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Age of Initiation, Psychopathology and Other Substance Use Are Associated with Time to Use Disorder Diagnosis in Persons using Opioids Nonmedically

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Abstract

Background: Nonmedical use of prescription opioids (NMUPO) is an ongoing public health challenge, as NMUPO is associated with psychopathology, other drug use and fatal overdose. These concomitant risks are greatest in those with opioid use disorder (OUD), but the development of NMUPO-related use disorder is poorly understood. The primary aim of this study was to establish factors associated with the development of and time to OUD among persons engaged in NMUPO.

Methods: Data were from Wave 1 of the National Epidemiologic Study on Alcohol and Related Conditions, with 1,755 participants endorsing lifetime NMUPO. Analyses used sequential design-based logistic regression for DSM-IV opioid dependence correlates, followed by Cox regression of proportional hazards for correlates (e.g., sociodemographics, age of NMUPO initiation and psychopathology) of time to dependence in those who developed DSM-IV dependence.

Results: Earlier age of NMUPO initiation increased OUD odds (AOR= 0.95, 95%CI= 0.94–0.96) but slowed OUD development (AHR= 1.05, 95%CI= 1.04–1.06) in those who developed OUD (n= 118), after controlling for sociodemographics, psychopathology and ages of other drug use initiation. Psychopathology and earlier other drug use initiation were associated with higher OUD odds, but only having an alcohol use disorder was associated with shorter time to OUD.

Conclusions: Earlier NMUPO initiation is associated with increased odds of OUD, though those with early initiation had a slower progression to OUD. Programs that prevent early NMUPO initiation, which might lower rates of OUD, and/or identify the later initiators at highest risk for rapid OUD development could have great public health benefits.

Keywords

Opioid; misuse; nonmedical use; dependence; course

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AUTHOR CONTRIBUTIONS

Ty Schepis was the primary writer of the manuscript. Jahn Hakes conducted all statistical analyses. Both authors participated equally in devising the research plan, selecting statistical analyses and in editing the manuscript.

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INTRODUCTION

Nonmedical use of prescription opioids (NMUPO) continues to be a significant public health issue in the United States.[1] In 2013, over 1.5 million residents initiated NMUPO,[2] and in 2014, nearly four million adults engaged in NMUPO.[3] Estimates from 2006 and 2007 indicated that NMUPO cost US society over $50 billion,[4,5] and NMUPO is associated with numerous behavioral health risks, including psychopathology,[6] other substance use,[7] and fatal overdose.[8] More recent reports have highlighted the elevated risk of heroin initiation among those engaged in NMUPO,[9] though this may be largely in those with frequent NMUPO and/or NMUPO-related opioid use disorders (OUDs).[10]

Indeed, the evidence indicates that the costs and personal risks are greatest in those engaged in frequent NMUPO and/or with OUDs from NMUPO.[6,9–11] Past work using cross-sectional, nationally representative or large insurance database samples has uncovered consistent sociodemographic correlates of a NMUPO-related OUD diagnosis: male sex, young adult age, unmarried status, lower educational attainment and uninsured status.[12–14] In addition, OUD is associated with current psychopathology, trauma exposure, poor self-endorsed health and younger age of NMUPO initiation.[12,15–19] Work using longitudinal data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) added evidence that many health conditions (e.g., arthritis) at wave 1 were risk factors for an OUD diagnosis at wave 2.[14]

Thus, many correlates of an OUD diagnosis have been found, often in repeated investigations. What is unclear, however, is which factors are associated with the course of OUD. Parker and Anthony[20] investigated transitions from NMUPO initiation to DSM-IV opioid dependence in individuals aged 12 to 21 years, finding that one of every 11 to 16 initiators transitioned to dependence within 12 months. They also found a peak incidence of opioid dependence at younger ages, suggesting the importance of earlier NMUPO initiation for the speed of transition to such dependence.[20] Otherwise, the sociodemographic and psychiatric factors that influence the time from NMUPO initiation to OUD remain uninvestigated. Establishing these characteristics could allow for treatment that matches those at highest risk for rapid OUD development with more intensive interventions, limiting the morbidity and mortality associated with NMUPO.

