A comprehensive multivariate model of biopsychosocial factors associated with opioid misuse and use disorder in a 2017-2018 United States national survey

Francisco Alejandro Montiel Ishino (francisco.montielishino@nih.gov)  
National Institutes of Health  https://orcid.org/0000-0002-2837-726X

Tamika Gilreath  
Texas A&M University College Station

Bonita Salmeron  
National Institutes of Health

Faustine Williams  
National Institutes of Health

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Abstract

Background: Few studies have comprehensively and contextually examined the relationship of variables associated with opioid use. Our purpose was to fill a critical gap in comprehensive risk models of opioid misuse and use disorder in the United States by identifying the most salient predictors.

Methods: A multivariate logistic regression was used on the 2017 and 2018 National Survey on Drug Use and Health, which included all 50 states and the District of Columbia of the United States. The sample included all noninstitutionalized civilian adults aged 18 and older (N=85,580; weighted N=248,008,986). The outcome of opioid misuse and/or use disorder was based on reported prescription pain reliever and/or heroin use dependence, abuse, or misuse. Biopsychosocial predictors of opioid misuse and use disorder in addition to sociodemographic characteristics and other substance dependence or abuse were examined in our comprehensive model. Biopsychosocial characteristics included socioecological and health indicators. Criminality was the socioecological indicator. Health indicators included self-reported health, private health insurance, psychological distress, and suicidality. Sociodemographic variables included age, sex/gender, race/ethnicity, sexual identity, education, residence, income, and employment status. Substance dependence or abuse included both licit and illicit substances (i.e., nicotine, alcohol, marijuana, cocaine, inhalants, methamphetamine, tranquilizers, stimulants, sedatives).

Results. The comprehensive model found that criminality (adjusted odds ratio [AOR]=2.58, 95% confidence interval [CI]=1.98-3.37, p<0.001), self-reported health (i.e., excellent compared to fair/poor [AOR=3.71, 95%CI=2.19-6.29, p<0.001], good [AOR=3.43, 95%CI=2.20-5.34, p<0.001], and very good [AOR=2.75, 95%CI=1.90-3.98, p<0.001]), no private health insurance (AOR=2.12, 95%CI=1.55-2.89, p<0.001), serious psychological distress (AOR=2.12, 95%CI=1.55-2.89, p<0.001), suicidality (AOR=1.58, 95%CI=1.17-2.14, p=0.004), and other substance dependence or abuse were significant predictors of opioid misuse and/or use disorder. Substances associated were nicotine (AOR=3.01, 95%CI=2.30-3.93, p<0.001), alcohol (AOR=1.40, 95%CI=1.02-1.92, p=0.038), marijuana (AOR=2.24, 95%CI=1.40-3.58, p<0.001), cocaine (AOR=3.92, 95%CI=2.14-7.17, p<0.001), methamphetamine (AOR=3.32, 95%CI=1.96-5.64, p<0.001), tranquilizers (AOR=16.72, 95%CI=9.75-28.65, p<0.001), and stimulants (AOR=2.45, 95%CI=1.03-5.87, p=0.044).

Conclusions. Biopsychosocial characteristics such as socioecological and health indicators, as well as other substance dependence or abuse were stronger predictors of opioid misuse and use disorder than sociodemographic characteristics.

Background

Studies by Chen and colleagues[5] and Pitt and colleagues[6] have further revealed that current universal interventions are not enough to address the multidimensional and dynamic aspects of the opioid epidemic. Improving universal opioid prevention strategies to more tailored approaches has been suggested.[7] Non-Hispanic whites, for instance, have become the primary focus for multiple prevention programs and strategies as they have been found to misuse opioid at greater rates.[8-10] However, multiple racial/ethnic groups have been found to be affected by opioid misuse and are at differential risk.[8-10] Other racial/ethnic groups found to experience high disparities in misuse and related outcomes include American Indian/Alaska Natives[8], Asians[11], and Hispanics.[12] As such, these epidemiological studies have revealed a possible racial/ethnic disparity.

Opioid misuse and/or use disorder are also linked to multiple risk factors not limited to race and ethnicity. Scholl et al.[9] revealed a complex relationship between sociodemographic factors and opioid misuse where age was a significant indicator, particularly among
younger age groups. The current opioid misuse and/or use disorder literature has also found that the relationships of race/ethnicity and age are not strong predictors for misuse when considered in the context of other biopsychosocial factors. Other sociodemographic factors like sex/gender must be considered. For instance, Nicholson and Vincent [13] observed that the prevalence of prescription opioid misuse varied among Black women and men. Specifically, Black women with lower socioeconomic status had an increased probability of misuse, while older age, higher educational attainment, and rural residence were associated with a lower probability.[13] Although men have been found to be more likely to misuse opioids at the population level, women in certain cases have been found to be at higher odds of misuse.[14-16] For example, Serdarevic, Striley, and Cottler [15] found women to have higher rates of lifetime prescription opioid use when compared to men.

Other biopsychosocial factors like criminality and sexual identity, although understudied, have been associated with misuse and/or use disorder. Individuals with criminality or involvement with the legal system had a prevalence of 22.4% for prescription opioid use, 33.2% for prescription opioid misuse, 51.7% for prescription opioid use disorder, and 76.8% for heroin use.[17] Similarly, Pierce et al. [18] found that, when adjusting for cocaine use, sex/gender, age, and birth cohort, individuals testing positive for opioid use had higher rates of criminality. Sexual minorities, such as those identifying as gay/lesbian or bisexual, have also been situationally reported to be at risk of opioid misuse.[19-21]. For instance, Duncan et al. [19] found that those identifying as bisexual or gay/lesbian were at 78% or 115% increased odds for opioid misuse than heterosexuals, respectively.

