

Retrospective Study



Factors Associated With Prescription Opioid Abuse and Dependence Among Those Reporting Prescription Opioid Misuse: A Retrospective Cross-Sectional Study

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Background: Prescription opioid misuse is an ongoing epidemic in the United States. Though the number of people misusing prescription opioids is declining, the prevalence of abuse and dependence remains stable. This highlights the need to identify and intervene in factors leading to the escalation of prescription opioid misuse.

Objectives: The aim of this study was to explore the association of prescription opioid-specific misuse factors such as pill source, misuse motivation, and misuse habits with abuse and dependence.

Study Design: A retrospective cross-sectional study.

Setting: Participants in the 2015 to 2018 National Survey on Drug Use and Health (NSDUH) reporting prescription opioid misuse in the past 12 months.

Methods: Simple and multivariable logistic regression were used to estimate the association of prescription opioid-specific misuse factors with prescription opioid abuse and dependence, which were determined by participant responses to screening questions according to DSM-IV criteria.

Results: After multivariable adjustment, prescription opioid abuse was associated with use in greater amounts than prescribed and misuse for 3-19 days in the past month, whereas dependence was associated with use in greater amounts and more often than prescribed, and misuse for 6 or more days in the past month. Initiating misuse in the past year and misuse without one's own prescription in the past year were associated with lower odds of opioid dependence.

Limitations: Only associations and not causal relationships can be claimed between the factors and outcomes. Second, the survey relies on self-reported data, and there is likely both underreporting and overreporting, leading to bias towards the null. The survey target population was civilian, so it excluded individuals living in institutional group quarters such as hospitals, treatment facilities, nursing homes, and prisons. This study does not differentiate between prescription opioids used for acute versus chronic pain.

Conclusions: Study results suggest the importance of the frequency of prescription opioid misuse as a possible risk factor for dependence and emphasize the need to monitor for misuse even in instances of acute pain.

Key words: Opioids, prescription, abuse, dependence, misuse, comorbidities

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Despite significant efforts to curb misuse, non-medical use of prescription opioids remains a significant public health concern in the United States (US) (1,2). Countless policies and programs have been implemented to reduce the availability of prescription opioids over the past several years, and they have started to produce results (3). The prevalence of prescription opioid misuse has decreased from an estimated 4.7% of the US population in 2015 to 3.6% of the population in 2018 (4). However, these efforts have failed to significantly reduce the number of people reporting opioid abuse (OA) and opioid dependence (OD) each year (4).

Prescription OA and OD are critical to consider since they are both associated with an increased risk of opioid-related overdose and mortality, as well as decreased social functioning (5,6). These opioid use disorders also levy a significant societal burden and cost the US economy -an estimated \$78.5 billion in 2013 alone from healthcare and substance abuse treatment expenses, lost productivity, and criminal justice costs (7).

Prescription opioid misuse is but one factor contributing to prescription OA and OD; of the estimated 10 million individuals who misused prescription opioids in 2018, only an estimated 1.7 million (17%) became dependent (4). Thus, it is critical to determine the factors associated with abuse and dependence among those misusing prescription opioids.

Prior studies have revealed several sociodemographic characteristics, as well as physical and mental health comorbidities, associated with increased risk of misusing, abusing, and becoming dependent on prescription opioids (8-11). Chief among these risk factors include younger age, current or previous substance use, current or previous mental health diagnosis, and an increasing number of physical comorbidities (9,12-14). However, there is little research examining more dynamic, prescription opioid-specific misuse factors that could be intervened upon to prevent OA and OD.

The purpose of the current study was to identify factors associated with prescription opioid abuse and dependence among those reporting prescription opioid misuse (OM). This study sought to look beyond the patient demographics and comorbidities known to contribute to opioid use escalation and examine factors and behaviors specific to prescription opioid misuse, such as opioid source and misuse motivation, in a nationally-representative sample. Findings can help inform prescription monitoring practices by increasing awareness of how a patient's potential risk for OA and

OD may change based on certain factors and emphasize screening criteria to better capture high-risk use patterns.