Aims and Hypotheses

Using data from wave 1 of the NESARC, the primary aim of this work was to evaluate potential sociodemographic, psychiatric and substance use characteristics associated with a shorter time to DSM-IV prescription opioid dependence (described as opioid use disorder in the Results and Discussion to be more consistent with DSM-5 standards), conditional upon NMUPO initiation. In order to develop these models, initial models examined the association of the above factors with development of dependence. Models were constructed in four steps: initial models examined associations between sociodemographic factors and either opioid dependence or time to dependence; a second set included age of NMUPO initiation; a third set added a set of DSM-IV Axis I and II diagnoses; and, the fourth set examined ages of alcohol and other drug use initiation. Given their association with more

rapid development of use disorder with other substances and their association with opioid us disorder, we hypothesized that earlier ages of NMUPO[17], alcohol and other drug initiation[15] and that having a DSM-IV psychiatric diagnosis[18,19] would be associated with shorter times to DSM-IV opioid dependence.

METHODS

The NESARC is a longitudinal, nationally representative survey funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The survey targets the US non-institutionalized adult population, including military personnel living off-base and those in group housing (e.g., shelters). The NESARC used the Census 2000–2001 Supplementary Survey to structure sampling, and each wave included weights to create nationally representative data. Weighting also adjusted for selection procedures, the need to oversample young adults and non-response at either wave 1 or 2. Participants were asked all sensitive questions (including those on NMUPO) using computer-assisted personal interviewing methods. The US Census Bureau and the US Office of Budget and Management approved the NESARC protocol, and the first author's IRB exempted this work from review. More comprehensive accounts of the NESARC are available elsewhere.[21,22]

This investigation only used data from wave 1 (conducted in 2001–2002), with 43,093 participants and a response rate of 81.2%.[21,22] After weighting, the sample is 52% female, 71% Caucasian, 12% Hispanic/Latino, 11% African-American; 13% of the sample was under 25 years of age.

Measures

Nonmedical use of prescription opioids is defined in the NESARC as opioid use "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." Here, only wave 1 NMUPO data were used because of concerns about the inclusion of non-opioid medications (i.e., Cox II inhibitors) in wave 2.[23,24]

Age of NMUPO initiation was assessed in all individuals who endorsed lifetime NMUPO via "How old were you when you FIRST used painkillers?", with similar questions for age of initiation of alcohol or non-opioid drug use. Ages of alcohol and other (non-opioid) drug use initiation were assessed in all individuals endorsing lifetime alcohol or drug use, respectively. Also, we used an investigator-created variable capturing lifetime non-opioid drug use. A similar variable for lifetime alcohol use was excluded because all but one individual with lifetime NMUPO initiated alcohol use.

Psychiatric diagnoses were obtained through the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV Edition (AUDADIS-IV).[25,26] The AUDADIS-IV is a structured diagnostic interview that assesses DSM-IV[27] Axis I and II disorders. Here, psychiatric outcomes included alcohol use disorders (AUD; abuse or dependence), substance use disorders (SUD; abuse or dependence), depressive disorders (major depression or dysthymia), bipolar disorders (bipolar I or II) and anxiety disorders (panic disorder with and without agoraphobia, social phobia, specific phobia or generalized

anxiety disorder). Seven of ten Axis II personality disorder (PD) diagnoses were included. These are antisocial, avoidant, dependent, obsessive-compulsive, paranoid, schizoid, and histrionic PD (the remaining PDs were not assessed at wave 1). The AUDADIS-IV has good reliability and validity in assessing the psychiatric disorders of interest.[25,26]

Age of onset of DSM-IV opioid dependence was assessed in all individuals endorsing the presence of at least three opioid dependence symptoms in the AUDADIS-IV interview. In those individuals, the following questions were asked to assess age of opioid dependence onset: "You just mentioned some other experiences you had with painkillers in the past, that is, before 12 months ago. Before last (Month one year ago) was there ever a period when SOME of these experiences with painkillers were happening around the same time most days for at least a month, on and off for a few months or longer or within the same 1-year period?" and "About how old were you the FIRST time SOME of these experiences with painkillers BEGAN to happen around the same time?"

Assessed sociodemographic control variables were age, gender, race/ethnicity, marital status, education level, household income, employment/full-time student status, and region of participant residence.