When considering opioid misuse and/or use disorder general health and health access have been found to have a role, although it is not clearly understood outside the context of physical pain or noninstitutionalized populations. Nicholson et al. [13] found that those who identified as being in poor health were more likely to misuse opioids. The relationship between opioid misuse and use disorder in the context of mental health is unclear. Epidemiological studies have not focused solely on the role of mental health indicators such as depression, anxiety, or suicidality. Opioid misuse and/or use disorder have been found to be associated with severe mental illness [22, 23] and suicidality [23-25]. Health insurance has also been identified as having a role in opioid misuse, but the relationship is not well defined. Schatman [26] argues that health insurance companies may perpetuate suboptimal pain management that facilitates opioid misuse whereby health insurance may in turn facilitate opioid misuse. On the other hand, Wettstein [27] observed a dose-response relationship with access to insurance on opioid overdose deaths in which an increase of health insurance coverage among young adults reduced opioid related deaths.

The role of other substance dependence, abuse, and/or misuse, whether legal, illicit, or prescribed, has also been linked to opioid misuse and/or use disorder. Concurrent substance use such as nicotine and tobacco dependence [28, 29], alcohol [30], sedatives [31], methamphetamines [32], tranquilizers [33-35], other analgesics [36], and marijuana [37] have been positively associated with opioid misuse and use disorder [37, 38]. Marijuana may be context dependent as it has a mixed relationship with opioid use, misuse, and use disorder.[39] Medical cannabis use, specifically, has been suggested to reduce opioid use in general, and may also reduce opioid overdose deaths in states with medical cannabis laws.[39]

While epidemiologic studies have examined the relationship of various risk factors on opioid misuse and use disorder among noninstitutionalized populations, comprehensive models are relatively absent. To ameliorate the effect of the opioid epidemic, we must identify the risk factors associated with the etiology of misuse to intervene and prevent the distal events of use disorder like overdose. Secondly, it is crucial to understand biopsychosocial characteristics in the presence of multiple sociodemographic factors and other substance dependence or abuse that underpin the risk profiles of misuse and use disorder at the population-level in order to stem overdose deaths. Biopsychosocial characteristics for our research purposes include socioecological (e.g., criminality) and health factors (e.g., self-reported general health; mental health, suicidality; access to health services). Therefore, to understand what factors are contributing to the increasing opioid epidemic, we comprehensively examined the relationship of opioid misuse and/or use disorder and biopsychosocial characteristics using four domains: (1) sociodemographic factors; (2) socioecological factors; (3) health factors; and (4) other substance dependence or abuse. We took this approach to determine the most salient risk factors for opioid misuse and/or use disorder in a representative, noninstitutionalized US adult sample.

We hypothesized that sociodemographic factors, while crucial to the comprehensive risk model, would not be critical predictors when included with socioecological and health factors, or other substance dependence or abuse. The purpose of this study was to add to a critical gap in the literature to improve population-level prevention strategies by identifying the most salient predictors of opioid misuse and/or use disorder.

**Methods**
We used multivariate logistic regression on the combined 2017[40] and 2018[41] National Survey on Drug Use and Health (NSDUH) to examine the relationship of biopsychosocial characteristics and opioid misuse and/or use disorder. Opioid misuse was characterized as heroin use and/or prescription pain reliever misuse in the past year based on NSDUH definitions.[42] Individuals taking prescribed pain relievers may develop a tolerance to pain relief that can lead to taking the prescription at higher doses and/or more frequently, which would constitute misuse.[42] Furthermore, heroin was included with misuse as any opioid creates the same adverse effects as prescription pain relievers, which in turn may develop into opioid use disorder.[42] Use disorder was characterized by heroin use disorder, prescription pain reliever use disorder, or heroin and prescription pain reliever use disorder as they may not be mutually exclusive in the NSDUH.[42] Biopsychosocial characteristics, as well as sociodemographic and other substance dependence or abuse were tested independently in unadjusted models. Adjusted models were then built using a block entry method to test biopsychosocial characteristics on opioid misuse and/or misuse disorder in the following order: (Model 1) sociodemographic indicators; (Model 2) socioecological indicator; (Model 3) health indicators; and (Model 4) other substance dependence or abuse. All variables were retained as controls and covariates in subsequent models. We accounted for the complex survey design of the NSDUH by the strata and clusters provided, as well as adjusting the analytical weights to account for two years. All analyses were conducted on Stata 16 (StataCorp LLC, College Station, TX). The study received exemption from the Institutional Review Board as no human participants were involved in this research. The analysis was not pre-registered, and the results should be considered exploratory.

Sociodemographic variables and factors. Five age categories were used: (1) 18 to 25; (2) 26 to 34; (3) 35 to 49; (4) 50 to 64; and (5) 65 and older. The binary category of male and female was used for sex/gender. Race/ethnicity was divided into seven categories: (1) non-Hispanic white; (2) non-Hispanic Black/African American; (3) non-Hispanic Native American/Alaska Native; (4) non-Hispanic Native Hawaiian/other Pacific Islander; (5) non-Hispanic Asian; (6) non-Hispanic more than one race; and (7) Hispanic. Sexual identity had three categories: (1) heterosexual; (2) gay/lesbian; and (3) bisexual. Place of residence was based on 2009 Core-Based Statistical Areas (CBSAs) defined by the Office of Management and Budget[43]: (1) CBSA with 1 million or more persons; (2) CBSA with fewer than 1 million persons; and (3) segment not in a CBSA. Total family income was divided into four categories: (1) less than $20,000; (2) $20,000 to $49,999; (3) $50,000 to $74,999; and (4) $75,000 or more. Employment status was divided into five categories: (1) full-/part-time job; (2) unemployed; (3) retired; (4) disabled; and (5) other which included keeping house full time and in school/training. Educational attainment was divided into four categories: (1) less than high school; (2) high school graduate; (3) some college/associate's degree; and (4) college graduate.

