



Short communication

The association between frequency of opioid misuse and opioid use disorder among youth and adults in the United States

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ABSTRACT

Background: Studies have shown the frequency of drug misuse is important in the development of a substance use disorder, but little is known about this relationship in the context of opioid misuse and opioid use disorder and withdrawal symptoms.

Methods: Our study included 2694 civilian respondents from the United States 12 years and older who had misused prescription opioids in the past year from the 2014 National Survey on Drug Use and Health. Logistic regression was used to model the association between frequency of prescription opioid misuse and opioid use disorder and withdrawal symptoms, adjusting for age, sex, race/ethnicity, and income level.

Results: Misusing prescription opioids more frequently was significantly associated with opioid use disorder in a dose-dependent manner (daily misuse: OR = 14.92, 95% confidence interval (CI) 9.29, 23.95; 1–2 days/week: OR = 4.46 95% CI: 2.52, 7.89); 1–4 times/month: OR = 2.40, 95% CI: 1.37, 4.18) compared to use less than 1 time a month. OR = 2.89, 95% CI 1.90, 4.40, respectively) after controlling for sex, age, race/ethnicity, and income. A dose-dependent relationship was found between frequency of opioid misuse and withdrawal symptoms (daily misuse: OR = 2.89, 95% CI: 1.90, 4.40; 1–2 times/week: OR = 1.91, 95% CI: 1.05, 3.45; and 1–4 times/month: 1.74, 95% CI: 1.90, 4.40) after controlling for all covariates mentioned above.

Conclusions: Our results provide evidence that higher frequency of opioid misuse is associated with both opioid use disorder and withdrawal symptoms. Frequency of use should be considered in the development of more effective opioid use disorder prevention strategies.

1. Introduction

Opioid use is a growing problem in the United States, with mortality rates due to opioid overdoses more than tripling from 1999 to 2016 (Seth et al., 2018). In 2016, opioid overdoses caused 42,249 deaths and contributed to more than 66% of all fatal drug overdoses (Seth et al., 2018). Not only has legitimate opioid use increased in recent years, but opioid misuse, or use in a way not directed by a prescriber, is also on the rise. In 2017, over 11 million people misused opioids and of these, about 1.7 million or 15% were classified as having an opioid use disorder (OUD) (Substance Abuse and Mental Health Service Administration (SAMHSA), 2018). An OUD is defined as a pattern of opioid misuse that causes significant impairment and distress in an individual and is diagnosed using criteria defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association (APA), 2000).

This study explored the relationship between the frequency of prescription opioid misuse and opioid use disorder, which has not been described in previous studies examining OUD (Parker and Anthony, 2015; Schepis and McCabe, 2016; Salas et al., 2016; Vaughn et al., 2016). Previous research has shown a relationship between the frequency of both marijuana use and alcohol consumption and the development of a use disorder; with increased use being associated with increased risk of dependence (Chen et al., 1997; Grant, 1993). Other studies have shown poorer treatment outcomes are associated with more frequent opioid use (Dreifuss et al., 2013; Edlund et al., 2010). Additionally, differences between demographic groups have been shown, with females developing OUD more quickly than males, black individuals having higher opioid metabolism than white individuals, and opioid misuse being associated with lower income level (Compton et al., 2016; Lee and Ho, 2013; Smith, 2009).

Our study also examined the prevalence of withdrawal symptoms

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among those who misuse prescription opioids. The development of withdrawal symptoms upon the cessation of opioid use is an important indicator of physiological dependence or a “state in which an organism functions normally only in the presence of a drug” (National Institute on Drug Abuse (NIDA, 2007). Research suggests an association between increased drug use and the development of withdrawal symptoms, but this research does not consider frequency of use and instead focuses mostly on the amount of drug used (Amigoni et al., 2014). Limited studies on opioid withdrawal symptoms have found that men report worse and longer-lasting withdrawal symptoms than women hinting at possible demographic differences (Bodnar and Kest, 2010; Lee and Ho, 2013).

The purpose of our study was to assess the association between the frequency of prescription opioid misuse in the last year and OUD, as well as the association between frequency and withdrawal symptoms. These findings will add to the growing body of literature about OUD and can inform future treatment and policy decisions.