METHODS

Data Source

This study is a cross-sectional analysis of pooled data derived from the 2015 to 2018 National Surveys on Drug Use and Health (NSDUH) (15-18). NSDUH is a nationally representative survey conducted annually by RTI International, an independent non-profit research organization funded by the Substance Abuse and Mental Health Service Administration's (SAMHSA) Center for Behavioral Health Statistics and Quality, and is the leading source for national data and trends in substance use, mental health, and other health-related issues in the United States (19). The target population of the NSDUH survey is non-institutionalized US civilians age 12 and older; subpopulations excluded from the survey include individuals on active military duty or in institutional group quarters including hospitals, treatment facilities, nursing homes, and prisons (20). The NSDUH utilized multistage area probability sampling for each of the 50 states, including the District of Columbia. Data were collected via a combination of computer-assisted personal interviews and computer-assisted self-interviews (20). This survey received approval by RTI International's Institutional Review Board. A de-identified version of the survey data was made available to the public by the Substance Abuse and Mental Health Data Archive (20). There is no patient consent requirement given the deidentified nature of the data. These publicly available data are considered exempt from Institutional Review Board oversight as dictated by Title 45 Code of Federal Regulations (CFRs), Part 46 of the United States, specifically 45 CFR 46.101(b)(4). In accordance with The Health Insurance Portability and Accountability Act of 1996 Privacy Rule, disclosed data are considered de-identified per 45 CFR 164.514(b)(1) through the "Expert Determination" method; this falls under nonhuman subject research as defined by 45 CFR 46.102(e) since we had no interaction with the subjects, and we have no identifiable private information. Institutional Review Board approval was obtained (Mass General Brigham, Protocol #: 2021P002076).

Measures

Participants reporting misuse of prescription opioids in the past 12 months at the time of the survey were extracted from the 2015 to 2018 NSDUH databas-

es. Prescription OM was defined as use in any way not directed by a doctor, including use in greater amounts, more often or longer than directed, and use without one's own prescription. The 2 primary endpoints were prescription opioid abuse in the last 12 months and prescription opioid dependence in the last 12 months. Prescription OA and OD are mutually exclusive measures, determined by participant responses to screening questions accordant with Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria (19).

The independent variables of interest in our regression models included: past year initiation of prescription OM (yes, no); age at first misuse for past year prescription OM initiates (under 25 years of age, 25 years of age and older); opioid use without a prescription in the past 12 months (yes, no); opioid use in greater amounts than prescribed in the past 12 months (yes, no); opioid use more often than prescribed in the past 12 months (yes, no); opioid use in a way other than prescribed in the past 12 months (yes, no); main reason for OM in the past 12 months (to relieve pain, to relax/relieve tension, to experiment, to feel good/get high, for sleep, for emotions, to alter the effect of another drug, because hooked, other reason); source of opioid for last misuse (got/stole from doctor's office, clinic, hospital or pharmacy, got from a friend or relative, got from another source); number of days misused prescription opioids in the past month (1-2 days, 3-5 days, 6-19 days, 20-30 days).

Potential confounding characteristics were also controlled for in multivariable logistic regression. These characteristics included gender (male, female); race (non-Hispanic White, non-Hispanic Black/African American, non-Hispanic Native American/Alaska Native/Native Hawaiian/Other Pacific Islander/Asian, non-Hispanic more than one race, Hispanic); age (12-17, 18-25, 26-34, 35-49, 50-64, 65 and older); education level (no high school diploma, high school diploma, associate's degree, bachelor's degree or more); ever served in armed forces; perceived overall health (excellent, very good, good, fair/poor); employment status (full-time, part-time, unemployed, other); income (less than \$20,000; \$20,000-\$49,999; \$50,000-\$74,999; \$75,000 or more); health insurance (Medicaid/CHIP, Medicare, VA/TRICARE/CHAMPUS/CHAMPVA/Military, Commercial, other); illicit drug use other than marijuana in the past year (yes, no); mental health treatment in the past year (yes, no); non-medical use of other prescription drugs in the past year (yes, no); and residency (metropolitan area, non-metropolitan area).

Statistical Analysis

The association of prescription opioid misuse factors with the odds of prescription opioid abuse or dependence was assessed using simple and multivariable logistic regression. All summary statistics and regression models accounted for the complex NSDUH sampling design via incorporation of weights, stratification, and clustering. Associations are presented as odds ratios with 95% confidence intervals [CI] to quantify the magnitude and direction of the associations and the corresponding precision of these estimates. Factors with 5% or less missing data were included in the multivariable logistic regression model. Statistical analyses were performed using the SURVEYFREQ and SURVEYLOGISTIC procedures in SAS software version 9.4 (SAS Institute, Cary, NC), and forest plots were created using the forest plot package implemented in R software version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) (21).