Socioecological factors. Criminality was assessed if the participant had been arrested and booked for breaking the law; excluding minor traffic violations. Booked was defined as taken into custody and processed by the legal system, even if later released.

Health factors. Health factors included overall perceived health and having access to private health insurance, and included mental health indicators as well. Overall self-reported health was categorized as: (1) excellent; (2) very good; (3) good; and (4) fair/poor. The private health insurance category was based on if respondent had obtained it through: (1) employment by paying premiums to an insurance company; (2) the Health Insurance Marketplace; or (3) a health maintenance organization (HMO), fee-for-service plans, or single-service plans. Mental health indicators were assessed by severe psychological distress and suicidality. A severe psychological distress indicator within the past year was based on responses from past-month Kessler-6 (K6) items and the worst month in the past-year K6 items. K6 items are from a screening instrument for nonspecific psychological distress developed by Furukawa, Kessler, Slade, and Andrews,[44] and Kessler et al.[45] The K6 measures how frequently participants experience psychological distress during the past 30 days and during a month in the past year where they felt more depressed, anxious, or emotionally stressed than in the past month. Participants who had a score of 13 and above were in severe psychological distress. Suicidality was assessed if at any time in the past year a participant had seriously thought about trying to commit suicide.

Substance misuse, dependence, and/or abuse factors. Opioid misuse and/or use disorder was defined as misuse and/or dependence or abuse of prescription pain relievers and/or heroin use in the past year. Respondents were defined as having past year opioid misuse if they reported heroin use, prescription pain relievers misuse, or both heroin use and prescription pain reliever misuse during this time period based on NSDUH methodology and terminology. Opioid use disorder was classified using the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria for dependence or abuse criteria based on heroin use disorder, prescription pain reliever use disorder, or heroin and prescription pain reliever use disorder in the past year based on NSDUH methodology and terminology [See https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHMethodsSummDefs2018/NSDUHMethodsSummDefs2018.pdf]. Respondents were not counted as having opioid use disorder if they did not meet the full dependence or abuse criteria individually for either heroin or prescription pain relievers. While opioid substance use disorder was classified under the DSM-V, the NSDUH used the DSM-IV criteria of dependence or abuse, as such we opted to use the DSM-V terminology.[15,18] Nicotine dependence in the past month was assessed using Nicotine Dependence Syndrome Scale scores and the Fagerstrom Test of Nicotine Dependence scale in the past month. Alcohol dependence and abuse in the last year was also ascertained. Dependence and abuse in the past year for the following substances
were also determined: marijuana, cocaine, hallucinogens, inhalants, methamphetamine, tranquilizers, stimulants (i.e., independent of methamphetamine), and sedatives.[46]

**Statistical Analysis**

We performed descriptive analyses to detail the characteristics of NSDUH sample participants. We checked the data for normality of the residuals, homoscedasticity, multicollinearity, outliers and influence. After the data were found to be adequate for the logistic regression model, four weighted multivariate models were built using Stata survey procedure. All models were weighted and accounted for clustering and stratification of the complex survey design. All findings are reported in odds ratios (ORs) or adjusted odds ratios (AORs) using a 95% confidence interval (CI) and *p*-value for significance criteria.

**Results**

**Sample Characteristics**

The sample consisted of 85,580 individuals (weighted *N* = 248,008,986) over the age of 18. Male and female participants were represented about equally—48% male (weighted *N* = 119,711,438) and 52% female (weighted *N* = 119,711,438). The majority of the weighted sample was non-Hispanic white (63.6%), resided in a high population density CBSA (54.1%), identified as heterosexual (94.8%), had a family income of $75,000 or more (38.9%), were college graduates (32.1%), were employed (62.7%), had no history of arrest and booking (83.4%), were in very good health (36.1%), had private health insurance (66.6%), had no serious psychological distress in past year (88.6%), and displayed no suicidality (95.7%). See Table 1 for a detailed breakdown of the sample’s characteristics.
Table 1. Descriptive characteristics of biopsychical indicators using the 2017-2018 NSDUH (N=85,580; Weighted N=248,008,986)