2. Materials and methods

2.1. Study sample

Our study sample came from the 2014 National Survey on Drug Use and Health (NSDUH). The NSDUH is administered every year by the Substance Abuse and Mental Health Services Administration (SAMHSA) and uses a face-to-face computer-assisted interview design to ask a nationally representative sample of civilian, noninstitutionalized respondents aged 12 years or older about their use of drugs, mental health status, and basic demographic information. Those with no fixed address, the active military population, and residents of institutional group quarters such as jails and hospitals, are excluded (Substance Abuse and Mental Health Service Administration (SAMHSA, 2015).

This analysis also excludes respondents who have not used prescription pain relievers (referred to as opioids in this study) in the past year, since frequency of opioid misuse, OUD, and withdrawal are only assessed in the past year. Further, we excluded respondents who used opioids for medical reasons only and focused on individuals using opioids defined as 1) using a drug without a prescription or 2) taking the drug only for the experience or feeling it caused (Substance Abuse and Mental Health Service Administration (SAMHSA, 2016). The study sample included 2,694 respondents.

2.2. Study variables

Frequency of use was classified based on respondents' answers to the survey question: “On how many days in the past 12 months did you use any prescription pain reliever that was not prescribed for you or that you took only for the experience or feeling it caused?” We binned responses into: less than one time per month (1–12 days), 1–4 times per month (13–51 days), 1–2 times per week (52–151 days), and near daily or daily use (152–365 days) based on previous studies (Odgers et al., 1997).

OUD was classified by respondents' answers to several survey questions based on the DSM-IV criteria for substance dependence or abuse that assessed withdrawal, tolerance, use in dangerous situations, trouble with the law, and interference with major obligations at work, school, or home (Supplementary Appendix A). If the respondents answered yes to three or more of the dependency questions, they were classified as having substance dependence or if they answered yes to one or more of the abuse questions and weren't already determined to have substance dependence, they were classified as having substance abuse (Substance Abuse and Mental Health Service Administration (SAMHSA, 2016). This study includes individuals with substance dependence or abuse.

Presence of withdrawal symptoms was captured by the survey question: “During the past 12 months, did you have 3 or more of these

symptoms after you cut back or stopped using prescription pain relievers: feeling kind of blue or down, vomiting or feeling nauseous, having cramps or muscle aches, having teary eyes or a runny nose, feeling sweaty, having enlarged eye pupils, or having body hair standing up on your skin, having diarrhea, yawning, having a fever, or having trouble sleeping?”

We assessed confounding of the relationship between frequency of opioid misuse and OUD or withdrawal symptoms by age, race/ethnicity, income level, and sex. Age was binned into the following categories: 12–17 years, 18–25 years, 26–34 years, 35–49 years, and 50+ years. The following categories were used to define race/ethnicity: non-Hispanic white, non-Hispanic black, Native American/Alaska Native, Asian/Pacific Islander, Hispanic, and more than one race. Total household income was categorized as: less than \$20,000 per year, \$20,000–\$49,999 per year, \$50,000–\$74,000 per year, and more than \$75,000 per year. The NSDUH survey was approved by the Institutional Review Board (IRB) at RTI International.

2.3. Statistical analysis

SAS version 9.4 was used to conduct all analyses. Frequency statistics were calculated and chi-square tests were conducted between each covariate and OUD and withdrawal symptoms to look for significant differences between groups. Logistic regression was used to calculate both the crude and adjusted odds ratio of the frequency of opioid misuse and (1) OUD and (2) withdrawal symptoms. We stratified our analysis by each covariate: age, sex, race/ethnicity, and income level. Due to the complex sampling design, analyses were conducted using SAS survey procedures to account for design effects.

3. Results

3.1. Demographic characteristics

There were 2,694 respondents who misused opioids in the last year (Table 1). The prevalence of OUD among those individuals was 17.1%, which equates to about 1.9 million people in the total US population aged 12 and older. There were significant differences in the reporting of OUD by age category and income, but not by sex or race/ethnicity. Of those respondents who misused opioids in the last year, 16.8% of them reported having three or more withdrawal symptoms. There were significant differences in the reporting of withdrawal symptoms by race and income, but not by sex or age.