Participants

Only individuals who endorsed lifetime NMUPO at the wave 1 interview were included in analyses (unweighted n= 1,755). These individuals were most likely to be male (61.9%), between ages 36 and 50, inclusive (39.7%; ages 18 to 25: 25.5%; ages 26 to 35: 21.5%; ages 51 and older: 13.3%) and Caucasian (79.6%; Hispanic/Latino: 7.7%; African-American: 5.7%). Individuals endorsing lifetime NMUPO at wave 1 were also most likely to be either married (44.0%) or never married (31.0%), with a high school degree (29.2%) or some college (37.3%) and currently employed (71.9%; 10.4% are current students).

Of the 1,755 individuals engaged in lifetime NMUPO, 131 developed DSM-IV opioid dependence. The mean age of opioid initiation was 20.4 years and mean age of dependence was 23.1 years. Analyses of weighted cases indicated that individuals with dependence were slightly more likely to be male (54.2%), between ages 36 and 50, inclusive (45.4%; ages 18 to 25: 22.2%; ages 26 to 35: 17.9%; ages 51 and older: 14.4%) and Caucasian (75.1%; Hispanic/Latino: 4.5%; African-American: 5.6%). Also, those individuals were most likely to be married (41.1%), followed by never married (26.0%) or divorced (19.1%) individuals, have completed some college (36.9%; 28.0% had not completed high school and 27.1% completed high school), and currently employed (57.6%; 6.2% are current students). Finally, of those with a lifetime dependence diagnosis, 14 had a lifetime history of heroin use (10.7%) and only one had used heroin in the past year (0.8%).

Data Analysis

Descriptive statistics for all characteristics were analyzed using SAS SURVEYMEANS. Then, the three models (below) used a sequential strategy of design-based logistic regression, followed by Cox regression of proportional hazards. Model 1 included sociodemographic variables and age of NMUPO initiation. Model 2 added psychiatric disorders to the variables in model 1. Finally, model 3 added variables for age of alcohol use

initiation, age of other (non-NMUPO) drug use initiation or a variable capturing whether an individual initiated other, non-NMUPO, drug use. These variables were entered as independent variables in the models, with DSM-IV opioid dependence diagnosis (presence or absence) as the dependent variable in the logistic regressions and time to DSM-IV opioid dependence as the dependent variable in the Cox regressions. To allow unbiased estimation of regression parameters, missing values for age of substance initiation were recoded at the conditional mean, with an indicator variable used to estimate the effect of the missing value. The logistic regressions identified the correlates of dependence among persons engaged in lifetime NMUPO; inclusion in the Cox models was condition upon both a known initiation age and age of initiation of dependence (n= 118). Models censored follow-up time to DSM-IV opioid dependence at 10 years to prevent the influence of extreme outliers from biasing the parameter estimates.[28] All analyses controlled for the 8 sociodemographic variables listed above.

For the logistic regressions, we reported adjusted odds ratios (AORs) with 95% confidence intervals (95% CIs), and for the Cox regressions, we reported adjusted hazard ratios (AHRs) with 95% confidence intervals. Also, we weighted the data, clustered it on primary sampling units, and stratified it appropriately. We used Fischer's scoring algorithm to iteratively estimate regression parameters for logistic regression and employed the Taylor Series approximation, with adjusted degrees of freedom, to estimate variance. We included models only if they evidenced adequate fit and had a significant omnibus regression chi-square value. Analyses were performed in SAS, version 9.4 (Cary, NC).

RESULTS

Effects of Sociodemographics and Age of NMUPO Initiation on Development of and Time to OUD

All results on odds of developing OUD are in the online-only Supplemental Table 4. For sociodemographic factors, older adults (36 to 50-year-old AOR= 1.56, 95%CI= 1.13–2.17; 51 years and older AOR= 2.06, 95%CI= 1.41–3.01), as compared to those aged 18 to 25, and Asian-American or Native American adults (Native American AOR= 2.72, 95%CI= 1.57–4.71; Asian-American AOR= 2.68, 95%CI= 1.53–4.69), as compared to Caucasian adults, were more likely to develop OUD. Widowed individuals were more likely than married participants to develop OUD (AOR= 2.20, 95%CI= 1.40–3.47). Also, individuals who dropped out of high school were more likely to become dependent than those with a high school education (AOR= 1.95, 95%CI=1.33–2.85), and those living in either the southern US (AOR= 1.66, 95%CI= 1.23–2.26) or Midwest (AOR= 1.69, 95%CI= 1.22–2.33) were more likely to develop OUD than those in the northeastern US.

