curbing this growing problem. Data are robust, however, in demonstrating that rates of overdoses are

proportional to the rates of prescription (Centers for Disease Control and Prevention, 2011; Bohnert et al., 2011; Paulozzi et al., 2006), indicating the need for evidence-based prescribing practices. In many cases, despite being aware of an individual's risk of abuse, physicians are still prescribing opioids to these patients (Lembke, 2012). In acknowledging the relationship between rates of opioid prescription and rates of overdoses, it may be prudent to exhaust all other means of pain control, both pharmacologically with paracetamol and NSAIDs (Labianca et al., 2012) and non-pharmacologically, through lifestyle adjustments, before resorting to the more potent opioids. Moreover, non-pharmacological interventions such as cognitive-behavioral therapy may be particularly useful in the reduction of pain, as these types of treatments have been found to be effective in pain reduction and coping (Morley et al., 1999).

There are several streams of interventions currently in place to control the growing problem of prescription opioid overdoses, including patient, physician, pharmacist and emergency department education, opioid prescription guidelines, prescription drug monitoring programs, attempts to reduce illegal prescription, and improved access to substance abuse treatment programs (Centers for Disease Control and Prevention, 2012). Some programs in the United States involve the physicians prescribing naloxone, an opioid antagonist, to patients thought to be at high risk for overdose (Albert et al., 2011). In a review of current NMPOU prevention strategies, an algorithm was developed, highlighting screening and stratification of patients into low, medium and high-risk groups. Some prevention strategies among the high risk group include urinary drug screens, prescription monitoring, and low prescription doses, with those who display aberrant behavior being weaned off (Atluri et al., 2012). The current findings demonstrate the need to study these interventions among a comorbid sample, in order to determine the best approach for clinicians when confronted with the dilemma of whether to prescribe or not. The implications of this would likely help us to reduce the numbers of individuals abusing opioids, which may have health and economic benefits.

It is important to put these findings in the context of certain limitations. First, Wave 1 of the NESARC was collected earlier in the prescription opioid epidemic, which has been growing over the past 10 years (Paulozzi, 2012); therefore, the incident findings at follow-up may be overinflated. Second, although the study aimed to capture all individuals who were using a prescription opioid in ways other than prescribed by a physician or without a prescription at all, it may not capture all those who receive opioids from other sources and does not capture the motivation for NMPOU. Additionally, this study could not address the amount of NMPOU, and while we can speculate that misusing opioids once or twice would not lead to an abuse/dependence disorder, we cannot comment as to the degree of NMPOU that would lead to an abuse/dependence disorder. Third, all physical conditions were past-year and based on self-report. Although this study examined self-reported physical conditions based on physician diagnoses, there may be reporting bias; however, studies have shown good reliability of self-report as compared to physical health measures (Baumeister et al., 2010; Edwards et al., 1996; Kinley et al., 2012). Fourth, the NESARC does not include a measure of past-year chronic pain, which is an important potential pathway in the relationships described here. Similarly, although Axis I and II mental disorders were included in these analyses, the study excluded individuals with subclinical manifestations, who may also be an

at-risk population. Additionally, when adjusting for Axis II mental disorders when, for example, we investigated Axis I mental disorders as our predictor, due to power issues, we could not additionally adjust for comorbid individual Axis I mental disorders alone. Last, mental disorders were diagnosed by trained-lay interviewers, rather than clinicians, which may contribute to inflated rates of diagnoses (Kessler et al., 1998).