3.2. Frequency of opioid misuse and OUD

We found a statistically significant relationship between opioid use disorder and the frequency of opioid misuse (Table 2). The frequency of misuse increased the odds of meeting the criteria for OUD in a dose-response manner. Near daily or daily misuse (aOR = 14.92, 95% CI: 9.29, 23.95), misuse 1–2 days per week (aOR = 4.46, 95% CI: 2.52, 7.89) and misuse 1–4 times per month (aOR = 2.40, 95% CI: 1.37, 4.18) had significantly higher odds of OUD than misuse that occurred less than one time a month.

3.3. Frequency of opioid misuse and withdrawal symptoms

We found a statistically significant relationship between having three or more withdrawal symptoms and the frequency of opioid misuse (Table 2). Specifically, we found a dose-dependent relationship between misuse frequency and experiencing withdrawal symptoms. Respondents misusing opioids 1–4 times per month (aOR = 1.74, 95% CI: 1.90, 4.40), 1–2 times per week (aOR = 1.91, 95% CI: 1.05, 3.45) and those using opioids near daily or daily (aOR = 2.89, 95% CI: 1.90, 4.40) all had higher odds of endorsing having three or more withdrawal symptoms than individuals who misuse opioids less than once a month.

Table 1
Prevalence of opioid use disorder and withdrawal symptoms (N = 2694).*

| Characteristic | Opioid Use Disorder [†] | | No Opioid Use Disorder | | Withdrawal Symptoms [‡] | | No Withdrawal Symptoms | | | |
|-----------------------------------|----------------------------------|------|------------------------|------|----------------------------------|-----|------------------------|------|------|----------------------|
| N (%) | 461 (17.1) | | 2233 (82.9) | | 452 (16.8) | | 2242 (83.2) | | | |
| n, weighted | 1,878,056 | | 8,438,521 | | 1,878,056 | | 8,573,806 | | | |
| | N | % | n | % | p-value [§] | n | % | n | % | p-value [§] |
| Sex | | | | | 0.999 | | | | | 0.111 |
| Male | 225 | 48.8 | 1139 | 51.0 | | 203 | 44.9 | 1161 | 43.1 | |
| Female | 236 | 51.2 | 1094 | 49.0 | | 249 | 55.1 | 1081 | 40.1 | |
| Age Category | | | | | 0.001 | | | | | 0.121 |
| 12–17 Years | 86 | 18.7 | 554 | 24.8 | | 107 | 23.7 | 533 | 19.8 | |
| 18–25 Years | 159 | 34.5 | 820 | 36.7 | | 145 | 32.1 | 834 | 31.0 | |
| 26–34 Years | 113 | 24.5 | 393 | 17.6 | | 103 | 22.8 | 403 | 15.0 | |
| 35–49 Years | 67 | 14.5 | 325 | 14.6 | | 71 | 15.7 | 321 | 11.9 | |
| 50 Years or Older | 36 | 7.8 | 141 | 6.3 | | 26 | 5.8 | 151 | 5.6 | |
| Race/Ethnicity | | | | | 0.357 | | | | | 0.022 |
| White | 309 | 67.0 | 1,314 | 58.8 | | 297 | 65.7 | 1326 | 49.2 | |
| Black | 48 | 10.4 | 314 | 14.1 | | 43 | 9.5 | 319 | 11.8 | |
| Hispanic | 57 | 12.4 | 401 | 18.0 | | 71 | 15.7 | 387 | 14.4 | |
| Native American | 13 | 2.8 | 45 | 2.0 | | 11 | 2.4 | 47 | 1.7 | |
| Asian or Pacific Islander | 14 | 3.0 | 58 | 2.6 | | 8 | 1.8 | 64 | 2.4 | |
| More than One | 20 | 4.3 | 101 | 4.5 | | 22 | 4.9 | 99 | 3.7 | |
| Total Household Income | | | | | 0.030 | | | | | 0.033 |
| Less than \$20,000 | 167 | 36.2 | 591 | 26.5 | | 152 | 33.6 | 606 | 22.5 | |
| \$20,000–\$49,999 | 159 | 34.5 | 754 | 33.8 | | 152 | 33.6 | 761 | 28.2 | |
| \$50,000–\$74,999 | 56 | 12.1 | 370 | 16.6 | | 60 | 13.3 | 366 | 13.6 | |
| \$75,000 or more | 79 | 17.1 | 518 | 23.2 | | 88 | 19.5 | 509 | 18.9 | |
| Frequency of Opioid Misuse | | | | | < 0.0001 | | | | | < 0.0001 |
| < 1 time per month | 88 | 19.1 | 1247 | 55.8 | | 111 | 24.6 | 1224 | 54.6 | |
| 1–4 times per month | 82 | 17.8 | 423 | 18.9 | | 86 | 19.0 | 419 | 18.7 | |
| 1–2 days per week | 124 | 26.9 | 404 | 18.1 | | 120 | 26.5 | 408 | 18.2 | |
| Near daily or daily | 167 | 36.2 | 159 | 7.1 | | 135 | 29.9 | 191 | 8.5 | |