|                         | N     | Weighted N       | %    |
|-------------------------|-------|------------------|------|
| **Age Groups**          |       |                  |      |
| 18-25 years old         | 27,477| 34,171,330       | 13.8%|
| 26-34 years old         | 17,580| 39,791,188       | 16.0%|
| 35-49 years old         | 22,902| 61,084,084       | 24.6%|
| 50-64 years old         | 9,935 | 62,285,999       | 25.1%|
| 65 or older             | 7,686 | 50,676,385       | 20.4%|
| **Sex/Gender**          |       |                  |      |
| Male                    | 40,156| 119,711,438      | 48.3%|
| Female                  | 45,424| 128,297,548      | 51.7%|
| **Race/Ethnicity**      |       |                  |      |
| Non-Hispanic White      | 51,704| 157,708,305      | 63.6%|
| Non-Hispanic Black/African American | 10,630 | 29,520,476     | 11.9%|
| Native American/Alaska Native | 1220  | 1,387,749       | 0.6% |
| Native Hawaiian/other Pacific Islander | 417   | 939,268         | 0.4% |
| Non-Hispanic Asian      | 4,190 | 14,061,853       | 5.7% |
| Non-Hispanic more than one race | 2,786 | 4,250,536       | 1.7% |
| Hispanic                | 14,633| 40,140,798       | 16.2%|
| **Area of Residence by Population Density** |       |                  |      |
| Segment in a CBSA > 1 million | 36,272 | 134,292,992    | 54.1%|
| Segment in a CBSA < 1 million | 42,433 | 99,166,152     | 40.0%|
| Segment not in a CBSA   | 6,875 | 14,549,842       | 5.9% |
| **Sexual Identity**     |       |                  |      |
| Heterosexual, i.e., straight | 77,811 | 230,292,107      | 94.8%|
| Lesbian or gay          | 1,884 | 4,774,123        | 2.0% |
| Bisexual                | 4,204 | 7,875,005        | 3.2% |
| **Family Income**       |       |                  |      |
| Less than $20,000       | 16,488| 39,520,535       | 15.9%|
| $20,000-$49,999 99      | 26,460| 72,948,368       | 29.4%|
| $50,000-$74,999 99      | 13,376| 38,994,110       | 15.7%|
| $75,000 or more         | 29,256| 96,545,973       | 38.9%|
| **Level of Education**  |       |                  |      |
| Less than high school   | 10,832| 30,482,047       | 12.3%|
| High school graduate    | 22,532| 61,032,429       | 24.6%|
| Some                    | 28,608| 76,994,245       | 31.0%|
| college/associate’s degree | | |
|---------------------------|--|--|
| College graduate          | 23,608 | 79,500,265 | 32.1% |
| Employment Status (past week) | | |
| Employed full/part-time    | 57,686 | 153,914,559 | 62.7% |
| Unemployed                 | 4,840  | 10,241,227  | 4.2%  |
| Retired                    | 6,329  | 41,374,848  | 16.9% |
| Disabled                   | 3,035  | 11,545,013  | 4.7%  |
| Other                      | 12,717 | 28,404,275  | 11.6% |
| Ever Arrested and Booked   | | |
| No                         | 70,625 | 205,996,442 | 83.4% |
| Yes                        | 14,628 | 41,013,634  | 16.6% |
| Overall Health Status      | | |
| Fair/poor                  | 9,675  | 34,313,374  | 13.8% |
| Good                       | 23,960 | 72,114,751  | 29.1% |
| Very good                  | 32,368 | 89,447,218  | 36.1% |
| Excellent                  | 19,555 | 52,070,096  | 21.0% |
| Covered by Private Health Insurance | | |
| No                         | 30,721 | 82,568,583  | 33.4% |
| Yes                        | 54,422 | 164,350,599 | 66.6% |
| Serious Psychological Distress Indicator (past year) | | |
| No                         | 72,141 | 219,851,056 | 88.6% |
| Yes                        | 13,439 | 28,157,930  | 11.4% |
| Suicidality (past year)    | | |
| No                         | 79,598 | 235,697,531 | 95.7% |
| Yes                        | 5,327  | 10,703,135  | 4.3%  |

Of the sample, 865 individuals (weighted N = 1,976,471) reported opioid misuse. Other substances that the sample had dependence on or abused were nicotine, alcohol, marijuana, cocaine, inhalants, methamphetamine, tranquilizers, stimulants, hallucinogens, and sedatives. See Table 2 for a complete report of the sample’s substance dependence and abuse profile.
Table 2. Descriptive characteristics of substance dependence or abuse from the 2017-2018 NSDUH (N=85,580; Weighted N=248,008,986)

| Substance                        | N      | Weighted N    | %   |
|---------------------------------|--------|---------------|-----|
| **Nicotine dependence (past month)** |        |               |     |
| No                              | 75,397 | 221,362,313   | 89.26% |
| Yes                             | 10,183 | 26,646,673    | 10.74% |
| **Alcohol dependence or abuse (past year)** |        |               |     |
| No/Unknown                      |        |               |     |
| n                               | 79,239 | 133,842,026   | 94.29% |
| Yes                             | 6,341  | 14,166,959    | 5.71% |
| **Marijuana dependence or abuse (past year)** |        |               |     |
| No/Unknown                      |        |               |     |
| n                               | 83,439 | 244,355,720   | 98.53% |
| Yes                             | 2,141  | 36,532,266    | 1.47% |
| **Cocaine dependence or abuse (past year)** |        |               |     |
| No/Unknown                      |        |               |     |
| n                               | 85,147 | 247,063,145   | 99.62% |
| Yes                             | 433    | 945,841       | 0.38% |
| **Inhalant dependence or abuse (past year)** |        |               |     |
| No                              | 85,535 | 247,914,187   | 99.96% |
| Yes                             | 45     | 94,798        | 0.04% |
| **Methamphetamine dependence or abuse (past year)** |        |               |     |
| No                              | 85,146 | 246,985,929   | 99.59% |
| Yes                             | 434    | 1,023,057     | 0.41% |
| **Tranquilizer dependence or abuse (past year)** |        |               |     |
| No                              | 85,260 | 247,362,108   | 99.74% |
| Yes                             | 320    | 646,877       | 0.26% |
| **Stimulant dependence or abuse (past year)** |        |               |     |
| No                              | 85,309 | 247,499,633   | 99.79% |
| Yes                             | 271    | 509,353       | 0.21% |
| **Sedative dependence or abuse (past year)** |        |               |     |
| No                              | 85,519 | 247,855,708   | 99.94% |
| Yes                             | 61     | 153,278       | 0.06% |
| **Opioid dependence or abuse (past year)** |        |               |     |
| No                              | 84,715 | 246,032,515   | 99.20% |
| Yes                             | 865    | 1,976,471     | 0.80% |

Logistic Regression

**Independent unadjusted models.** All sociodemographic and biopsychosocial characteristics, as well as other substance dependence or abuse were tested independently in unadjusted models to examine the relationship of each characteristic on opioid misuse. All characteristics tested with exception of residence at some level were found to be a significant factor predictive of opioid misuse. See Table 3 for all associations.

