HHS Public Access

Author manuscript

J Addict Dis. Author manuscript; available in PMC 2024 October 01.

Published in final edited form as:

J Addict Dis. 2023 ; 41(4): 266–273. doi:10.1080/10550887.2022.2108287.

Detoxification, 12-Step Meeting Attendance, and Non-Fatal Opioid Overdoses Among a Suburban/Exurban Population with Opioid Use Disorder

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Abstract

Background: Drug overdoses are the leading cause of injury death in the United States with an estimated 105,752 individuals dying from an overdose in the United States in a 12-month period ending October 2021. Given that people who have opioid use disorder (OUD) are at an increased risk of death, it is crucial to assess risk factors associated with opioid overdose to improve interventions.

Objectives: We examine factors associated with non-fatal overdose among a suburban/exurban population with OUD in Southern California.

Methods: Participants were recruited by convenience sampling (n=355) and were interviewed between November 2017 to August 2018. Participants were eligible for the study if they had a history of pharmaceutical opioid use.

Results: A total of 198 (55.8%) participants reported at least one overdose in their lifetime. A total of 229 participants identified as male, 124 identified as female, and 2 identified as non-binary. When controlling for demographic factors, non-oral opioid administration at first opioid use (AOR 2.82, 95% CI 1.52-5.22), having a history of methadone detoxification, (AOR 2.23, 95% CI 1.27-3.91), history of buprenorphine detoxification (AOR 1.77, 95% CI 1.02-3.07), and history of 12 step attendance (AOR 1.89, 95% CI 1.12-3.20) were found to be independently and positively associated with lifetime opioid overdose.

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Conflict of interest: None

Ethics approval

This study was approved by the University of California San Diego's Institutional Review Board on 11/09/2018 (approval number 181654).

Conclusions: Detoxification with buprenorphine and methadone was found to be associated with having a non-fatal opioid overdose. Buprenorphine and methadone should not be prescribed as a detoxification medication as long-term use of medication for OUD results in better outcomes than medication that is used short-term.

Keywords

opioid overdose; risk factors; medication for opioid use disorder

Introduction

Drug overdoses are the leading cause of injury death in the United States[1] and have risen sharply during the COVID-19 pandemic.[2] Provisional data from the CDC estimated 105,752 individuals died from an overdose in the United States in a 12-month period ending October 2021, the highest number of overdose deaths recorded in Unites States history.[3,4] Opioid overdose death rates are increasing at an alarming rate, and those most at risk are people who have opioid use disorder (OUD).

Given that there is an increased risk of death from an opioid overdose among individuals with OUD it is imperative that we assess risk factors associated with an opioid overdose to improve targeted interventions. Previous research has shown an increased risk for an overdose among those who are white, educated, or homeless.[5-9] Furthermore, males tend to be at a greater risk for an overdose than females[10,11] but the research in this area is conflicting[6,7]. For instance, females recently released from jail may be at an elevated risk for an opioid overdose in comparison to males.[6] In addition, the drug used (e.g., prescription drug vs other) might affect the differential risk of overdose among males and females.[7]

Some groups tend to have higher rates of overdose, such as people who were recently released from jail[6] or substance use treatment.[10] Tolerance diminishes rapidly after an opioid is stopped,[12] and individuals who use opioids after periods of abstinence may not reduce their consumption of opioids to a ‘safe dose.’ These changes are likely responsible for the increased risk of overdose following discharge from abstinence-based treatment or jail.[13,14] Additionally, having had a previous opioid overdose[15-16] and/or having been diagnosed with OUD[17] are the strongest predictors of having a fatal drug overdose, making it important to consider risk factors of opioid overdoses so that future and potentially fatal overdoses can be avoided.

Previous research has looked at medication and treatments for opioid use disorder as possible risk factors for an opioid overdose, but the research is limited.[7,9] Schiavon and colleagues, assessed factors associated with having a non-fatal opioid overdose with a high-risk sample. They found that having more buprenorphine treatment episodes was associated with increased odds of having an opioid overdose, and having more methadone treatment episodes was associated with decreased odds of having an opioid overdose.[9] This research is noteworthy because research suggests medication adherence to buprenorphine or methadone reduces the risk of overdose.[18] However, when these medications are stopped overdose risk goes back to baseline.[19] Another study found detoxification, intensive behavioral health, and naltrexone treatments were not related to reduced overdoses at 3 or 12 months but

treatment with buprenorphine and methadone were associated with reduced overdoses at 3 or 12 months.[20] Similarly, buprenorphine but not injectable naltrexone has been found to be significantly related to reduced risk of opioid overdose compared to no treatment.[21] Additionally, a study with a sample of young people found residential drug treatment attendance and detoxification were associated with past-year drug overdose on any drug.[5]