* The study sample includes respondents aged 12 and older from the 2014 NSDUH.

[†] Opioid use disorder was defined by answers to survey questions about opioid misuse and is based on past year use.

[‡] Withdrawal symptoms were assessed by a survey question asking about having 3 or more withdrawal symptoms at the same time in the past year.

[§] Pearson’s chi-square test for differences between groups. Statistically significant p-values are bolded.

4. Discussion

4.1. Study significance and implications

This is the first study to use nationally representative data to examine the association between the frequency of prescription opioid misuse and OUD. Increased frequency of opioid misuse was associated with increased odds of OUD. This study also examined misuse frequency and withdrawal; increased frequency of use is associated with a higher likelihood of experiencing withdrawal symptoms.

The findings in this paper highlight the importance that frequency of misuse plays in developing OUD and withdrawal symptoms, indicating that reducing frequency of prescription opioid misuse is a worthy policy goal. The new CDC Guideline for Prescribing Opioids for Chronic Pain indicates that the lowest possible amount of opioid should be prescribed, and urges providers to consider whether opioids are the appropriate treatment for patients in the first place (Dowell et al., 2016).

In addition, this analysis found that while odds of OUD were higher in older adults, the opposite was seen with withdrawal symptoms. All other age groups were less likely to endorse withdrawal symptoms than individuals aged 12–17 years, but the relationship was only statistically significant in those aged 18–25 years. We also found that all adult age categories had higher odds of OUD than those aged 12–17; however, the results were only statistically significantly for those aged 26–34. This finding may be due to the fact that older respondents who misuse opioids may have been misusing for a longer period of time and have had more time to develop an OUD than younger people who misuse. Further, if older adults have been misusing opioids for a longer period of time, they may also need to use a larger dose of opioid to get the

same effect. Further research controlling for duration and amount of opioid misuse could help elucidate this relationship.

We also found that black respondents had lower odds of withdrawal symptoms compared with white respondents; consistent with previous findings that higher opioid metabolism is found among black individuals, compared to white individuals (Smith, 2009).

4.2. Limitations

The NSDUH survey excludes homeless, incarcerated, and institutionalized populations, as well as active military and these populations may be at the greatest risk for prescription opioid misuse. Second, OUD was defined using answers to survey questions and was not based on a psychiatric diagnosis made by a clinician., but any misclassification that occurred is likely non-differential and will bias our results towards the null. Because of the cross-sectional design of this study, prescription opioid misuse and OUD were measured at the same time so we cannot be sure which came first.. However, it is unlikely that one would develop OUD before misusing opioids so we can be relatively certain prescription opioid use preceded the development of OUD.

5. Conclusion

Given the extent of the opioid crisis in the United States, it is necessary to better understand the relationship between frequency of prescription opioid misuse and OUD, as well as frequency of use and withdrawal symptoms. Our research can inform the development of more effective opioid use disorder prevention strategies as well as in the optimization of treatments for opioid use.