RESULTS

Sample Characteristics

Of the 226,632 participants surveyed from 2015 to 2018, 11,079 (4.9%) reported misusing prescription opioids in the past year, representing a weighted sample size of 11,218,451. The study population was 53.9% male and 66.5% non-Hispanic white; 70.2% of participants held a high school diploma or less, and 20.7% held a bachelor's degree or more; 50.9% were employed full time, and 8.7% were unemployed; 21.9% reported an annual income less than \$20,000 and 30.9% reported an income of \$75,000 or greater. Complete sample characteristics are shown in Table 1. Of the 11,079 respondents, 401 (3.6%) and 1374 (12.4%) screened positive for prescription OA and OD in the past year, respectively (Table 2). Of those screening positive for prescription OA, 53.2% report being under the age of 25 when they misused prescription opioids for the first time in the past year. Of those screening positive for prescription OD, 56.8% report using without their own prescription in the past 12 months, and 48.6% report receiving their last prescription opioid from a friend or relative.

Unadjusted Analysis

Results of the unadjusted and adjusted analysis using simple and multivariable logistic regression are presented in Table 3. Univariable analysis revealed use of prescription opioids in greater amounts than prescribed in the past 12 months was associated with 1.98

Table 1. Patient characteristics (unweighted sample n = 11,079; weighted sample n = 11,218,451).

Characteristics	Unweighted Frequency N	Weighted Percent %
Gender		
Male	5626	53.9
Female	5453	46.1
Race		
Non-Hispanic White	6790	66.5
Non-Hispanic Black/African American	1262	10.9
Non-Hispanic Native American/Alaska Native or Non-Hispanic Native Hawaiian/Other Pacific Islander or Non-Hispanic Asian	506	3.5
Non-Hispanic More Than One Race	585	2.7
Hispanic	1936	16.4
Age		
12-17 Years Old	1879	7.4
18-25 Years Old	3982	21.7
26-34 Years Old	2309	23.0
35-49 Years Old	2064	24.1
50-64 Years Old	650	18.2
65 Years Old or Older	195	5.6
Education Level		
No High School Diploma	3287	20.6
High School Diploma	5397	50.2
Associate's Degree	803	8.6
Bachelor's Degree or More	1592	20.7
Served in Armed Forces	387	6.1
Perceived Overall Health		
Excellent	778	13.7
Very Good	1827	34.9
Good	1643	32.6
Fair/Poor	797	18.7
Employment Status		
Full-Time	4575	50.9
Part-Time	1498	14.6
Unemployed	995	8.7
Other	2132	25.8
Income		
Less than \$20,000	2770	21.9
\$20,000-\$49,999	3699	31.8
\$50,000-\$74,999	1622	15.3
\$75,000 or more	2988	30.9

Characteristics	Unweighted Frequency N	Weighted Percent %
Health Insurance		
Medicaid/CHIP	3225	23.9
Medicare	523	9.7
VA/TRICARE/CHAMPUS/CHAMPVA/MILITARY	360	3.4
Commercial	5850	55.2
Other	350	15.6
Illicit Drug Use Other Than Marijuana in the Past Year		
Illicit Drug Use Other Than Marijuana in the Past Year	3501	26.2
Mental Health Treatment in the Past Year		
Mental Health Treatment in the Past Year	1264	30.2
Non-Medical Use of Other Prescription Drugs		
Non-Medical Use of Other Prescription Drugs	4201	33.4
Residency		
Metropolitan Area	8828	86.1
Non-Metropolitan Area	2251	13.9

(95% CI: 1.39-2.81) times the odds of OA and 3.78 (95% CI: 3.15-4.54) times the odds of OD. Use in a way other than prescribed (excluding amount and frequency) in the past 12 months was associated with 1.58 (95% CI: 1.03-2.44) times the odds of OA and 1.32 (95% CI: 1.05-1.66) times the odds of OD. Misuse for 3-5 days in the past month versus misuse for zero days was associated with 2.00 (95% CI: 1.22-3.26) times the odds of OA and 1.51 (95% CI: 1.11-2.04) times the odds of OD. Misuse for 6-19 days in the past month was associated with 2.52 (95% CI: 1.38-4.58) times the odds of OA and 5.13 (95% CI: 4.15-6.34) times the odds of OD. Misuse for 20-30 days in the past month was associated with 2.06 (95% CI: 1.05-4.07) times the odds of OA and 9.05 (95% CI: 6.54-12.51) times the odds of OD. Misuse because hooked in the past 12 months was associated with lower odds of prescription OA (OR [95% CI]: 0.16 [0.03-0.94]), but greater odds of OD (OR [95% CI]: 11.99 [6.92-20.78]). Use of prescription opioids more often than directed in the past 12 months was associated with 3.74 (95% CI: 3.07-4.57) times the odds of OD; use to feel good or get high was associated with 1.49 (95% CI: 1.02-2.17) times the odds of OD; use to help with emotions was associated with 2.16 (95% CI: 1.4-3.34) times the odds of OD; and use of opioids acquired from a source other than a doctor, friend or relative was associated with 1.69 (95% CI: 1.24-2.32) times the odds of OD. Misuse initiation in the last year and use without a prescription in the past year were both associated with lower odds of OD (OR [95% CI]: 0.29 [0.22-0.37] and