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Table 3. Odds ratios, 95% confidence intervals, and p-values of independent biopsychosocial indicators and other substance dependence or abuse on opioid misuse: 2017-2018 National Survey on Drug Use and Health

|                          | 95% CI | OR  | Lower | Upper | p-value |
|--------------------------|--------|-----|-------|-------|---------|
| **Age**                  |        |     |       |       |         |
| 18-25 years old          |        | 6.55| 3.10  | 13.83 | 0.000   |
| 26-34 years old          |        | 7.97| 3.77  | 16.84 | 0.000   |
| 35-49 years old          |        | 4.95| 2.33  | 10.52 | 0.000   |
| 50-64 years old          |        | 4.86| 2.35  | 10.04 | 0.000   |
| 65 years and older       | ref.   |     |       |       |         |
| **Sex/Gender**           |        |     |       |       |         |
| Male                     |        | 1.43| 1.14  | 1.80  | 0.003   |
| Female                   | ref.   |     |       |       |         |
| **Race/Ethnicity**       |        |     |       |       |         |
| Non-Hispanic White       |        | 5.15| 2.31  | 11.46 | 0.000   |
| Non-Hispanic Black/African American |             | 3.95| 1.60  | 9.77  | 0.004   |
| Native American/Ale Native |       | 8.64| 3.28  | 22.75 | 0.000   |
| Native Hawaiian/Pacific Islander |       | 3.39| 0.65  | 17.61 | 0.142   |
| Non-Hispanic more than one race |             | 7.48| 2.84  | 19.65 | 0.000   |
| Hispanic                 |        | 3.18| 1.42  | 7.12  | 0.006   |
| Non-Hispanic Asian       | ref.   |     |       |       |         |
| **Sexual Identity**      |        |     |       |       |         |
| Lesbian or gay           |        | 1.21| 0.70  | 2.08  | 0.484   |
| Bisexual                 |        | 2.70| 1.89  | 3.84  | 0.000   |
| Heterosexual, i.e., straight |     | ref.|       |       |         |
| **Educational attainment** |       |     |       |       |         |
| Less than high school    |        | 4.01| 2.54  | 6.34  | 0.000   |
| High school grad         |        | 3.55| 2.30  | 5.49  | 0.000   |
| Some college/associate’s degree |     | 2.75| 1.79  | 4.24  | 0.000   |
| College graduate         | ref.   |     |       |       |         |
| **Family Income**        |        |     |       |       |         |
| Less than $20,000        |        | 3.55| 2.57  | 4.91  | 0.000   |
| $20,000-$49,999          |        | 1.95| 1.44  | 2.64  | 0.000   |
|                              | $50,000-$74,999 | $75,000 or more | Population Density |
|------------------------------|-----------------|-----------------|--------------------|
|                              |                 |                 | Segment in a CBSA > 1 million |
|                              |                 |                 | Segment in a CBSA < 1 million |
|                              |                 |                 | Segment not in a CBSA |
| Employment (past week)        |                 |                 | Employed full/part-time |
| Unemployed                   | 4.23            | 3.11            | 5.76               | 0.000 |
| Retired                      | 0.29            | 0.14            | 0.59               | 0.001 |
| Disabled                     | 4.10            | 2.88            | 5.84               | 0.000 |
| Other                        | 1.85            | 1.44            | 2.37               | 0.000 |
| Arrested and Booked for Breaking the Law | No | ref. | - | - |
| Yes                          | 7.73            | 6.18            | 9.68               | 0.000 |
| Overall Health Status        |                 |                 |                     |
| Fair/Poor                    | 10.70           | 7.25            | 15.78              | 0.000 |
| Good                         | 6.15            | 4.17            | 9.05               | 0.000 |
| Very Good                    | 3.52            | 2.49            | 4.96               | 0.000 |
| Excellent                    | ref.            | -               | -                  |      |
| Serious Psychological Distress in Past Year | No | ref. | - | - |
| Yes                          | 9.15            | 7.55            | 11.08              | 0.000 |
| Suicidality in Past Year     |                 |                 |                     |
| No                           | ref.            | -               | -                  |      |
| Yes                          | 8.14            | 6.61            | 10.04              | 0.000 |
| Private Health Insurance     |                 |                 |                     |
| No                           | ref.            | -               | -                  |      |
| Yes                          | 4.14            | 3.34            | 5.14               | 0.000 |
| Nicotine Dependence (past month) | No | ref. | - | - |
| Yes                          | 10.46           | 8.44            | 12.96              | 0.000 |
| Alcohol Dependence or Abuse (past year) | No/Unknown | ref. | - | - |
| Yes                          | 5.80            | 4.72            | 7.13               | 0.000 |
| Marijuana Dependence or Abuse (past year) | No/Unknown | ref. | - | - |
| Yes                          | 12.82           | 9.33            | 17.62              | 0.000 |
| Cocaine Dependence or Abuse (past year) | No/Unknown | ref. | - | - |
### Adjusted multivariate logistic regression models

Model 1 found that sociodemographic factors such as age, sex/gender, race/ethnicity, sexual identity, educational attainment, family income, and employment status were positively predictive of opioid misuse. In Model 2, we added the socioecological factor of past criminality, which was predictive of opioid misuse, while controlling for sociodemographic factors. In Model 3, health factors such as overall reported health, serious psychological distress in past year, suicidality in the past year, and not having private health insurance were added (while controlling for sociodemographic and socioecological factors) and were predictive of opioid misuse. In Model 4, other substance dependence and abuse were added to the model, which was controlled for sociodemographic, socioecological, and health factors. Model 4 was selected for interpretation.

