



Psychiatric symptoms and recent overdose among people who use heroin or other opioids: Results from a secondary analysis of an intervention study

Michael Fendrich^{a,*}, Jessica Becker^a, Jennifer Hernandez-Meier^b

^a School of Social Work, University of Connecticut, 38 Prospect St., Hartford, CT 06103, United States of America

^b Department of Emergency Medicine, Medical College of Wisconsin, 8701 Watertown Plank Rd., Milwaukee, WI 53226, United States of America

ABSTRACT

Background: Drug overdose (OD) is the leading cause of accidental death in the United States and most of these deaths involve opioids. Despite research linking opioid abuse to mental illness, and evidence suggesting a large portion of opioid OD deaths are suicides, OD prevention strategies scarcely take into account mental health risk factors.

Methods: We examined a sample of heroin or other opioid users enrolled in an intervention study to determine the prevalence of overdose, the prevalence of suicide attempts in overdose, and whether those with higher levels of psychiatric symptomatology would be more likely to experience a recent OD compared to other opioid users. By performing bivariate analyses and multivariate logistic regression models that controlled for poly drug use, criminal justice status, age, race, gender, and education, we evaluated the association of severe depression, severe anxiety, posttraumatic stress disorder (PTSD) and, psychosis and past three-month OD.

Results: Just over 12% (45/368) of recent opioid users reported a recent overdose. Four of these recent overdose victims reported that the overdose was a suicide attempt. Multiple logistic regression analysis revealed that severe depression (odds ratio 2.46; 95% CI: 1.24, 4.89), PTSD (odds ratio: 2.77; 95% CI: 1.37–5.60) and psychosis (odds ratio 2.39; 95% CI: 1.10–5.15) were significantly associated with elevated odds for OD.

Conclusions: Findings suggest systematic mental health symptom screening and connection to mental health treatment for opioid users—especially those identified with OD—may be critical for OD prevention.

1. Introduction

Drug overdose (OD) is the leading cause of accidental death in the United States (American Society of Addiction Medicine, 2016) and most OD deaths involve opioids, such as heroin (Rudd, Seth, David, & Scholl, 2016). The OD death epidemic is growing exponentially, with incidence increasing six-fold from 1999 to 2017 (Centers for Disease Control and Prevention; CDC, 2018). Between 2000 and 2014, Rudd, Aleshire, Zibbell, and Gladden (2016) found significant increases in OD deaths in the U.S. for “both sexes, persons aged 25–44 years and > 55 years, non-Hispanic whites and non-Hispanic blacks, and in the Northeastern, Midwestern, and Southern regions of the United States” (p. 1378). Both the number of people who received treatment for heroin dependence and the number of people who received treatment for pain relievers more than doubled from 2002 to 2015 (Center for Behavioral Health Statistics and Quality, 2014; Center for Behavioral Health Statistics and Quality, 2016).

The response to this crisis has mainly focused on evaluating and expanding the availability of effective medications. Medications such as buprenorphine and methadone can treat opioid dependence and prevent OD (National Academies of Sciences, Engineering, and Medicine, 2019). Widespread adulteration of opioids and other substances with

fentanyl and carfentanyl has increased lethality associated with use and has resulted in focused community prevention efforts to increase the distribution of naloxone, which directly reverses the physical symptoms of OD (Faul et al., 2017; Morgan & Jones, 2018). Knowledge of naloxone administration and effective and safe use of the drug on OD victims by first providers and civilians has increased (Lewis, Vo, & Fishman, 2017; McDonald & Strang, 2016). Community distribution of naloxone has reduced rates of OD deaths (Rando, Broering, Olson, Marco, & Evans, 2015; Walley et al., 2013; Wheeler, Davidson, Jones, & Irwin, 2012). Implementation of “drug checking” strategies for lethal fentanyl (using chemical “test strips”) by people who use drugs (usually in safe use sites) also serves as a vehicle for preventing ODs (Karamouzian et al., 2018).