Risk of Opioid Dependence

Table 2. Factor and outcome prevalence.

unweighted sample n = 11,079; weighted sample n = 11,218,451	Prescription Opioid Abuse		Prescription Opioid Dependence	
	Unweighted N (Weighted %) with outcome	Unweighted N (Weighted %) without outcome	Unweighted N (Weighted %) with outcome	Unweighted N (Weighted %) without outcome
Outcome	401 (3.3)	10678 (96.7)	1374 (13.0)	9705 (87.0)
Factor				
Past Year Initiate for Prescription Opioid Misuse	78 (15.6)	2245 (18.5)	116 (6.7)	2207 (20.1)
Under 25 Years of Age at 1st Misuse for Past Year Prescription Opioid Misuse Initiates	68 (53.2)	13 (46.8)	76 (41.5)	1554 (42.1)
Prescription Opioid Use Without Own Prescription in Past 12 Months	213 (55.1)	6551 (62.0)	816 (56.8)	5948 (62.6)
Used Prescription Opioid in Greater Amounts Than Prescribed in Past 12 Months	117 (34.4)	2093 (21.0)	597 (45.1)	1613 (17.8)
Used Prescription Opioid More Often Than Prescribed in Past 12 Months	81 (21.9)	1467 (15.9)	455 (35.9)	1093 (13.0)
Used Prescription Opioid In a Way Other Than Prescribed in Past 12 Months	114 (32.3)	2346 (23.2)	405 (28.1)	2055 (22.8)
Main Reason Used Prescription Opioid: Not as Prescribed in the Past 12 Months				
To Relieve Pain	60 (45.2)	1431 (45.3)	229 (38.5)	1262 (47.1)
To Relax or Relieve Tension	16 (11.4)	494 (15.3)	52 (6.0)	458 (17.5)
To Experiment	9 (3.1)	139 (2.5)	9 (0.8)	139 (3.0)
To Feel Good or Get High	37 (17.2)	690 (18.0)	146 (21.0)	581 (17.2)
For Sleep	10 (6.0)	187 (5.2)	22 (3.7)	175 (5.6)
For Emotions	22 (13.1)	292 (7.1)	94 (11.2)	220 (6.3)
To Alter Effect of Other Drug	2 (1.5)	40 (1.3)	10 (2.9)	32 (0.9)
Because Hooked	3 (0.7)	137 (4.5)	100 (15.1)	40 (1.5)
Other Reason	4 (1.7)	31 (0.7)	9 (1.0)	26 (0.8)
Source of Prescription Opioids for Last Misuse				
Got/Stole from Dr. Office, Clinic, Hospital, or Pharmacy	60 (37.1)	1482 (37.4)	189 (36.9)	1353 (37.5)
Got From a Friend or Relative	85 (45.8)	2465 (52.1)	274 (46.8)	2276 (52.8)
Got From Another Source	24 (17.2)	560 (10.4)	125 (16.3)	459 (9.8)
Source of Friend/Relative's Prescription Opioids for Last Misuse				
Got/Stole from Dr. Office, Clinic, Hospital, or Pharmacy	33 (85.0)	1325 (85.6)	87 (83.3)	1271 (85.8)
Got From a Friend or Relative	3 (6.0)	202 (10.0)	24 (13.7)	181 (9.6)
Got From Another Source	6 (9.0)	82 (4.4)	6 (3.0)	82 (4.7)
Number of Days Misused Prescription Opioid in the Past Month				
1-2 days	58 (10.3)	1361 (12.0)	126 (7.7)	1293 (4.8)
3-5 days	47 (11.7)	749 (7.1)	123 (7.8)	673 (2.8)
6-19 days	40 (13.2)	601 (6.4)	228 (18.0)	413 (1.9)
20-30 days	20 (6.1)	348 (3.6)	187 (13.8)	181 (0.8)

0.74 [0.6-0.92], respectively). The use of prescription opioids to relax or relieve tension and to experiment were also associated with lower odds of OD (OR [95% CI]: 0.42 [0.27-0.65] and 0.33 [0.12-0.91], respectively).