### Comprehensive model of opioid misuse

Compared to no prior history, having past criminality was a positive predictor of opioid misuse (adjusted odds ratio [AOR] = 2.58, 95% confidence interval [CI]: 1.98-3.37, \( p < 0.001 \)). Overall self-reported health status was associated with opioid misuse when individuals reported fair/poor (AOR = 3.71, 95% CI: 2.19-6.29, \( p < 0.001 \)), good (AOR = 3.43, 95% CI: 2.20-5.34, \( p < 0.001 \)), and very good health (AOR = 2.75, 95% CI: 1.90-3.98, \( p < 0.001 \)) compared to those that reported excellent health. Among individuals with no private health insurance, there was a 2.12 increased adjusted odds (95% CI: 1.55-2.89, \( p < 0.001 \)) of opioid misuse compared to participants with health insurance. Similarly, participants who experienced past serious psychological distress or suicidality had 3.05 adjusted odds (95% CI: 2.20-4.23, \( p < 0.001 \)) and 1.58 odds (95% CI: 1.17-2.14, \( p = 0.004 \)) of opioid misuse, respectively, when compared to those with no history. Participants exhibiting substance dependence or abuse, with the notable exception of inhalants and sedatives, were positively associated with increased adjusted odds of opioid misuse compared to those with no substance dependence or abuse (nicotine: AOR = 3.01, 95% CI: 2.30-3.93, \( p < 0.001 \); alcohol: AOR = 1.40, 95% CI: 1.02-1.92, \( p = 0.038 \); marijuana: AOR = 2.24, 95% CI: 1.40-3.58, \( p = 0.001 \); cocaine: AOR = 3.92, 95% CI: 2.14-7.17, \( p < 0.001 \); methamphetamine: AOR = 3.32, 95% CI: 1.96-5.64, \( p < 0.001 \); tranquilizers: AOR = 16.7, 95% CI: 9.75-28.7, \( p < 0.001 \); stimulants: AOR = 2.45, 95% CI: 1.03-5.87, \( p = 0.044 \)). See Table 4 for more detail.
Table 4. Multivariate logistic regression examining opioid misuse and/or use disorder: 2017-2018 NSDUH

| Model 1 | Model 2 | Model 3 | Model 4 |
| --- | --- | --- | --- |
| Sociodemographic Indicators | Socioecological Indicator | Health Indicators | Other Substance Abuse or Dependence |

| 95% CI | 95% CI | 95% CI | 95% CI | 95% CI | 95% CI | 95% CI | 95% CI | 95% CI |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| AOR | Lower | Upper | p-value | AOR | Lower | Upper | p-value | AOR | Lower | Upper | p-value |
| Age | | | | | | | | | | | |
| 18-25 years old | 4.06 | 1.53 | 10.77 | 0.006 | 4.08 | 1.54 | 10.85 | 0.006 | 2.52 | 0.96 | 6.63 | 0.060 |
| 26-34 years old | 6.65 | 2.55 | 17.30 | 0.000 | 4.58 | 1.74 | 12.11 | 0.003 | 2.88 | 1.12 | 7.43 | 0.029 |
| 35-49 years old | 4.43 | 1.71 | 11.46 | 0.003 | 2.99 | 1.14 | 7.81 | 0.026 | 2.06 | 0.80 | 5.33 | 0.132 |
| 50-64 years old | 3.57 | 1.47 | 8.69 | 0.006 | 2.65 | 1.09 | 6.47 | 0.033 | 2.30 | 0.95 | 5.55 | 0.065 |
| 65 years and older | ref. | - | - | ref. | - | - | ref. | - | - | ref. | - |
| Sex/Gender | | | | | | | | | | | |
| Male | 1.45 | 1.13 | 1.85 | 0.004 | 1.02 | 0.82 | 1.27 | 0.855 | 1.26 | 1.00 | 1.59 | 0.055 |
| Female | ref. | - | - | ref. | - | - | ref. | - | - | ref. | - |
| Race/Ethnicity | | | | | | | | | | | |
| Non-Hispanic White | 4.31 | 1.89 | 9.84 | 0.001 | 3.16 | 1.37 | 7.33 | 0.008 | 2.87 | 1.18 | 6.97 | 0.021 |
| Non-Hispanic Black/African American | 1.90 | 0.72 | 5.00 | 0.189 | 1.40 | 0.53 | 3.74 | 0.493 | 1.46 | 0.52 | 4.09 | 0.463 |
| Native American/Alaskan Native | 3.87 | 1.47 | 10.19 | 0.007 | 2.49 | 0.93 | 6.63 | 0.067 | 2.53 | 0.91 | 7.01 | 0.074 |
| Native Hawaiian/Pacific Islander | 1.66 | 0.31 | 8.88 | 0.547 | 1.55 | 0.30 | 7.98 | 0.592 | 1.47 | 0.27 | 7.95 | 0.647 |
| Non-Hispanic | 4.60 | 1.87 | 12.67 | 0.004 | 2.99 | 1.04 | 8.63 | 0.043 | 2.40 | 0.79 | 7.27 | 0.119 |

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| Sexual Identity | Less than high school | High school grad | Som e college/associate’s degree | College graduate | Popul ation Dens ity of Residence |
|-----------------|-----------------------|-----------------|--------------------------------|----------------|----------------------------------|
| Lesbian or gay   | 1.96 1.36 2.81 0.001  | 2.59 1.65 4.05 0.000 | 2.08 1.32 3.26 0.002 | ref. - - - | ref. - - - |
| Bisexual        | 1.04 0.59 1.83 0.887  | 1.15 0.79 1.67 0.450 | 1.18 0.81 1.71 0.392 | ref. - - - | ref. - - - |
| Heterosexual, i.e., straight | ref. - - - | ref. - - - | ref. - - - | ref. - - - | ref. - - - |

| Educational Attainment | Less than high school | High school grad | Som e college/associate’s degree | College graduate | Popul ation Dens ity of Residence |
|------------------------|-----------------------|-----------------|--------------------------------|----------------|----------------------------------|
| Hispanic                | 1.56 0.69 3.55 0.281  | 1.40 0.60 3.24 0.425 | 1.34 0.56 3.19 0.506 | 1.38 0.55 3.46 0.486 |
| Non-Hispanic Asian      | ref. - - - | ref. - - - | ref. - - - | ref. - - - |
| Non-Hispanic Asian      | ref. - - - | ref. - - - | ref. - - - | ref. - - - |
| Non-Hispanic Asian      | ref. - - - | ref. - - - | ref. - - - | ref. - - - |
| Population Density of Residence | ref. - - - | ref. - - - | ref. - - - | ref. - - - |