Protective factors (i.e., those associated with lower OUD odds) included completing at least some postgraduate work (AOR= 0.25, 95%CI= 0.11–0.57), current employment (AOR= 0.54, 95% CI= 0.41–0.72), current student status (AOR= 0.45, 95%CI=0.24–0.85) and household incomes at or above US$ 40,000 ($40,000–69,999 AOR= 0.55, 95%CI= 0.40–0.76; $70,000–99,999 AOR= 0.41, 95%CI= 0.21–0.81; $150,000 or more AOR= 0.68, 95%CI= 0.54–0.86), except those with incomes between $100,000 and $149,999.

The outcomes for time to OUD are summarized in Table 1. The following sociodemographic characteristics were associated with more rapid development of OUD: Asian-American or multiracial ethnicity (Asian-American AHR= 1.56, 95%CI= 1.17–2.12; multiracial AHR= 3.15, 95%CI= 1.85–5.33), those who were separated, widowed or co-habitating (versus married adults; separated AHR= 1.67, 95%CI= 1.20–2.33; widowed AHR= 2.36, 95%CI= 1.54–3.63; co-habitating AHR= 1.52, 95%CI= 1.40–1.64), those with household incomes above US$ 100,000 (as compared to those with incomes below $40,000; $100,000–149,999 AHR= 1.19, 95%CI= 1.00–1.42; $150,000 or more AHR= 4.71, 95%CI= 3.01–7.35), and those living in the southern US (as compared to northeastern US residents; AHR= 1.54, 95%CI= 1.13–2.11).

In contrast, these factors were associated with significantly slower OUDdevelopment: older adulthood (as compared to those aged 18 to 25; 36 to 50-year-old AHR= 0.47, 95%CI= 0.29–0.76; 51 years and older AHR= 0.51, 95%CI= 0.36–0.73), Hispanic/Latino or Native American ethnicity (as compared to Caucasians; Hispanic/Latino AHR= 0.38, 95%CI= 0.27–0.53; Native American AHR= 0.47, 95%CI= 0.35–0.63), never married status (as compared to married adults; AHR= 0.78, 95%CI= 0.63–0.97), current employment (AHR= 0.74, 95%CI=0.60–0.90) and residence in the Midwest (as compared to the northeastern US; AHR= 0.74, 95%CI= 0.63–0.89).

Earlier age of NMUPO initiation was associated with increased odds of OUD (AOR= 0.95, 95%CI= 0.94–0.96) but also with slower development of OUD (AHR= 1.05, 95%CI= 1.04–1.06), after controlling for sociodemographic factors.

Effects of Psychiatric Diagnosis and Age of NMUPO Initiation on Development of and Time to OUD

Models of psychiatric and age of initiation variables related OUD odds are summarized in the online-only Supplemental Table 5. After controlling for sociodemographic factors, having a bipolar (AOR= 2.12, 95%CI= 1.53–2.92), anxiety (AOR= 1.80, 95% CI= 1.29–2.52), depressive (AOR= 1.66, 95%CI= 1.14–2.41) or alcohol use disorder (AOR= 3.81, 95%CI= 2.88–5.04) significantly increased the odds of developing OUD among those with a lifetime history of NMUPO. In contrast, those with a non-opioid substance use disorder did not have significantly higher odds of developing OUD (AOR= 1.01, 95%CI= 0.76–1.35). Those with one or more of the seven examined personality disorders also had greater odds of developing OUD (AOR= 1.72, 95%CI= 1.33–2.25). Earlier age of NMUPO initiation also remained a significant predictor of OUD development in this model (AOR= 0.96, 95%CI= 0.95–0.97).