Noticeably absent from harm reduction-oriented discussions of OD prevention are the personal risk factors among people who use heroin or other opioids (PWUHO) which may reduce the potential to seek treatment or to engage in strategies to minimize self-harm. Research suggests that those experiencing mental health symptoms are more likely to be prescribed (Braden et al., 2009; Howe & Sullivan, 2014; Richardson et al., 2012; Seal et al., 2012) and abuse (Becker, Sullivan, Tetrault, Desai, & Fiellin, 2008; Cicero & Ellis, 2017) opioids. Research also suggests that those who are prescribed opioids and develop

* Corresponding author at: School of Social Work, University of Connecticut, 38 Prospect Street, Hartford, CT 06103-2814, United States of America.

E-mail addresses: michael.fendrich@uconn.edu (M. Fendrich), jessica.becker@uconn.edu (J. Becker), jhernandez@mcw.edu (J. Hernandez-Meier).

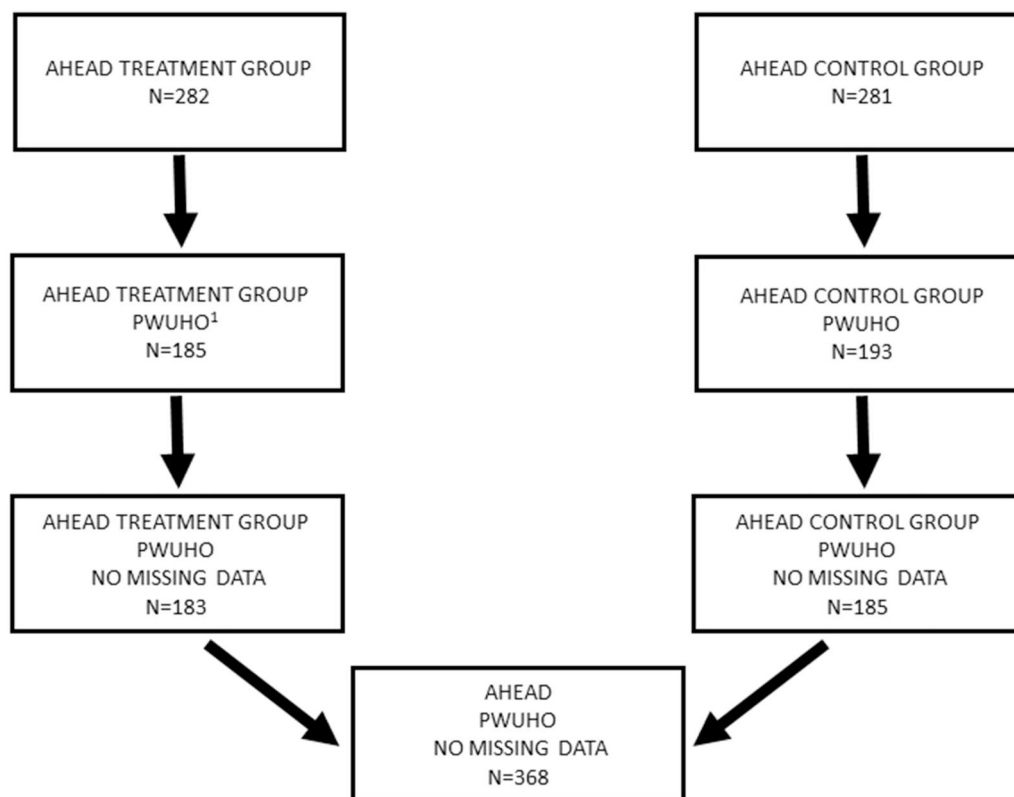


Fig. 1. Sample participation flowchart.

¹PWUHO = people who use heroin or other opioids.

substance use problems tend to present with higher levels of psychiatric symptoms (depression and anxiety; Edlund, Sullivan, Steffick, Harris, & Wells, 2007). A growing number of reports suggesting that psychiatric symptoms (especially depression) may increase OD risk (Foley & Schwab-Reese, 2019; Johnson et al., 2013; Porucznik, Johnson, Sauer, Crook, & Rolfs, 2011; Tobin & Latkin, 2003; Wines, Saitz, Horton, Lloyd-Travaglini, & Samet, 2007; Yokell et al., 2014) underscore the need for more research on this topic since these are potentially modifiable risk factors.