| **Sexual Identity** | **Lesbian or gay** | **Bisexual** | **Heterosexual, i.e., straight** |
|---------------------|-------------------|-------------|-------------------------------|
| He                  | 1.04 0.59 1.83 0.887 | 1.96 1.36 2.81 0.001 | ref. - - - |
| Female              | 1.00 0.56 1.79 0.830 | 1.75 1.24 2.48 0.002 | ref. - - - |
| Missing             | ref. - - - | ref. - - - | ref. - - - |

| **Educational Attainment** | **Less than high school** | **High school grad** | **Some college/associate’s degree** | **College graduate** | **Population Density of Residence** |
|---------------------------|--------------------------|----------------------|-----------------------------------|----------------------|-------------------------------------|
| Hispanic                  | 1.56 0.69 3.55 0.281     | 1.40 0.60 3.24 0.425 | 1.34 0.56 3.19 0.506             | 1.38 0.55 3.46 0.486 |
| Non-Hispanic Asian        | ref. - - -                | ref. - - -           | ref. - - -                        | ref. - - -           |
| Non-Hispanic Asian        | ref. - - -                | ref. - - -           | ref. - - -                        | ref. - - -           |
| Non-Hispanic Asian        | ref. - - -                | ref. - - -           | ref. - - -                        | ref. - - -           |
| Population Density of Residence | ref. - - - | ref. - - - | ref. - - - | ref. - - - |
### Income

| Income Level | Mean | SD  | Median | P-value |
|--------------|------|-----|--------|---------|
| Less than $20,000 | 2.24 | 1.53 | 3.28 | 0.000 |
| $20,000-$49,999 | 1.58 | 1.13 | 2.21 | 0.009 |
| $50,000-$74,999 | 1.32 | 0.91 | 1.92 | 0.145 |
| $75,000 or more | ref. | ref. | ref. | ref. |

### Employment Status

| Status                  | Mean | SD  | Median | P-value |
|-------------------------|------|-----|--------|---------|
| Unemployed              | 3.02 | 2.17 | 4.21 | 0.000 |
| Retired                 | 0.71 | 0.28 | 1.84 | 0.478 |
| Disabled                | 2.68 | 1.67 | 4.30 | 0.000 |
| Other                   | 1.58 | 1.17 | 2.14 | 0.003 |

### Overall Health

| Quality    | Mean | SD  | Median | P-value |
|------------|------|-----|--------|---------|
| Fair/poor  | 4.58 | 2.89 | 7.26 | 0.000 |
| Good       | 4.06 | 2.76 | 5.96 | 0.000 |
| Very good  | 2.94 | 2.07 | 4.16 | 0.000 |
| Excellent  | ref. | ref. | ref. | ref. |
| No private health insurance | 2.29 | 1.73 | 3.04 | 0.000 |

### Serious Psychological Distress

| Distress | Mean | SD  | Median | P-value |
|----------|------|-----|--------|---------|
| 4.20     | 3.25 | 5.44 | 0.000  |

### Suicide in Past Year

| Year | Mean | SD  | Median | P-value |
|------|------|-----|--------|---------|
| 2.14 | 1.64 | 2.79 | 0.000  |

### Nicotine Dependence

| Nicotine Dependence | Mean | SD  | Median | P-value |
|---------------------|------|-----|--------|---------|
| 3.01                | 2.30 | 3.93 | 0.000  |
| Substance                  | Adjusted Odds Ratio (AOR) | 95% Confidence Interval (CI) | p-value |
|---------------------------|---------------------------|-----------------------------|---------|
| Alcohol Dependence or Abuse | 1.40                      | 1.02 1.92                   | 0.038   |
| Marijuana Dependence or Abuse | 2.24                      | 1.40 3.58                   | 0.001   |
| Cocaine Dependence or Abuse | 3.92                      | 2.14 7.17                   | 0.000   |
| Inhalant Dependence or Abuse | 1.80                      | 0.23 14.23                  | 0.571   |
| Methamphetamine Dependence or Abuse | 3.32                      | 1.96 5.64                   | 0.000   |
| Tranquilizer Dependence or Abuse | 16.72                     | 9.75 28.65                  | 0.000   |
| Stimulant Dependence or Abuse | 2.45                      | 1.03 5.87                   | 0.044   |
| Sedative Dependence or Abuse | 3.16                      | 0.52 19.21                  | 0.206   |

Notes: ref. = reference group; AOR = adjusted odds ratio; CI = confidence interval

Discussion

Opioid misuse and use disorder prevention strategies and programs must focus on multiple associated misuse factors in the context of the person and their environment to ameliorate the ongoing epidemic. Epidemics do not occur in a vacuum, as such we accounted for the biopsychosocial characteristics associated with opioid misuse in context of sociodemographic factors and substance use. Analyses revealed sociodemographic, socioecological, and health factors, as well as other substance dependence or abuse, were significant biopsychosocial risk factors for opioid misuse. Specifically, we found that socioecological indicators like criminality and health status factors, including serious psychological distress and suicidality, as well as private health insurance were significant risk characteristics.
Nicotine, alcohol, marijuana, cocaine, methamphetamine, tranquilizer, and stimulant substance dependence or abuse were also significant predictors of opioid misuse.