The results for time to OUD in these models are summarized (below) in Table 2. Having an alcohol use or a depressive disorder significantly altered time to OUD. While having an alcohol use disorder was associated with more rapid development of OUD (AHR= 1.97, 95%CI= 1.71–2.28), having a depressive disorder (AHR= 0.77, 95%CI= 0.66–0.90) was associated with significantly slower development of OUD. Having a drug use, anxiety, bipolar or personality disorder did not significantly affect time to OUD. Earlier age of NMUPO initiation remained significantly associated with slower development of OUD in this model (AHR= 1.05, 95%CI= 1.04–1.06).

Effects of Age of Alcohol Use and Other Drug Use Initiation and Age of NMUPO Initiation on Development of and Time to OUD

All results on models evaluating other drug use and age of NMUPO initiation are summarized in the online-only Supplemental Table 6, for odds of OUD, or Table 3, for time to OUD. Earlier age of initiation of other drug use (among initiators; AOR= 0.93, 95%CI= 0.91–0.96) was associated with higher odds of OUD among those engaged in lifetime NMUPO, after controlling for sociodemographic characteristics. Neither age of alcohol use initiation among persons engaged in lifetime alcohol use (AOR= 0.97, 95%CI= 0.93–1.02) nor non-initiation of drug use (AOR= 0.78, 95%CI= 0.56–1.09) were associated with OUD. Earlier age of NMUPO initiation remained significant in this model (AOR= 0.96, 95%CI= 0.95–0.97).

For time to OUD in Table 3, never initiating other drug use was significantly associated with slower development of OUD (AHR= 0.45, 95%CI= 0.39–0.53), and earlier age of NMUPO initiation remained significantly associated with slower development of OUD (AHR= 1.05, 95%CI= 1.04–1.06). Age of alcohol use initiation (AHR= 0.99, 95%CI= 0.96–1.01) and age of drug use initiation (AHR= 1.03, 95%CI= 0.99–1.08) were not associated with time to OUD.

DISCUSSION

Across models, earlier NMUPO initiation was associated with higher odds of OUD, but it was also associated with a slower transition to OUD. These associations were significant even when including sociodemographic characteristics, psychopathology and age of alcohol or drug use initiation in models. Thus, earlier initiation of NMUPO is a robust risk factor for OUD, with a 4 to 5% decrease in odds for every year NMUPO is delayed, but development of OUD somewhat later in life may predispose individuals to develop consequences (i.e., OUD symptoms) more rapidly than younger initiators.

This is consistent with findings in those who use alcohol or marijuana, where those who initiate use earlier are at greater risk for heavy later adolescent and adult use, development of a use disorder and poorer psychosocial outcomes.[29–36] Most saliently, earlier NMUPO initiation is associated with greater odds of later OUD and initiation of heroin use in adolescence.[17,37,38] Our findings lend further weight to the importance of early initiation of use as a key risk factor for the development of later substance use problems. Less research has examined the relationship between age of initiation and time to OUD, with some work finding earlier age of initiation is related to more rapid dependence,[39] and other work finding the opposite.[40] Sex[40,41] and race/ethnicity[39,42] were likely to influence the inconsistent findings, and further work is needed to clarify if these characteristics influence time to OUD in NMUPO.

Many of the significant correlates of OUD were similar to those found in previous work, including lower educational achievement and socioeconomic status and the presence of other psychopathology. Earlier other drug use initiation, while not specifically examined in other work, was associated with greater odds of OUD, as anticipated. One somewhat discrepant finding was that older adults, aged 36 and older, were more likely to have developed OUD.

This, however, was likely to be the result of methodological differences: this work examined lifetime OUD, whereas other studies examined much shorter windows for OUD development.

Interestingly, while psychopathology was a robust correlate of the development of OUD, only having an alcohol use disorder predicted a shorter time to OUD. Conversely, a lifetime depressive disorder diagnosis was associated with longer time to OUD, even while it was associated with increased odds of OUD. Also, higher incomes, while predictive of lower OUD odds, were associated with a more rapid development of OUD among those engaged in NMUPO. The final sociodemographic characteristics to note were that persons of either Native American or Asian-American ethnicity had higher odds of OUD. Notably, though, those of Native American descent had slower transitions to OUD, while those of Asian descent had more rapid transitions to OUD. Further investigation is needed for both findings, as both run contrary to recent US epidemiological data,[43] but our combination of Hawaiian Natives and Pacific Islanders in the Asian-American category may have impacted that outcome, as Hawaiian Natives and Pacific Islanders may have higher rates of NMUPO-related OUD.[43] Nonetheless, these findings may highlight both members of ethnic groups as particularly vulnerable to and NMUPO-related OUD.