Relatedly, the notion that some portion of ODs are intentional suicides needs emphasis and evaluation. Researchers estimate that suicides account for 20–30% of opioid OD deaths (Oquendo & Volkow, 2018). The proportion of suicides by opioid OD nearly doubled in the US from 1999 to 2014 (Oquendo & Volkow, 2018), echoing a 24% increase in suicide rates overall in the US over the same time (McCarthy, 2016). Information about the extent to which OD is motivated by suicidal intentions or other mental health conditions and symptoms is needed to more broadly inform harm reduction approaches.

To address the above gaps in knowledge, the current study sought to answer the following research questions: 1) What was the prevalence of recent opioid-related OD in a treatment sample of opioid users; 2) How prevalent were suicide attempts among opioid users reporting OD?; and 3) How did those reporting elevated psychiatric symptoms differ from other opioid users in terms of their probability of reporting a recent OD? We hypothesized that those with higher levels of psychiatric symptomatology would be more likely to experience a recent OD than other opioid users.

2. Methods

2.1. Data source

This study performed secondary analyses on data from the Addiction Health Evaluation and Disease (AHEAD) Management Study

(Saitz et al., 2013). The AHEAD treatment study recruited 563 patients aged 18 or older with alcohol and/or other drug dependence in Boston, Massachusetts between 2006 and 2008. Of the 563 participants, 282 were randomized to receive a chronic care management (CCM) intervention, and 281 did not receive CCM. CCM was offered at the AHEAD clinic, which was staffed by social workers, nurse care managers, internists, a psychiatrist with addiction expertise, and physicians (see Fendrich & Becker, 2018; Saitz et al., 2013).

Study participants were interviewed at baseline, 3-, 6-, and 12 months, with data collection spanning 2006–2010. This study utilized AHEAD's baseline questionnaire data. The baseline interview included demographic questions as well as the following psychosocial assessment tools: the Addiction Severity Index (ASI), the Patient Health Questionnaire (PHQ-9), the Beck Anxiety Inventory (BAI), the Mini International Neuropsychiatric Interview (MINI), and the Behavior and Symptom Identification Scale-24 (BASIS-24).

2.2. Sample & Measures

2.2.1. Subsample of heroin and other opioid users

This study utilized a subsample of current heroin or other opioid users (PWUHO), which was defined as past month use of heroin, methadone, or other opiates/analgesics reported on the relevant baseline ASI question. The flowchart on Fig. 1 shows that there were 185 PWUHO in the treatment group and 193 PWUHO in the control group. When the small group with missing values on any of the variables employed in this study are eliminated, the final combined sample consists of 183 treatment group participants and 185 control group participants for a final sample size of 368 (65.4% of the original study sample).

2.2.2. OD measure

Any respondent indicating they experienced an OD in the past 3 months on the ASI was counted as having a “recent OD” at baseline.

Table 1
Bivariate analysis: OD risk by symptom and background characteristics (n = 368).

| Variable | PWUHO with recent OD (%) | p-Value |
|--------------------------------------|--------------------------|---------|
| Severe depression ^a | | 0.004 |
| Yes (n = 149) | 18.1 | |
| No (n = 219) | 8.2 | |
| PTSD ^b | | 0.020 |
| Yes (n = 146) | 17.1 | |
| No (n = 222) | 9.0 | |
| Psychosis ^c | | 0.118 |
| Yes (n = 231) | 14.3 | |
| No (n = 137) | 8.8 | |
| Severe anxiety ^d | | 0.940 |
| Yes (n = 129) | 12.4 | |
| No (n = 239) | 12.1 | |
| Poly drug use ^e | | 0.017 |
| Yes (n = 115) | 18.3 | |
| No (n = 253) | 9.5 | |
| Criminal justice status ^f | | 0.013 |
| Yes (n = 150) | 17.3 | |
| No (n = 218) | 8.7 | |
| Age | | 0.007 |
| 18–29 (n = 137) | 18.3 | |
| > 29 (n = 231) | 8.7 | |
| Race/ethnicity | | 0.094 |
| Non-Hispanic White (n = 211) | 14.7 | |
| Other ^g (n = 157) | 8.9 | |
| Gender | | 0.217 |
| Male (n = 266) | 13.5 | |
| Female (n = 102) | 8.8 | |
| Education | | 0.003 |
| High school diploma (n = 278) | 15.1 | |
| No high school diploma (n = 90) | 3.3 | |

^a Severe depression was assessed by the PHQ-9, scored from 0 to 27. A score above 19 indicates severe depression.