Some forms of abstinence-based approaches such as 12-step programs (e.g., Narcotics Anonymous) may not address the unique needs of individuals on medication for OUD (MOUD)[22] and may contribute to MOUD stigma.[23] Experiencing MOUD stigma in a recovery group may lead some people on MOUD to stop attending groups that provide social support[24] or could lead some people on MOUD to stop medication[23] which could lead to negative outcomes and possibly even overdose death.[25] Therefore, we seek to add to the existing research on risk factors for an overdose and fill gaps in knowledge by explicitly focusing on factors that have been suggested in the literature to increase overdose risk.

The objective of this study is to investigate methadone detoxification, buprenorphine detoxification, injectable naltrexone, and 12 step attendance among participants with OUD. We hypothesize that lifetime history of non-fatal opioid overdose will be associated with having a history of opioid detoxification using methadone, a history of opioid detoxification using buprenorphine, a history of opioid treatment with injectable naltrexone, and a history of 12 step attendance.

Methods

Recruitment

Participants were recruited by referral from community organizations, through snowball sampling,[26] and by attending areas where individuals with OUD frequent (e.g., methadone clinics). Potential participants were asked a few screening questions, and if eligible and still interested, arrangements were made to conduct a one-on-one face-to-face interview. Participants were eligible for the current study if they were 14 years of age or older and misused pharmaceutical opioids in the past 12 months or used heroin in the past 30 days where prior to first heroin use, the participant used pharmaceutical opioids. All study procedures were approved by the Institutional Review Board at the University of California, San Diego. All participants were given a $40 cash incentive for time and travel.

Data collection

The interviewer-administered questionnaire was conducted at a location of the participants' choosing and measured self-reported behaviors. The questionnaire lasted 30 minutes to an hour, and information in multiple domains were asked: Sociodemographic characteristics; substance use history; MOUD history; 12-step history; and opioid overdose history. Opioid use was asked about in a timeline format. Data collection was conducted on tablet computers or cellphones connected to the internet and uploaded to a secure web server. All interviewers were either seasoned quantitative interviewers or were trained by senior staff.

Participants

Data for the current study was acquired between November 2017 and August 2018 in San Diego County, Orange County, and Ventura County. A total of 365 participants took part in the study, as 10 were excluded from the final analysis because they were missing data across the opioid timeline (n = 3), they never misused prescription opioids or never used heroin (n = 3), or the interviewer had no confidence in their responses (n = 4).

Measures

The primary outcome of interest was lifetime non-fatal opioid overdose, where overdose was defined by the following question: “The next questions are about overdosing on heroin or other opioids. Different people have different ideas about what an overdose is. For these questions, we mean only those times when someone loses consciousness, and something had to be done if they were going to come back.” The prompt was designed to provide participants with a clear understanding of what the study investigators considered an overdose to be.

Age, gender, education level, and race/ethnicity were obtained by self-report. Questions regarding gender were open-ended, and three categories were obtained. Education was collapsed into 3 categories (less than high school, high school, and more than a high school). Race/ethnicity categories included Asian, African American, Hawaiian/other Pacific Islander, Hispanic/Latino, Native American/American Indian/Alaska Native, white, and other and were not mutually exclusive. Race/ethnicity was collapsed into two categories (white versus other) for analysis because past research has shown that being white is a risk factor for having an opioid overdose.[9] Using an opioid drug by non-oral methods was constructed by the question, “The first time you took opioids, how did you take them?” The main independent variables of interest were ascertained by asking participants if they ever received drug treatment with methadone detoxification, buprenorphine detoxification, injectable naltrexone (e.g., Vivitrol), and/or 12-steps. Each response option was yes, no, or N/A and duration of treatment was not ascertained.

Data analytic approach

All analyses were performed using SAS version 9.4. Initial descriptive analyses were conducted on all variables of interest. Next, between-group comparisons were conducted using a chi-square test for categorical data and *t*-tests for continuous data at the alpha 0.05 level. Next, a chi-square test was conducted on methadone detoxification, buprenorphine detoxification, and 12-step attendance by lifetime non-fatal opioid overdose. Finally, two multivariate logistic regression models were performed and sociodemographic factors and other factors significant at the alpha .10 level in the bivariate tests were included in the model as covariates except for covariates that were conceptually similar to each other. Prior to all analyses, assumptions for performing logistic regression were performed (e.g., verify there was no violation of the assumption of the linearity of the logit). Hosmer and Lemeshow goodness of fit test was used to assess model fit ($X^2 = 5.62$, df = 8, p>05).[27]

Participants on average were 34.3 years old (SD = 10.53) and ages ranged from 19 to 76 years old. A total of 229 participants identified as male, 124 identified as female, and 2

identified as non-binary. A majority of the sample identified as white only (61%) followed by Latino/Hispanic only (19%), Black/African-American only (4%), Asian/Asian-American only (<1%), and Native American or American Indian or Alaska Native only (2%). The remaining identified as multiracial (12.5%). A total of 46.8% of the sample reported having more than a high school education (see Table 1).