Adjusted Analysis

After multivariable adjustment, taking prescription opioids at higher doses than prescribed, misusing prescription opioids 3-5 days in the past month, and 6-19

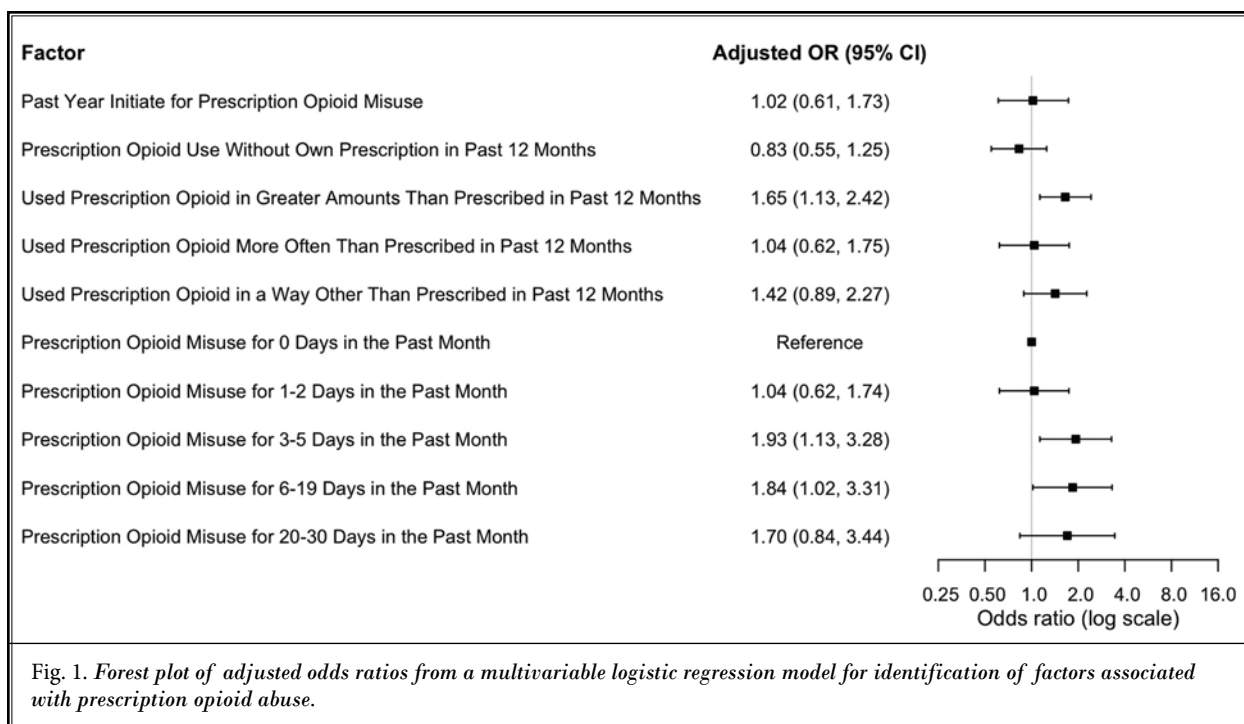
Table 3. Simple and multivariable logistic regression models for identification of factors associated with prescription opioid abuse and dependence.