Limitations

The most important limitation is the potential for retrospective bias, as participants recalled ages of initiation and DSM-IV opioid dependence onset that may have occurred many years prior. Reliability estimates from the National Survey on Drug Use and Health, which uses a similar measurement for initiation, found good to excellent test-retest reliabilities when ages could have one year of discrepancy.[44] While some misreporting of age of initiation or onset is probable, we believe it is limited in degree and impact. Furthermore, by controlling for current age in the analyses, systematic bias those with longer times since initiation or onset should be mitigated. A second limitation was the use of self-report data, which could lead to inaccurate reporting of psychiatric symptoms. A second limitation is that there is not a consensus definition of NMUPO,[23,45–47] impacting the ability to compare these results with those of other studies with alternative definitions of NMUPO. Also, this was a secondary analysis of previously collected data, so the measures were not specifically designed to meet the aims of this work. Finally, although the response rate of the NESARC is excellent and statistical methods corrected for non-response, bias could have resulted from selective drop-out. Such bias should be minimal, though.[48]

Clinical Implications and Conclusions

These results highlight the importance of earlier age of NMUPO initiation for the development of OUD and the potential for development of more rapid OUD in later NMUPO initiators. With other work linking earlier NMUPO initiation to OUD and a greater likelihood of heroin initiation,[17,37] this work corroborates a need to identify early NMUPO initiators in order to prevent these problematic outcomes; similarly, work that identifies the subgroups of older initiators at risk for rapid development of OUD is also needed. Also echoing previous work, psychopathology was a robust correlate of lifetime OUD, though only having an alcohol use disorder predicted more rapid OUD onset. Intervention programs

in school[49] and community settings should consider screening for earlier initiation of NMUPO, with consideration of a more intensive intervention in younger initiators. Screening in college/university or medical settings may need to concentrate on preventing rapid development of use and consequences. Universal prevention programs[49] may be most efficacious, as they would potentially limit both early NMUPO initiation and the consequent higher odds of OUD, and other drug use and development of other substance use disorders. Such early prevention and intervention could be crucial in limiting the morbidity and mortality associated with the ongoing public health challenge of nonmedical opioid use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Cox Regression Model for Time to Opioid Dependence using Sociodemographics and Age of Opioid Initiation (n = 118)

Characteristic	B	SE	*t*-value	*p*-value	HRs	95% CIs
Age of Opioid Initiation	0.047	0.003	16.94	< 0.001	1.05	1.04–1.06
Young Adults (18–25)	***Reference Group***					
Ages 26–35	−0.014	0.103	−0.14	0.90	0.99	0.74–1.31
Ages 36–50	−0.758	0.012	−4.4	0.011	0.47	0.29–0.76
Ages 51 and older	−0.671	0.127	−5.27	0.006	0.51	0.36–0.73
Male	***Reference Group***					
Female	−0.304	0.057	−5.32	0.006	0.74	0.63–0.86
Caucasian	***Reference Group***					
Hispanic/Latino	−0.975	0.120	−8.12	0.001	0.38	0.27–0.53
Native American	−0.755	0.108	−7.03	0.002	0.47	0.35–0.63
Asian-American	0.454	0.106	4.27	0.013	1.58	1.17–2.12
African-American	−0.096	0.067	−1.43	0.22	0.91	0.75–1.09
Multiracial	1.146	0.190	6.02	0.004	3.15	1.85–5.33
Married	***Reference Group***					
Co-Habitating	0.416	0.029	14.29	0.0001	1.52	1.40–1.64
Widowed	0.859	0.154	5.57	0.005	2.36	1.54–3.63
Divorced	−0.142	0.064	−2.21	0.09	0.87	0.73–1.04
Separated	0.515	0.119	4.32	0.013	1.67	1.20–2.33
Never Married	−0.243	0.077	−3.14	0.035	0.78	0.63–0.97
HS Graduate	***Reference Group***					
HS Dropout	−0.162	0.068	−2.39	0.08	0.85	0.70–1.03
Some College	0.300	0.120	2.50	0.07	1.35	0.97–1.89
College Graduate	−0.045	0.105	−0.43	0.69	0.96	0.71–1.28
Postgraduate Work	−0.121	0.522	−0.23	0.28	0.83	0.21–3.77
Less than 40,000 USD	***Reference Group***					
40,000–69,999 USD	0.174	0.106	1.65	0.18	1.19	0.89–1.60
70,000–99,999 USD	−0.362	0.322	−1.12	0.32	0.70	0.29–1.70
100,000–149,999 USD	0.175	0.062	2.82	0.048	1.19	1.00–1.42
150,000 or more USD	1.549	0.161	9.64	0.0006	4.71	3.01–7.35
Currently Employed	−0.304	0.072	−4.22	0.014	0.74	0.60–0.90
Current Student	0.125	0.180	0.69	0.53	1.13	0.69–1.87
Northeastern US	***Reference Group***					
Midwest	−0.291	0.064	−4.57	0.01	0.75	0.63–0.89
Southern US	0.283	0.096	2.94	0.042	1.33	1.02–1.73
Western US	0.032	0.072	0.44	0.68	1.03	0.85–1.26