A total of 198 (55.8%) of participants reported at least one overdose in their lifetime (Table 1). The average age of first opioid misuse was 20.3 years old and ranged from 7 to 72 years. On average, participants used opioids for 14 years, and years of use ranged from less than a year to 49 years.

Table 1 presents a comparison between those who had a non-fatal opioid overdose and those who did not on sociodemographic, methadone detoxification, buprenorphine detoxification, injectable naltrexone, 12-step attendance and opioid history. No sociodemographic variables tested were found to be associated with lifetime non-fatal overdose. Initial bivariate analyses showed that injectable naltrexone was not associated with opioid overdose. However, participants who had an opioid overdose in their lifetime were more likely than participants who had not had an opioid overdose in their lifetime to have had a history of methadone detoxification (32.3% vs. 15.29%, p <.01), buprenorphine detoxification (33.8% vs. 20.4%, p <.01), and a history of 12 step attendance (79.3% vs. 63.7, p <.01). Using an opioid drug by non-oral methods at first opioid use (e.g., inhalation versus swallowing) was also significantly associated with having a non-fatal opioid overdose (27.8% vs. 10.83%, p <.01). Younger age at first opioid misuse (19.2 years vs. 21.8 years) was also found to be associated with lifetime opioid overdose (Table 1).

When controlling for demographic factors, non-oral opioid administration at first opioid use (AOR 2.82, 95% CI 1.52-5.22), having a history of methadone detoxification, (AOR 2.23, 95% CI 1.27-3.91), history of buprenorphine detoxification (AOR 1.77, 95% CI 1.02-3.07), and history 12 step attendance (AOR 1.89, 95% CI 1.12-3.20) were found to be independently and positively associated with lifetime opioid overdose (see Table 2).

To assess the cumulative associated overdose risk with variables of interest, we constructed a variable that included methadone detoxification, buprenorphine detoxification, and 12-step attendance. The variable ranged from 0 to 3 with 0 indicating no history of methadone detoxification, buprenorphine detoxification, and/or 12-step attendance and 3 indicating having a history of all three. Injectable naltrexone was not included in the count variable as it was found to not be associated with opioid overdose. Among the 355 participants 77 (21.7%) reported that they have never attended any, 143 (40.3%) reported that they have been to one type, 104 (29.3.8%) reported that they have been to two types, and the remaining 31 (8.7%) reported that they had been to three different types. A significant chi-square test showed an association between the number of variables of interest and opioid overdose, X^2 (3) = 23.5, p< .001. Figure 1 shows the relationship between methadone detoxification, buprenorphine detoxification, and/or 12-step attendance and lifetime opioid overdose.

Discussion

This study shows the association of methadone detoxification, buprenorphine detoxification, 12-step attendance, and opioid administration at first use with lifetime opioid overdose. While some studies have documented the associations between methadone, buprenorphine, and substance use disorder treatment with opioid overdose[5,8,9,29] the association has not been well studied. Thus, our study makes an important contribution to the literature by specifically focusing on variables that have been suggested in the literature to increase overdose risk among individuals with OUD.

Among a suburban/exurban opioid-using population in Southern California, over half reported having had at least one opioid overdose in their lifetime. The high number of reported overdoses in our sample is consistent with the literature,[9,14] and highlights the health risks of opioid use. Our study also found an association between younger age of first opioid misuse and opioid overdose and is consistent with previous findings.[11] For instance, Chang and colleagues found that having a non-fatal opioid overdose was associated with younger age (36.53 vs 39.17).[11] These findings further highlight the need for targeted intervention for younger people who use opioids. Furthermore, how opioids are used (e.g., smoking opioids vs. taking opioids by mouth) is an important factor in predicting overdose risk. For instance, we found using an opioid drug by non-oral methods at first opioid use (e.g., inhalation vs. swallowing pills) was a reliable predictor of having a later opioid overdose. Using an opioid for the first time by any other method except oral administration placed opioid misusers at almost 3 times the risk of experiencing an opioid overdose in their lifetime. These findings seem reasonable given that injection drug use is a reliable predictor of having an opioid overdose in other studies.[8]