Despite these limitations, this study yields important clinical implications. We have shown that chronic physical conditions are important independent predictors of prescription opioid abuse/dependence. We have proposed that perhaps those with a physical condition have either severe physical pain, or increased access to opioids that push past the NMPOU category into abuse/dependence. We do not yet understand this relationship, but speculate that self-medication and/or recreational use of an available opioid prescription might mediate this relationship. Even further, those with a physical condition plus an Axis I and/or Axis II mental disorder are at an elevated risk of NMPOU and abuse/dependence. These results tell us that physicians must carefully screen patients when prescribing opioids, even those outside of the mental health system, to elicit an indication of risk. No universal screening tool exists, therefore this may be an area of future investigation (Solanki et al., 2011). As mentioned above, some of the intervention techniques consist of prescribing naloxone along with opioid in high-risk cases (Albert et al., 2011), whereas other research suggests that non-pharmacological treatments may be appropriate. This way, physicians are able to address the patient's pain while potentially mitigating the risk. Other techniques such as pill counting, dose limitation, and other methods as outlined above could be utilized once stratification based on nonmedical use risk has occurred. Further investigation of the intervention techniques currently employed to control opioid NMPOU is warranted. Such techniques may be increasingly helpful in a population with chronic physical conditions and mental health comorbidity.

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Table 1

Summary of primary variables (n=34,653).

Variable	N weighted (%)
Sociodemographic variables	
Sex	
Female	20 089(52.08)
Male	14 564(47.92)
Race/Ethnicity	
White, non-hispanic	20 174(70.93)
Black, non-hispanic	6577(l1.04)
Other	1546(6.47)
Hispanic, any race	6356(l1.56)
Education	
Less than high school	5744(14.65)
High school or equivalent	9955(29.03)
Some college or more	18 954(56.32)
Marital status	
Married/common law	18 413(63.06)
Widowed/separated/divorced	8564(16.47)
Never married	7676(20.46)
Past-year household income	
$0–$19 999	8959(20.35)
$20 000–$34 999	7309(19.62)
$35 000–$59 999	8812(26.27)
$60 000+	9573(33.76)
Primary dependent variables	
Incident opioid abuse/dependence	191(0.63)
Incidence non-medical prescription opioid use	585(1.82)
Mental health variables	
Any anxiety disorder	4013(11.16)
Any mood disorder	3365(9.17)
Any substance use disorder, excluding opioids	556(1.76)
Any axis II disorder	7783(21.52)
Nicotine dependence	4017(12.41)
Any alcohol use disorder	2694(8.27)
Physical health variables	
Arteriosclerosis or Hypertension	7265(19.67)
Hepatic disease	236(0.64)
Cardiovascular disease	2710(7.38)
Gastrointestinal disease	2178(5.80)
Arthritis	6343(17.60)
Any medical condition	12 135(33.97)

Variable	N weighted (%)
Variable	Mean (SE)
Age	45.08 (0.001)
# of physical health conditions	0.55 (<0.001)

[a] AH variables are based on Wave 1 prevalence, with exception of incidence variables.

Table 2

Physical conditions predicting non-medical prescription opioid use and abuse/dependence.

Physical health	NMPOU, *n* (%)		Abuse/Dep, *n* (%)		OR (95% Cl)		AOR1 (95% Cl)		AOR2 (95% Cl)	
	No	Yes	No	Yes	NMPOU	Abuse/Dep	NMPOU	Abuse/Dep	NMPOU	Abuse/Dep
Number of physical health conditions (0–9)	–	–	–	–	0.93(0.82–1.04)	1.14(0.97–1.35)	1.19(1.07–1.32) ***	1.62(1.42–1.84) ***	1.12(1.00–1.25)	1.42(1.23–1.63) ***
Arteriosclerosis or hypertension	479(1.93)	92(1.33)	150(0.61)	33(0.66)	0.69(0.51–0.92) **	1.08(0.64–1.84)	1.15(0.82–1.60)	2.53(1.50–4.28) ***	1.05(0.75–1.46)	2.02(1.18–3.46) **
Hepatic disease	565(1.81)	6(2.44)	181(0.61)	3(2.90)	1.36(0.49–3.77)	–	1.60(0.58–4.42)	–	1.30(0.48–3.54)	–
Cardiovascular disease	520(l.79)	51(2.15)	162(0.59)	20(1.06)	1.21(0.82–1.78)	1.81(0.89–3.71)	1.80(1.22–2.66) **	3.20(1.49–6.87) **	1.53(1.02–2.28) *	2.22(1.01–4.89) *
Gastrointestinal disease	526(1.78)	44(2.20)	166(0.61)	18(0.88)	1.24(0.84–1.83)	1.44(0.78–2.65)	1.58(1.06–2.36) *	1.98(1.08–3.60) *	1.33(0.89–1.98)	1.36(0.75–2.44)
Arthritis	482(1.86)	92(1.61)	146(0.60)	37 (0.70)	0.86(0.65–1.15)	1.18(0.73–1.91)	1.49(1.09–2.03) **	2.71(1.51–4.85) ***	1.34(0.99–1.82)	2.09(1.20–3.63) **
Any assessed medical condition	388(1.92)	183(1.61)	112(0.54)	70(0.77)	0.84(0.67–1.05)	1.42(0.94–2.16)	1.44(1.12–1.85) **	3.38(2.25–5.07) ***	1.25(0.97–1.61)	2.47(1.66–3.67) ***