Table 2:

Cox Regression Model for Time to Opioid Dependence using Sociodemographics, Age of Nonmedical Opioid Use Initiation and Psychopathology (n = 118)

Characteristic	B	SE	*t*−value	*p*−value	HRs	95% CIs
Age of Opioid Initiation	0.048	0.004	12.87	0.0002	1.05	1.04–1.06
Alcohol Use Disorder	0.679	0.05	13.06	0.0002	1.97	1.71–2.28
Drug Use Disorder	0.078	0.08	1.01	0.37	1.08	0.87–1.34
Depressive Disorder	−0.266	0.06	−4.73	0.01	0.77	0.66–0.90
Anxiety Disorder	−0.059	0.05	−1.09	0.34	0.94	0.81–1.10
Bipolar Disorder	−0.181	0.09	−2.13	0.10	0.83	0.66–1.06
Personality Disorder	0.057	0.06	0.91	0.42	1.06	0.89–1.26
Ages 18–25	***Reference Group***					
Ages 26–35	−0.137	0.11	−1.22	0.29	0.87	0.64–1.19
Ages 36–50	−0.842	0.16	−4.96	0.008	0.44	0.28–0.70
Ages 51 and older	−0.808	0.14	−5.61	0.005	0.45	0.30–0.67
Males	***Reference Group***					
Female	−0.138	0.05	−2.95	0.04	0.87	0.76–0.99
Caucasian	***Reference Group***					
Hispanic/Latino	−0.556	0.12	−4.52	0.01	0.57	0.41–0.81
Native American	−0.744	0.11	−6.81	0.002	0.48	0.35–0.64
Asian-American	0.342	0.13	2.64	0.06	1.41	0.98–2.02
African-American	−0.088	0.07	−1.27	0.27	0.92	0.76–1.11
Multiracial	1.208	0.18	6.68	0.003	3.35	2.03–5.53
Married	***Reference Group***					
Co-Habitating	0.368	0.03	13.86	0.0002	1.44	1.34–1.56
Widowed	1.567	0.19	8.37	0.001	4.79	2.85–8.06
Divorced	−0.102	0.08	−1.36	0.25	0.90	0.73–1.11
Separated	0.518	0.13	4.00	0.02	1.68	1.17–2.41
Never Married	−0.358	0.08	−4.72	0.009	0.70	0.57–0.86
HS Graduate	***Reference Group***					
HS Dropout	−0.222	0.07	−3.22	0.03	0.80	0.66–0.97
Some College	0.217	0.12	1.84	0.14	1.24	0.90–1.73
College Graduate	0.011	0.12	0.09	0.93	1.01	0.73–1.41
Postgraduate Work	−0.027	0.56	−0.05	0.96	0.97	0.20–4.64
Less than 40,000 USD	***Reference Group***					
40,000–69,999 USD	0.111	0.08	1.38	0.24	1.12	0.89–1.40
70,000–99,999 USD	−0.489	0.39	−1.25	0.28	0.61	0.21–1.82
100,000–149,999 USD	0.176	0.08	2.35	0.08	1.19	0.97–1.47
150,000 or more USD	1.580	0.21	7.37	0.002	4.85	2.68–8.80
Currently Employed	−0.270	0.08	−3.28	0.03	0.76	0.61–0.96
Current Student	0.086	0.18	0.49	0.65	1.09	0.67–1.78
Northeastern US	***Reference Group***					