Factor	Prescription Opioid Abuse		Prescription Opioid Dependence	
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Past Year Initiate for Prescription Opioid Misuse	0.82 (0.5, 1.33)	1.02 (0.61, 1.73)	0.29 (0.22, 0.37)	0.46 (0.35, 0.6)
Under 25 Years of Age at 1st Misuse for Past Year Prescription Opioid Misuse Initiates	1.58 (0.7, 3.59)	-	0.98 (0.62, 1.54)	-
Prescription Opioid Use Without Own Prescription in Past 12 Months	0.75 (0.54, 1.05)	0.83 (0.55, 1.25)	0.79 (0.64, 0.96)	0.74 (0.6, 0.92)
Used Prescription Opioid in Greater Amounts Than Prescribed in Past 12 Months	1.98 (1.39, 2.81)	1.65 (1.13, 2.42)	3.78 (3.15, 4.54)	2.13 (1.67, 2.7)
Used Prescription Opioid More Often Than Prescribed in Past 12 Months	1.49 (0.98, 2.25)	1.04 (0.62, 1.75)	3.74 (3.07, 4.57)	2.07 (1.63, 2.63)
Used Prescription Opioid In a Way Other Than Prescribed in Past 12 Months	1.58 (1.03, 2.44)	1.42 (0.89, 2.27)	1.32 (1.05, 1.66)	0.96 (0.76, 1.22)
Main Reason Used Prescription Opioid Not as Prescribed in the Past 12 Months				
To Relieve Pain	Ref	-	Ref	-
To Relax or Relieve Tension	0.75 (0.37, 1.51)	-	0.42 (0.27, 0.65)	-
To Experiment	1.25 (0.52, 2.98)	-	0.33 (0.12, 0.91)	-
To Feel Good or Get High	0.96 (0.52, 1.76)	-	1.49 (1.02, 2.17)	-
For Sleep	1.17 (0.33, 4.08)	-	0.81 (0.39, 1.71)	-
For Emotions	1.86 (0.87, 3.94)	-	2.16 (1.4, 3.34)	-
To Alter Effect of Other Drug	1.12 (0.19, 6.67)	-	3.87 (0.88, 17.16)	-
Because Hooked	0.16 (0.03, 0.94)	-	11.99 (6.92, 20.78)	-
Other Reason	2.3 (0.48, 11.09)	-	1.2 (0.35, 4.12)	-
Source of Prescription Opioids for Last Misuse				
Got/Stole from Dr. Office, Clinic, Hospital, or Pharmacy	Ref	-	Ref	-
Got From a Friend or Relative	0.89 (0.48, 1.63)	-	0.9 (0.69, 1.17)	-
Got From Another Source	1.66 (0.66, 4.14)	-	1.69 (1.24, 2.32)	-
Source of Friend/Relative's Prescription Opioids for Last Misuse-				
Got/Stole from Dr. Office, Clinic, Hospital, or Pharmacy	Ref	-	Ref	-
Got From a Friend or Relative	0.61 (0.09, 4.01)	-	1.47 (0.76, 2.84)	-
Got From Another Source	2.05 (0.61, 6.95)	-	0.65 (0.19, 2.24)	-
Number of Days Misused Prescription Opioid in the Past Month:				
1-2 days	1.04 (0.63, 1.72)	1.04 (0.62, 1.74)	0.85 (0.62, 1.18)	0.92 (0.66, 1.29)
3-5 days	2.00 (1.22, 3.26)	1.93 (1.13, 3.28)	1.51 (1.11, 2.04)	1.25 (0.89, 1.75)
6-19 days	2.52 (1.38, 4.58)	1.84 (1.02, 3.31)	5.13 (4.15, 6.34)	3.41 (2.66, 4.37)
20-30 days	2.06 (1.05, 4.07)	1.70 (0.84, 3.44)	9.05 (6.54, 12.51)	5.56 (3.79, 8.15)

Note: Only factors with 5% or less missing observations were included in the multivariable logistic regression model.

days in the past month were all associated with greater odds of OA (OR [95% CI]: 1.65 [1.13-2.42], 1.93 [1.13-3.28] and 1.84 [1.02-3.31], respectively) (Fig. 1). Taking prescription opioids at higher doses than prescribed and misusing prescription opioids 6-19 days in the past month were also found to be associated with greater odds of OD (OR [95% CI]: 2.13 [1.67-2.7] and 3.41 [2.66-

4.37], respectively), as was taking prescription opioids more often than prescribed and misusing prescription opioids 20-30 days in the past month (OR [95% CI]: 2.07 [1.63-2.63] and 5.56 [3.79-8.15], respectively). In contrast, initiating prescription OM in the past year and use without a prescription in the past year were both associated with lower odds of OD (OR [95% CI]:



0.46 [0.35-0.6] and 0.74 [0.6-0.92], respectively) (Fig. 2). There were insufficient data to include age at first OM for past year OM initiates, main reason for OM in past 12 months, source of misused prescription opioids, and source of family or friends' opioids for last misuse into the multivariable logistic regression model.