^b PTSD was assessed by the PTSD module of the MINI. Clients are determined to meet the criteria for PTSD if they indicate one or more traumatic events has caused problems that significantly interfere with their work or social activities, or caused significant distress.

^c Psychosis was assessed by the BASIS-24 psychosis subscale. Participants met the criteria for psychosis if they experienced one or more types of delusions or hallucinations.

^d Severe anxiety was assessed by the Beck Anxiety Inventory, scored from 0 to 63. A score above 35 indicates severe anxiety.

^e Poly drug use was based on use of 3 or more non-opioid drugs in the past month at baseline.

^f Criminal justice status was based on any current or prior involvement in the criminal justice system.

^g Other = non-Hispanic black, Hispanic, and non-Hispanic other.

2.2.3. Psychiatric measures

Severe depression was measured by dichotomizing the PHQ-9 (Kroenke & Spitzer, 2002) at a score of 20 and above, which is well above the typical cutoff of 10 and consistent with the PHQ-9's threshold for "severe depression." This cutoff (20 and above) was deemed appropriate since 82% of the sample scored above the typical cutoff of 10. **Severe Anxiety** was measured by dichotomizing the BAI (Beck, Epstein, Brown, & Steer, 1988) at a score of 36. Participants were classified as having **PTSD** if they answered affirmatively to questions on the MINI (Sheehan et al., 1998) about whether they experienced traumatic events, about whether these events caused them to experience problems, and whether these problems significantly interfered with their work or social activities, or caused significant distress in the past month. Respondents were classified as having **psychosis** if they answered affirmatively to any one of four questions on the BASIS-24 (Idiculla & Eisen, 2012) about whether they experienced delusions or

hallucinations in the past week.

2.2.4. Poly drug use and criminal justice involvement

We included two additional variables in the data set that have been shown to increase the risk for overdose, **poly drug use** (e.g., Coffin et al., 2003; Darke & Hall, 2003) and **criminal justice involvement** (e.g. Binswanger, Blatchford, Mueller, & Stern, 2013; Joudrey et al., 2019; Seal et al., 2001). Participants who reported use of at least 3 non-opioid drugs in the past month were considered to be poly drug users. Participants who indicated any prior or current involvement in probation, parole, pretrial release, diversion, incarceration, or other criminal justice process were classified as having criminal justice involvement. No study participants were incarcerated at baseline.

2.2.5. Other measures

Our goal was to estimate the effect of our substantive variables on overdose outcomes independent of the influence of extraneous variables and free from potential bias that may arise from subgroup differences with respect to demographic variables that have been found in prior literature to potentially impact substance misuse-related outcomes. Accordingly, we controlled for the following demographic variables: **gender**, **age** (dichotomized at age 30 years and above), **race/ethnicity** (dichotomized as non-Hispanic whites and others) and **education** (dichotomized as those who had less than a high school education and those who had at least a high school degree).

3. Results

3.1. Analysis sample demographics

Overall, the sample included in our analyses was 72.3% male. With respect to race/ethnicity, 57.3% were non-Hispanic white. The age of participants ranged from 18 to 60 years, with a mean age of 35. Over one third (37.2%) of the sample were ages 18–29 years. Three quarters (75.5%) of the sample reported they had graduated from high school.

3.2. Recent OD

To address our first research question, we looked at the number of people who reported a recent OD in our sample of PWUHO with complete data. In the final study sample of 368 PWUHO with complete data, 45 respondents reported a recent overdose. Thus, the overall prevalence of recent overdose in our study sample of PWUHO was 12.2% (45/368).