Sociodemographic factors have generally been identified as a definitive risk factors in opioid misuse, and overdose death.[8, 9, 17, 47, 48] In the presence of biopsychosocial factors and other substance abuse we found that sociodemographic characteristics were no longer significant predictors but served as controls for our comprehensive opioid misuse model. Our model further revealed that socioecological and health factors are significant predictors. Examining opioid misuse using nationally representative data, Mojtabai, Amin-Esmaeili, Nejat, and Olfson [49] also found that prescribed-opioid misuse was associated with criminality, mental health distress, and other substance abuse or dependence. Similarly, Grigsby and Howard [37] and found that prescription opioid and polysubstance users had the greatest probability of past-year criminality and mental health distress. Moreover, Prince [23] found that individuals with opioid misuse disorder who had a severe mental illness were at an increased risk of criminality and suicidality. The risk increased between those using only heroin, both heroin and prescription opioids, and all other substance use disorders, in that order.

Other substance dependence or abuse has been associated with opioid misuse based on varying risk factors.[13, 28, 33, 47, 50] In this study, we specifically found that nicotine,[28, 29] alcohol,[28, 30] cocaine,[50] methamphetamine,[32] tranquilizers,[34, 35, 51] other illicit stimulants [20], and marijuana [28] have a positive relationship with opioid misuse and use disorder. The stimulant effect from nicotine, cocaine, methamphetamine, and other illicit stimulants have been stipulated to mitigate the depressive effects of opioids and may increase the “high” effect.[32] Substances such as tranquilizers have been reported to be used to heighten, maintain, and extend the effect of the “high” [34-36], which may explain the elevated odds ratio of 16.7 when compared to all other substance dependence or abuse. Further research would be necessary to capture this context. Tranquilizer dependence and abuse is also of particular note as most opioid overdose reports in the US involved some type of tranquilizer, i.e., benzodiazepine.[52]

Although the present study revealed an increased association of opioid misuse with marijuana compared to non-marijuana users, the relationship in the literature has been mixed. In the cases of marijuana dependence or abuse there is a positive relationship with opioid misuse.[37] A more recent review, however, found that medical marijuana use may decrease the probability of opioid use.[39] Campbell et al. [39] further revealed that medical cannabis laws may slow the increase of opioid overdose deaths in states with medical cannabis laws compared to states with none. Alcohol has been another substance with mixed associations for opioid misuse and use disorder. For instance, Fernandez et al. [30] reported that alcohol dependence or abuse was not associated with opioid misuse. We found, however, in our comprehensive adjusted model that alcohol dependence or abuse was associated with a higher probability for opioid misuse, in line with the findings of Witkiewitz et al. [53] Overall, prevention strategies and prevention programs must focus on both the combined use of legal and illicit substances.

Although comprehensive models can be cumbersome, they provide the ability to examine multiple risk factors in context to understand profiles of misuse and use disorder at a population level. Our study took a comprehensive approach to understand how multiple biopsychosocial characteristics in context relate to opioid misuse and/or use disorder. Since the current opioid crisis is not unlike prior substance use disorder crises of the past, our goal was to provide etiological data that can be used to inform preventive intervention efforts along the continuum from opioid misuse to use disorder. By identifying risk factors within our model, we were able to contextually examine biopsychosocial characteristics to inform future research and prevention strategies to intervene upon opioid use disorder and related distal outcomes for noninstitutionalized US adults.

**Limitations**

To our knowledge, this is the first US population-level study to comprehensively address risk profiles of opioid misuse using the latest national survey data available. Like most surveys of this kind, there are limitations to the NSDUH. The most prominent limitation is the use of self-reported data. These data are subject to the individual participant's bias, truthfulness, recollection, and knowledge. Second, although the data are nationally representative, it is cross-sectional, excludes some subsets of the population, and does not directly account for pain. The NSDUH only targets noninstitutionalized US citizens, so active-duty military members and institutionalized groups (e.g., prisoners, hospital patients, treatment center patients, and nursing home members) are excluded. Thus, if substance use differs between US noninstitutionalized and institutionalized groups by more than 3%, data may be problematic for the total US population.[46] Another issue that may have introduced bias is participant knowledge or lack thereof concerning opioids and other substances.[54] Moreover, heroin is a less commonly used opioid and there are issues in accounting for the true prevalence of this substance use.[54, 55] Finally, the opioid misuse data does not fully account for synthetic opioids like fentanyl.

**Conclusion**
This study provides the most recent and comprehensive risk assessment of possible biopsychosocial characteristics indicative of opioid misuse. Findings provide the population-level risk factors to improve risk assessments and to tailor future interventions to stem and ameliorate the opioid epidemic. For instance, at-risk individuals had a history of criminality, serious psychological distress, suicidality, no private health insurance, and substance dependence or abuse. Individuals, however, are not variables representative of risk factors on an outcome to opioid misuse and/or use disorder. At a population-level analysis, we must acknowledge that results of a person-centered approach such as this work only represent findings based on a population average.[56] More specialized approaches, such as variable-centered ones, are necessary to study specific at-risk groups. Thus, these findings serve as a population-level risk profile using the most recent US nationally-representative data to inform epidemiological trends and possible large-scale interventions.

List Of Abbreviations

AOR Adjusted odds ratio
CBSA Core-based statistical areas
OR Odds ratio
US United States

Declarations

Ethics approval and consent to participate
The study received exemption from the Texas A&M University Institutional Review Board as no human participants were involved in this research.

Consent for publication
Not applicable.

Availability of data and materials
All National Survey on Drug Use and Health datasets analyzed during the current study are available in the Substance Abuse & Mental Health Data Archive (SAMHDA) repository, https://www.datafiles.samhsa.gov/study-series/national-survey-drug-use-and-health-nsduh-nid13517

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
FAMI and TG conceived the study. FAMI designed the study. FAMI acquired, cleaned, managed, and analyzed the data under supervision of TG. All authors interpreted the results. FAMI and BS drafted the manuscript, supervised by TG and FW. TG and FW substantially modified and approved the submitted version of the manuscripts. All authors read and approved the final version of the manuscript. The content is solely the responsibility of the authors and does not necessarily reflect the views of the National Institutes of Health.

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