DISCUSSION

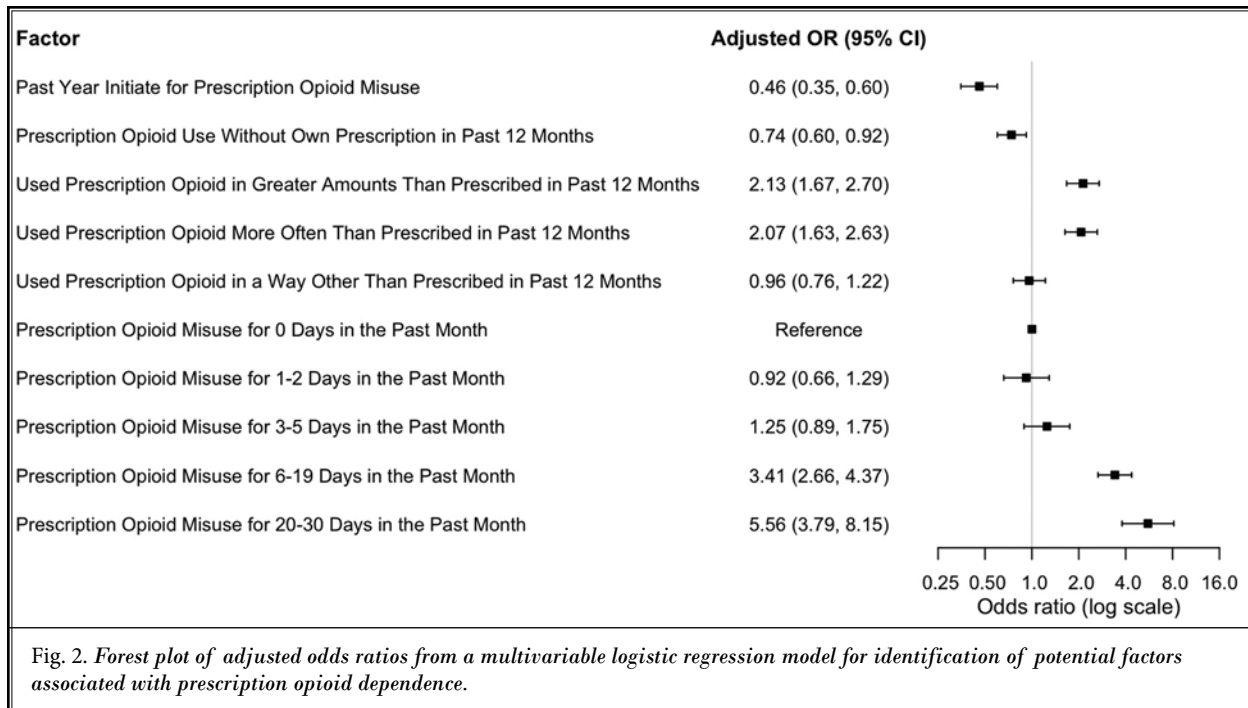
The great personal and societal costs associated with OA and OD necessitate investigation into possible factors associated with this pattern of drug use among those reporting prescription OM (22,23). This is the first study to use combined NSDUH data to assess the association of prescription opioid-specific misuse factors such as prescription source, misuse motivation, and misuse habits with prescription OA and OD.

The findings suggest that the strongest association with prescription OD is the duration of misuse. Adjusting for patient characteristics, the misuse of prescription opioids for 6-19 days is associated with 3.5 times the odds of becoming dependent on prescription opioids, whereas misuse for 20-30 days is associated with over 5.5 times the odds of becoming dependent. These findings are consistent with previous literature examining the association of misuse frequency with opioid use disorder and withdrawal symptoms, including Shah et al's finding that the probability of long-term opioid use

starts to increase after only 3 days of prescription opioid use, and increases substantially after 5 days (24,25).

Even though the 2016 CDC prescribing guidelines and subsequent state opioid prescription limits work toward curbing the availability of prescription opioids, the average duration of opioid prescriptions continues to grow. The average days' supply per prescription has steadily increased from 13.3 days in 2006 to 18.3 in 2018, which is long enough to accommodate high-risk OM (26). It is also possible that refills during this high-risk window of misuse play a role. Studies have found that each additional prescription opioid refill can increase the rate of misuse by nearly 50% when controlling for other variables (25,27). While it is unknown if our subjects were using prescription opioids for acute or chronic pain, it is possible that those with dependence reporting misuse for 6 to 19 days in the past month requested a refill during that time.

While more research is needed to elucidate the exact reasons patients are at increased risk of dependence after 6 to 19 days of misuse, this highlights the need for policies and practices targeted at the reduction of misuse duration. Consistent use of risk assessment monitoring tools such as the Current Opioid Misuse Measure, which asks patients about the duration of OM along with other risk factors, is recommended and should be considered for patients undergoing treat-



ment for acute pain as well since a relatively short duration of misuse can significantly increase the odds of dependence (28). Importantly, misuse duration should be screened in conjunction with other psychosocial and genetic risk factors, as it represents just one screening component of what should be a multi-faceted approach to opioid dependence risk reduction (23,29).

There was also a strong correlation between the misuse of prescription opioids in greater amounts and at more frequent intervals than prescribed and prescription OD in the past year. It is well-documented in the literature that individuals taking opioids at a high morphine milligram equivalent per day and those taking prescription opioids over a longer duration are at increased risk for developing prescription OD (30-32). While there is little data looking at the effect of these use patterns among those reporting prescription OM, these findings are consistent with the existing literature and confirm that misusing prescription opioids at higher doses and longer durations than prescribed is high-risk.