3.3. OD and suicide

To address our second research question, we looked at the number and percentage of recent ODs that were suicide attempts. The study found that four (8.9%; 4/45) of the PWUHO study sample with a recent OD indicated their most recent OD was a suicide attempt (one participant did not give an answer for this question). Overall 1.1% (4/368) of the PWUHO attempted suicide through a recent OD.¹

3.4. OD and psychiatric symptoms

To address our third research question, we looked at the association between four mental health indicators and recent overdose.

¹ If the 2 overdose victims who were excluded from the analyses due to missing data are added back into the analysis, an additional suicide attempt is identified in the group. This would increase the number of suicide attempts to 5 and increase the rate to 10.6% (5/47).

Table 2
Logistic regression models: symptom and background predictors of recent overdose (OD) (n = 368).

| Variable | Model 1 Odds ratio (95% CI) | Model 2 Odds ratio (95% CI) | Model 3 Odds ratio (95% CI) | Model 4 Odds ratio (95% CI) |
|--|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Severe depression ^a | 2.46 (1.24–4.89) | | | |
| PTSD ^b | | 2.77 (1.37–5.60) | | |
| Psychosis ^c | | | 2.39 (1.10 - 5.15) | |
| Severe anxiety ^d | | | | 1.04 (0.51–2.13) |
| Poly drug use ^e | 2.21 (1.13–4.35) | 2.25 (1.14–4.42) | 2.08 (1.06–4.07) | 2.19 (1.13–4.26) |
| Criminal justice status ^f | 2.01 (1.01–4.01) | 2.30 (1.16–4.53) | 2.31 (1.17–4.55) | 2.32 (1.18–4.55) |
| Age (18–29 vs > 29) | 2.56 (1.24–5.29) | 2.81 (1.33–5.91) | 2.83 (1.35–5.90) | 2.47 (1.20–5.05) |
| Race/ethnicity (non-Hispanic white vs other ^g) | 1.13 (0.53–2.39) | 1.35 (0.62–2.94) | 1.32 (0.61–2.85) | 1.13 (0.53–2.42) |
| Gender (male vs female) | 2.47 (1.06–5.79) | 2.63 (1.11–6.22) | 2.29 (0.99–5.33) | 2.15 (0.93–4.98) |
| Education (high school diploma + vs < high school diploma) | 6.16 (1.78–21.33) | 6.54 (1.87–22.80) | 6.80 (1.96–23.54) | 6.40 (1.86–21.99) |

^a Severe depression was assessed by the PHQ-9, scored from 0 to 27. A score above 19 indicates severe depression.

^b PTSD was assessed by the PTSD module of the MINI. Clients are determined to meet the criteria for PTSD if they indicate one or more traumatic events has caused problems that significantly interfere with their work or social activities, or caused significant distress.

^c Psychosis was assessed by the BASIS-24 psychosis subscale. Participants met the criteria for psychosis if they experienced one or more types of delusions or hallucinations.

^d Severe anxiety was assessed by the Beck Anxiety Inventory, scored from 0 to 63. A score above 35 indicates severe anxiety.

^e Poly drug use was based on use of 3 or more non-opioid drugs in the past month at baseline.

^f Criminal justice status was based on any current or prior involvement in the criminal justice system.

^g Other = non-Hispanic black, Hispanic, and non-Hispanic other.

3.4.1. Correlates of OD

Bivariate analyses (exact *p* values are listed on Table 1) revealed that severe depression and PTSD—but not psychosis and severe anxiety—showed statistically significant associations (i.e., *p* values smaller than 0.05) with recent OD among PWUHO. Poly drug use and criminal justice involvement were also significantly associated with recent OD among PWUHO. In terms of demographics, age and graduation from high school showed a significant association with recent OD. PWUHO under the age of 30 were significantly more likely to report recent OD relative to PWUHO aged 30 or older. Additionally, PWUHO with at least a high school education were significantly more likely to report recent OD compared to PWUHO who did not graduate from high school.