Table 2
Adjusted odds of opioid use disorder at varying frequencies of opioid misuse (N = 2694).*

| Risk Factor | Opioid Use Disorder | | | Withdrawal Symptoms | | | | |
|---------------------------------|---------------------|--------|--------|----------------------|------------------|--------|--------|----------------------|
| | aOR [†] | 95% CI | | p-value [‡] | aOR [×] | 95% CI | | p-value [‡] |
| Frequency of Opioid Misuse | | | | | | | | |
| < 1 time per month [‡] | 1.00 | | | | 1.00 | | | |
| 1–4 times per month | 2.40 | (1.37, | 4.18) | 0.003 | 1.74 | (1.04, | 2.91) | 0.035 |
| 1–2 days per week | 4.46 | (2.52, | 7.89) | < 0.0001 | 1.91 | (1.05, | 3.45) | 0.033 |
| Near daily or daily | 14.92 | (9.29, | 23.95) | < 0.0001 | 2.89 | (1.90, | 4.40) | < 0.001 |
| Sex | | | | | | | | |
| Female [‡] | 1.00 | | | | 1.00 | | | |
| Male | 0.87 | (0.64, | 1.20) | 0.390 | 0.75 | (0.50, | 1.12) | 0.158 |
| Age Category | | | | | | | | |
| 12–17 Years Old [‡] | 1.00 | | | | 1.00 | | | |
| 18–25 Years Old | 1.16 | (0.72, | 1.74) | 0.495 | 0.49 | (0.29, | 0.82) | 0.008 |
| 26–34 Years Old | 1.72 | (1.19, | 2.85) | 0.015 | 0.65 | (0.38, | 1.11) | 0.115 |
| 35–49 Years Old | 0.98 | (0.71, | 1.71) | 0.943 | 0.76 | (0.40, | 1.44) | 0.389 |
| 50 Years or Older | 1.67 | (0.93, | 3.02) | 0.084 | 0.53 | (0.27, | 1.04) | 0.064 |
| Race/Ethnicity | | | | | | | | |
| White [‡] | 1.00 | | | | 1.00 | | | |
| Black | 0.85 | (0.41, | 1.55) | 0.598 | 0.35 | (0.18, | 0.65) | 0.003 |
| Hispanic | 0.59 | (0.36, | 1.25) | 0.116 | 0.70 | (0.39, | 1.26) | 0.385 |
| Asian or Pacific Islander | 1.53 | (0.64, | 3.61) | 0.244 | 1.04 | (0.24, | 4.49) | 0.777 |
| Native American | 0.85 | (0.33, | 2.20) | 0.735 | 0.91 | (0.38, | 2.17) | 0.931 |
| More than one Race | 1.34 | (0.61, | 3.33) | 0.398 | 2.00 | (0.98, | 4.09) | 0.012 |
| Total Household Income | | | | | | | | |
| Less than \$20,000 [‡] | 1.00 | | | | 1.00 | | | |
| \$20,000 - \$49,999 | 0.80 | (0.57, | 1.28) | 0.207 | 0.66 | (0.40, | 1.08) | 0.097 |
| \$50,000 - \$74,999 | 0.94 | (0.59, | 1.61) | 0.781 | 0.83 | (0.48, | 1.45) | 0.504 |
| \$75,000 or More | 0.74 | (0.43, | 1.23) | 0.248 | 0.56 | (0.29, | 1.07) | 0.079 |
| Opioid Use Disorder | | | | | | | | |
| No [‡] | | | | | 1.00 | | | |
| Yes | | | | | 14.43 | (9.84, | 21.17) | < 0.001 |

aOR: adjusted odds ratio, CI: confidence interval.

* The study sample includes respondents aged 12 and older from the 2014 NSDUH.

[†] Model adjusted for all other covariates; frequency of opioid misuse, sex, age category, race/ethnicity, and total household income.

[×] Model adjusted for all other covariates; frequency of opioid misuse, sex, age category, race/ethnicity, total household income, and OUD.

[‡] Significant odds ratios are bolded (p-value < 0.05).

[‡] Reference category.

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Kathleen R. Elliott designed the study and carried out the analyses. Kathleen Elliott and Emily Jones drafted the manuscript. All authors approved the final version of the manuscript for submission.

Conflicts of interest

No conflict declared.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.drugalcdep.2019.01.008>.

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