Methadone detoxification, buprenorphine detoxification, and 12-step attendance were shown to be associated with lifetime opioid overdose. These results align with other studies.[9,28] For instance, a study conducted in the United Kingdom found that people who inject drugs who recently stopped taking detoxification or a maintenance treatment (as opposed to currently taking or never taking a detoxification/maintenance treatment) were more likely to have had an overdose in the past year.[28] While some studies have shown a potential risk of opioid overdose related to treatment with injectable naltrexone, we did not find this relationship. Our cross-sectional study design may have contributed to these findings, as the risk of opioid overdose for injectable naltrexone may be greatest post-treatment.[29]

The association between 12-step attendance and lifetime opioid overdose may be explained by diminished tolerance after being abstinent from opioids.[12,14] Thus, individuals with OUD who use opioids after being in a 12-step abstinence-based program are at a greater risk for having an opioid overdose. Research has shown that post-prison release is a high-risk time for overdose[13,31,32] and further supports these conclusions. For instance, Ranapurwala and colleagues found that inmates recently released from prison (two weeks post-release) in North Carolina were 40 times more likely to die from an opioid overdose than the general population. They also found that former inmates who had participated in substance use and mental health treatment in prison were at a higher risk of death from an opioid overdose post-release than inmates who did not participate in such treatments.[32] Similarly, stopping

MOUD prematurely may put individuals with OUD at an increased risk for an opioid overdose. MOUD is most effective with longer durations,[33] and risk for opioid overdose is less when buprenorphine is taken for a longer time.[11] These results along with the literature in this area, show how important it is to educate individuals with OUD about their risk for an opioid overdose after leaving abstinent-based substance use treatment, detoxification units, or 12-step programs.

Our study has a few limitations that need to be addressed. Our study used self-reported information, and this could result in recall bias and motivation to present themselves in a more positive light. For instance, we asked participants to report on the first time they misused an opioid, and for some participants, this could have happened 20 years ago. However, drug use was asked in a timeline format to limit recall bias, and all interviewers were trained in an attempt to reduce socially desirable responses. Secondly, our study was cross-sectional, and we are unable to determine when an opioid overdose occurred in relation to methadone detoxification, buprenorphine detoxification, and 12-step attendance. However, we speculate that the relationship is bi-directional. For instance, having a history of methadone detoxification, buprenorphine detoxification, and 12-step attendance, in general, may represent the severity of OUD and subsequent increase in opioid overdose risk. Research has shown that the severity of OUD is associated with non-fatal overdoses.[34] Individuals with OUD who have greater severity of OUD may seek out more treatment options or may seek detoxification more often than individuals with OUD who have less severe OUD. Detoxification attempts and 12-step attendance, therefore, represent the severity of drug use and may further explain why we found an association between methadone detoxification, buprenorphine detoxification, and 12-step attendance with opioid overdose. Finally, the convenience sample and potential lack of representation of all individuals with OUD limit our ability to generalize these findings. However, we recruited from three diverse counties in California in an attempt to reduce selection bias.

Conclusions

The current study furthers our understanding of the risk factors for a non-fatal opioid overdose among a suburban/exurban population in Southern California. Given these results, we believe more focused intervention needs to take place in detoxification programs. For example, providers could provide education at discharge on how to properly respond to an opioid overdose. Additionally, providers could provide naloxone supplies to individuals with OUD leaving detoxification units as these methods have been found to reduce opioid overdose-related mortality.[35,36] Conversely, buprenorphine and methadone should not be prescribed as a detoxification medication as long-term use of MOUD results in better retention rates and outcomes than medication that is used short-term.[37] Furthermore, many patients who participate in medical detoxification programs without later support of MOUD return to drug use soon after.[38-40] Likewise, increasing access to non-12 step or abstinent based recovery support services[41] should be prioritized as 12 step programs may stigmatize people on MOUD.[23] Finally, prospective studies need to be conducted to establish the causal pathways between detoxification, 12-step attendance, and opioid overdose.

Acknowledgments:

The authors of this study would like to acknowledge the participants for devoting their time and energy to this project. We would also like to thank Jen Bowles and Elizabeth Copulsky for conducting the interviews.

Role of funding source:

Research reported in this publication was supported by the National Institute On Drug Abuse of the National Institutes of Health under Award Number R01DA040648, and by the Centers for Disease Control and Prevention Grant number U01CE0022778. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or Centers for Disease Control and Prevention.