3.4.2. Adjusted models

We performed logistic regression models (Table 2) to evaluate the association of the four mental health indicators with likelihood of recent OD. All regression models controlled for poly drug use, criminal justice status, age, race, gender, and education. Compared with other PWUHOs, those with severe depression had 2.46 times the odds of recent overdose (model 1; 95% CI: 1.24–4.89); those with PTSD had 2.77 times the odds of recent overdose (model 2; 95% CI: 1.37–5.60); those with psychosis had 2.39 times the odds of recent overdose (model 3; 95% CI: 1.10–5.15). Severe anxiety (model 4) was not significantly associated with recent OD. Furthermore, involvement with the criminal justice system and poly drug use had positive and statistically significant relationships with recent OD in all four models. Race was not significantly associated with recent OD in any of the models. Males were more likely to report a recent overdose compared to females; this result was statistically significant in only models 1 and 2, and marginally significant (at the 0.1 level) in models 3 and 4. Consistent with bivariate analyses, those who were under the age of 30 as well as those who graduated from high school were significantly more likely to report a recent OD in all four models.

4. Discussion

Our findings suggest, first of all, that recent OD is highly prevalent in a sample of opioid users in treatment—over one in ten reported a recent OD. Furthermore, our findings also suggest that elevated psychiatric symptomatology may be an important risk factor for OD. The 8.9% rate of suicide attempts among PWUHO OD victims is 15 times the rate of attempts in the general population (CDC, 2015), underscoring the severity of psychiatric risk among OD victims. While suicide attempts are clearly a red flag for needed mental health-focused intervention in a substantial minority of OD victims, the high rates of elevated symptomatology are also problematic. Those reporting psychosis, elevated depressive symptoms, and PTSD had more than twice the odds of recent OD compared to other PWUHO in this sample. Furthermore, we note that the elevated risks for our mental health indicators were net of the effects of two other significant OD risk factors identified in the previous research literature: poly drug use and criminal justice involvement.

OD risk screening tools targeted specifically to patients with pain who have been prescribed opioids have proliferated in recent years (e.g., Butler, Fernandez, Benoit, Budman, & Jamison, 2008; Larence et al., 2016; Pouget et al., 2017). In light of our analyses, we believe that screening tools need to be more broadly targeted to a variety of opioid users in treatment as well as opioid and heroin users who come into contact with harm reduction settings (venues such as safe injection sites) and personnel (e.g., emergency responders carrying naloxone). Mental health risk factors, which are often given short shrift in these OD screens need to be more systematically assessed. That is, we note that some OD risk scales include a limited number of non-specific mental health measures (such as self-reported “depressed mood;” see Butler, Fernandez, Benoit, Budman, & Jamison, 2008). Many screens omit mental health measures entirely. Our study suggests that if existing, validated mental health screening measures were directly integrated

into OD risk assessment tools, a substantial number opioid patients at high risk for OD would be identified.

Conclusions are tempered by the retrospective design of the study; the retrospective (past 3-month) questions about OD are asked at the same time as questions about mental health symptoms. It is possible that mental health conditions were a consequence of the OD experience, coupled with participation in substance dependence treatment. Nevertheless, Wines et al. (2007) indicate that the research on the impact of OD on depressive symptoms is mixed—with some studies suggesting an increase and others a decrease in symptoms in the aftermath of OD. We also note that the generalizability of our findings may be limited by the location of the sample recruitment (Boston, MA) and the dates of study implementation (2006–2010). Nevertheless, these unique data capture rich information about patients in treatment for opioid dependence early on in a nationwide opioid epidemic that continues to grow.

5. Conclusion

Irrespective of the timing of the onset of the psychiatric symptomatology or its cause, the overall findings underscore the potentially important role of psychiatric comorbidity in treatment for opioid dependence. Our findings suggest that comorbidity correlates are not limited to depression. Macro-level analyses underscore the need for expansion of mental health services in locales experiencing OD increases (Foley & Schwab-Reese, 2019). Mental health screening and connections to mental health treatment for PWUHO, especially those identified with OD may be critically important. Failure to screen and provide access to mental health services may increase the risk for a subsequent, possibly fatal OD.

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