OR, odds ratio; AOR1, adjusted for sex, age, marital status, education, household income, race; AOR2, adjusted for sociodemographic factors and Axis I and II mental disorders. For prevalence rates, yes = percentage of individuals with the physical condition who have NMPOU or abuse/dependence, respectively; no = percentage of individuals without the physical condition who have NMPOU or abuse/dependence, respectively. NMPOU, non-medical prescription opioid use; abuse/dep, opioid abuse and/or dependence.

* $p \leq 0.05$.

** $p \leq 0.01$.

*** $p \leq 0.001$.

Table 3

Individual and comorbid disorders predicting non-medical prescription opioid use and abuse/dependence.

	NMPOU				Abuse/Dep			
	n (%)		OR (95%CI)	AOR1 (95% CI)	*n* (%)		OR (95%CI)	AOR1 (95% CI)
	No	Yes			No	Yes		
Reference[a]			1.00	1.00			1.00	1.00
Axis I only	205(1.41)	41 (2.48)	1.78 (1.20–2.64) **	1.54(1.02–2.33) *	36(0.25)	13(0.83)	3.29 (1.48–7.32) **	2.69 (1.17–6.16) *
Axis II only	205(1.41)	77(2.98)	2.14 (1.53–2.99) ***	1.98 (1.41–2.77) ***	36(0.25)	33(1.15)	4.60 (2.38–8.90) ***	4.04 (2.09–7.78) ***
Axis III only	205(1.41)	85(1.13)	0.80 (0.58–1.09)	1.26 (0.92–1.75)	36(0.25)	23(0.33)	1.29 (0.58–2.87)	2.31 (1.09–4.89) *
Axis I +Axis II only	205(1.41)	65 (4.83)	3.54 (2.58–4.85) ***	2.77 (2.01–3.80) ***	36(0.25)	30(2.02)	8.16 (4.44–14.99) ***	6.10 (3.26–11.43) ***
Axis I +Axis III only	205(1.41)	30(2.43)	1.74(1.04–2.91) *	2.51 (1.44–4.38) **	36(0.25)	3(0.39)	–	–
Axis II + Axis III only	205(1.41)	29(2.03)	1.45 (0.88–2.37)	2.16 (1.27–3.65) **	36(0.25)	16(1.67)	6.70 (3.12–14.39) ***	11.44 (5.80–22.56) ***
Axis I+Axis II + Axis III	205(1.41)	39(3.55)	2.57 (1.59–4.15) ***	3.11 (1.94–4.97) ***	36(0.25)	28(2.90)	11.80 (5.93–23.47) ***	17.89 (9.28–34.47) ***

[a]Reference category, No Axis I, II or III; AOR1, adjusted for sex, age, marital status, education, household income, race; NMPOU, non-medical prescription opioid use; abuse/dep, opioid abuse and/or dependence; Axis I, past-year; Axis II, lifetime; Axis III, past-year. For prevalence rates, yes = percentage of individuals with the independent variable who have NMPOU or abuse/dependence, respectively; no = percentage of individuals with no Axis I, II or III who have NMPOU or abuse/dependence, respectively

* $p \leq 0.05$.

** $p \leq 0.01$.

*** $p \leq 0.001$.