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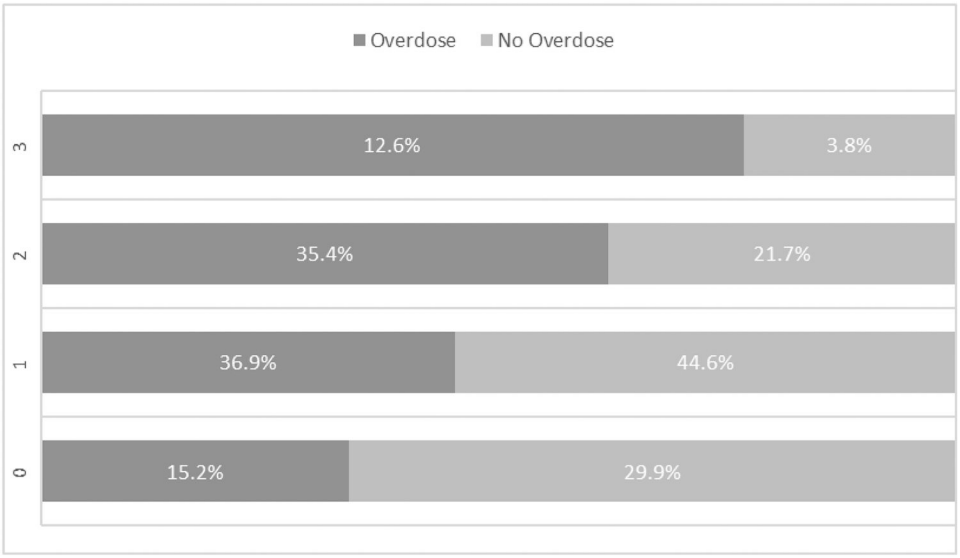

Figure 1. Opioid Overdose by number of conditions experienced

Note: Conditions include methadone detoxification, buprenorphine detoxification, and 12-step attendance.

Table 1

Characteristics of participants and associations with experiencing a non-fatal opioid overdose

	Total n = 355 n (%)	**Nonfatal overdose n = 198 (55.8%) n (%)**	**No nonfatal overdose n = 157 (44.2%) n (%)**	**X^2/t**	**p-value**
Age, M (SD)	34.29 (10.53)	34.07 (10.15)	34.58 (11.03)	0.46	.65
Female	124 (35.1)	72 (36.6)	52 (33.3)	0.39	.53
White	218 (61.4)	120 (60.6)	98 (62.4)	0.12	.73
Education					
Less than high school	73 (20.6)	45 (22.7)	28 (17.8)		
High school or GED	116 (32.7)	71 (35.9)	45 (28.7)		
More than high school	166 (46.8)	82 (41.4)	84 (53.5)	5.14	.07
Non-oral opioid administration at first opioid use	72 (20.28)	55 (27.8)	17 (10.83)	15.56	**<.01**
Age at first opioid misuse, M (SD)	20.3 (8.63)	19.2 (7.32)	21.8 (9.87)	2.86	**<.01**
Years of opioid misuse, M (SD)	13.95 (10.11)	14.87 (10.77)	12.8 (9.12)	1.94	.05
Methadone detoxification	88 (24.8)	64 (32.3)	24 (15.3)	13.63	**<.01**
Buprenorphine detoxification	99 (27.9)	67 (33.8)	32 (20.4)	7.88	**<.01**
Injectable Naltrexone	48 (13.5)	26 (13.1)	22 (14.0)	.06	.81
12-step attendance	257 (72.4)	157 (79.3)	100 (63.7)	10.66	**<.01**

Significant values p<0.05 bolded.

Table 2

Multivariate logistic regression model for ever having had an opioid overdose (n = 355)

	OR (95% CI)	AOR (95% CI)
Education (Reference high school)		
Less than high school	1.02 (0.56-1.86)	1.16 (0.61-2.21)
More than high school	**0.62 (0.38-1.00)**	0.62 (0.37-1.03)
Age at first opioid misuse	**0.96 (0.94-0.99)**	**0.97 (0.94-1.00)**
Non-oral opioid administration at first opioid use	**3.17 (1.75-5.72)**	**2.82 (1.52-5.22)**
Methadone detoxification	**2.65 (1.56-4.48)**	**2.23 (1.27-3.91)**
Buprenorphine detoxification	**2.00 (1.23-3.25)**	**1.77 (1.02-3.07)**
Injectable Naltrexone	0.93 (0.50-1.71)	0.73 (0.36-1.45)
12-step attendance	**2.18 (1.36-3.50)**	**1.89 (1.12-3.20)**

Significant values $p<0.05$ bolded.