Interestingly, our study also found that compared to those misusing their own prescription opioids, people misusing opioid prescriptions that are not their own have lower odds of OD. In other words, those misusing opioids obtained through a legal prescription have higher odds of dependence than those obtaining opioids solely through illicit means after adjusting for

confounders. It is likely that those with their own prescription have access to a larger and more stable supply of opioids for potential misuse and thus are at greater risk of dependence. It is unclear if those misusing their own prescription do so during an active care episode or misuse their unused opioids from a prior prescription at a later date when there is less clinician oversight. More investigation is required to understand these use patterns. However, this highlights an opportunity for physicians to either further refine their opioid prescribing practices so as to reduce unused opioids, or to integrate improved monitoring practices to quickly identify and intervene in patients misusing opioid prescriptions to prevent dependence.

Our univariable analysis showed that certain motivations for prescription OM are associated with prescription OD in the last year, whereas some are protective. Gathering enough data to include this in a multivariable analysis could lend insight into the risk associated with motivation for misuse versus past medical history or comorbidities. For example, opioids may cause short-term improvement in mood, and qualitative research has identified self-medication of emotional pain (i.e., pain that generates from a non-physical source) to be a leading cause of prescription OM and OD (33,34). Understanding the association between dependence and the misuse of prescription opioids for emotional regulation, absent confounders

like concurrent mental health treatment, would help providers properly address motivations for misuse and decrease the odds of dependence (35). Thus, further investigation into motivation for misuse is warranted.

As for prescription opioid abuse in the past year, our analysis revealed that it was associated with misusing opioids in greater amounts than prescribed and misusing for 3 to 19 days in the past 30 days. Because the rewarding effects of opioids are best achieved through rapid administration of large doses, the finding that misuse of opioids in large amounts is associated with abuse is consistent with the physiologic incentives for abuse (36). As compared to dependence, the duration of misuse associated with higher odds of abuse is shorter, likely because those who are dependent on opioids are compelled to continue to misuse opioids for an extended period of time to avoid withdrawal symptoms (33).

There are limitations of this study that deserve mention. First, because this is a cross-sectional analysis, only associations and not causal relationships can be claimed between the factors and outcomes. Second, because the survey relies on self-reported data, the information collected depends on respondents' truthfulness and accurate recall. While the survey was designed to mitigate this, there is likely both underreporting and overreporting, leading to bias towards the null. As DSM-IV criteria were used rather than DSM-V, this may have led to an overestimation of reported abuse and dependence. Third, the survey target population was civilian, so it excluded individuals living in institutional group quarters such as hospitals, treatment facilities, nursing homes, and prisons. Because some of these individuals are considered more vulnerable to substance use, the results of this study cannot be generalized to these subpopulations. Finally, this study does not differentiate between prescription opioids used for acute versus chronic pain. The literature suggests that the prescription OD rate is higher among those misusing prescription opioids intended for chronic pain, so further investigation is needed to determine how these opioid-specific factors might vary between those using

prescription opioids acutely versus chronically (37).

Nonetheless, this study has important implications for clinical practice. The finding that patients who misuse opioids typically misuse their own prescription emphasizes further opportunity for intervention at the provider level through enhanced counseling (coping skills, identifying negative thoughts and behaviors, patient and family education), and risk screening, even for acute episodes. Risk screening tools like the Opioid Risk Tool and Current Opioid Misuse Measure have proven effective in identifying potentially high-risk patients for OD in the context of chronic opioid use, though further investigation would be needed to optimize these tools for acute pain applications (28,38). Furthermore, the finding that prescription OD is directly associated with the duration of misuse highlights the need to implement procedures to decrease prescription duration through interventions like in-person evaluations prior to refills or opioid-sparing clinical pathways. Several pilot interventions have seen success in reducing the dose and duration of post-operative opioid prescriptions (39,40). For example, Hallway et al directed patients to take acetaminophen and ibuprofen with a prescribed opioid for breakthrough pain; 50 percent of patients reported no opioid use for procedures that historically received up to 40 tablets, with comparable pain control and satisfaction (39). While most opioid-sparing research is perioperative, similar approaches have been successful in the emergency department. For example, Chang et al found that ibuprofen and acetaminophen were just as effective as acetaminophen and an opioid for acute extremity pain (41). Further consideration should be given to novel approaches like these to decrease the risk of extended OM and thus OD.

Given the extent of the opioid epidemic in the United States and the consequences of prescription OA and OD, it is important to be able to identify those misusing opioids at high risk of OA and OD. This study has important findings that elucidate prescription opioid-specific misuse factors and can be used to inform the development of more effective prevention and monitoring programs.

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