Characteristic	B	SE	*t*−value	*p*−value	HRs	95% CIs
Midwest	−0.419	0.09	−4.71	0.01	0.66	0.51–0.84
Southern US	0.194	0.10	1.98	0.12	1.21	0.93–1.59
Western US	0.009	0.09	0.1	0.92	1.01	0.79–1.28

Table 3:

Cox Regression Model for Time to Opioid Dependence using Sociodemographics, Never Drug Use and Ages of Alcohol Use, Other Drug Use and Nonmedical Opioid Use Initiation (n = 118)

Characteristic	B	SE	*t*−value	*p*−value	HRs	95% CIs
Age of Opioid Initiation	0.047	0.003	15.89	<.0001	1.05	1.04–1.06
Age of Alcohol Initiation	−0.012	0.009	−1.41	0.23	0.99	0.96–1.01
Age of Other Drug Initiation	0.029	0.016	1.83	0.14	1.03	0.99–1.08
Never Other Drug Use	−0.794	0.06	−14.17	0.0001	0.45	0.39–0.53
Ages 18–25	***Reference Group***					
Ages 26–35	−0.074	0.11	−0.65	0.55	0.93	0.68–1.27
Ages 36–50	−0.788	0.19	−4.21	0.014	0.46	0.27–0.76
Ages 51 and older	−0.770	0.12	−6.3	0.003	0.46	0.33–0.65
Males	***Reference Group***					
Female	−0.186	0.06	−3.27	0.03	0.83	0.71–0.97
Caucasian	***Reference Group***					
Hispanic/Latino	−0.619	0.14	−4.55	0.01	0.54	0.37–0.79
Native American	−0.771	0.10	−7.55	0.002	0.46	0.35–0.61
Asian-American	0.432	0.15	2.88	0.045	1.54	1.02–2.33
African-American	−0.006	0.07	−0.08	0.94	0.99	0.83–1.20
Multiracial	1.044	0.19	5.55	0.005	2.84	1.69–4.79
Married	***Reference Group***					
Co-Habitating	0.338	0.04	9.36	0.0007	1.40	1.27–1.55
Widowed	1.427	0.19	7.63	0.002	4.17	2.48–7.01
Divorced	−0.256	0.07	−3.63	0.02	0.77	0.64–0.94
Separated	0.742	0.11	6.71	0.003	2.10	1.55–2.85
Never Married	−0.294	0.07	−4.03	0.02	0.75	0.61–0.91
HS Graduate	***Reference Group***					
HS Dropout	−0.133	0.09	−1.43	0.23	0.88	0.68–1.13
Some College	0.323	0.13	2.5	0.07	1.38	0.97–1.98
College Graduate	−0.123	0.15	−0.84	0.45	0.88	0.59–1.33
Postgraduate Work	0.195	0.50	0.39	0.72	1.22	0.30–4.86
Less than 40,000 USD	***Reference Group***					
40,000–69,999 USD	0.207	0.13	1.59	0.19	1.23	0.86–1.76
70,000–99,999 USD	−0.418	0.33	−1.25	0.28	0.66	0.26–1.67
100,000–149,999 USD	0.191	0.07	2.83	0.047	1.21	1.00–1.46
150,000 or more USD	1.393	0.14	9.86	0.0006	4.03	2.72–5.96
Currently Employed	−0.303	0.09	−3.21	0.033	0.74	0.57–0.96
Current Student	−0.010	0.20	−0.05	0.96	0.99	0.57–1.72
Northeastern US	***Reference Group***					
Midwest	−0.291	0.08	−3.45	0.03	0.75	0.59–0.95
Southern US	0.299	0.08	3.84	0.02	1.35	1.09–1.67
Western US	0.055	0.07	0.81	0.46	1.06	0.88–1.28