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Correlates of overdose risk perception among illicit opioid users

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Abstract

Background—Opioid-related mortality continues to increase in the United States. The current study assesses demographic and behavioral predictors of perceived overdose risk among individuals who use opioids illicitly. By examining these correlates in the context of established overdose risk factors, we aim to assess whether characteristics and behaviors that have been associated with actual overdose risk translate to higher perception of risk.

Methods—We conducted a cross-sectional survey of 172 adult illicit opioid users in San Francisco, CA and used multivariable logistic regression to identify predictors of perception of high risk for opioid overdose.

Results—Age (aOR=0.96, 95%CI=0.93-1.00) and number of injection days per month (0.91, 0.86-0.97) were associated with a lower odds of perceived high overdose risk. There was no independent association between use of opioid analgesics, concurrent use of opioids and benzodiazepines or cocaine, or HIV status and overdose risk perception.

Conclusions—Opioid users who injected more frequently and those who were older were less likely to perceive themselves as being at risk of overdose, notwithstanding that those who inject more are at higher risk of overdose and those who are older are at higher risk overdose mortality. In addition, despite being established overdose risk factors, there was no relationship between use of opioid analgesics, concurrent use of opioids and cocaine or benzodiazepines, or self-reported HIV status and overdose risk perception. These findings highlight key populations of opioid users

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and established risk factors that may merit focused attention as part of education-based overdose prevention and opioid management strategies.

Keywords

opioid overdose; risk perception; substance use; risk factors

1. Introduction

Opioid dependence is the largest contributor to the global burden of disease from illicit drug dependence and use of opioids increased globally from 2009-2014 (Degenhardt and Hall, 2012; United Nations Office on Drugs and Crime, 2014). Between 2002 and 2011 in the United States, more than 25 million people initiated nonmedical use of opioid analgesics and the drug-poisoning mortality rate more than doubled (Dart et al., 2015; Warner et al., 2014). A recent slowing in the long-consistent growth in abuse and mortality related to opioid analgesics has paralleled a stark increase in use of heroin and related mortality (Dart et al., 2015; Hedegaard and Warner, 2015; Rudd et al., 2014; Unick et al., 2013). Indeed, many individuals dependent on opioid analgesics transition to heroin (Cerda et al., 2015; Havens et al., 2012; Lankenau et al., 2012; Peavy et al., 2012; Warner et al., 2014). Additionally, there was a 37% yearly increase in heroin-related deaths in the U.S. from 2010 to 2013, contributing to a total of over 23,000 opioid overdose deaths in 2013 (Dart et al., 2015; Hedegaard and Warner, 2015; Rudd et al., 2014; Unick et al., 2013). Drug poisoning is now the leading cause of injury death among U.S. adults and accounts for over half of mortality among heroin users (Centers for Disease and Prevention, 2011; Centers for Disease Control and Prevention National Center for Injury Prevention and Control, 2013; Sporer, 1999).

Extensive research has established an array of circumstances and behaviors that increase the likelihood of opioid overdose, which has facilitated the development of evidence-based interventions (Darke and Hall, 2003). These established risk factors include having had a prior overdose, concurrent use of alcohol, cocaine, or benzodiazepines, more frequent injecting, and HIV infection (Brugal et al., 2002; Coffin et al., 2003, 2007; Darke et al., 2011, 2007, 2005; Evans et al., 2012; Green et al., 2012; Jenkins et al., 2011; Nielsen et al., 2011; Ochoa et al., 2005; Stoove et al., 2009; Wines et al., 2007). Despite these advances, young opioid analgesic users have been shown to be unaware or misinformed regarding overdose risk factors, and heroin users have been shown to present an “optimistic bias”, or tendency to perceive a lower personal susceptibility to overdose compared to one's peers (Frank et al., 2015; McGregor et al., 1998; Neira-Leon et al., 2006). In an effort to increase overdose knowledge and awareness and reduce opioid-related morbidity and mortality, community-based opioid overdose prevention programs provide overdose-related education and training and, increasingly, distribute naloxone to non-medical persons, including those who use opioids and are at risk for overdose (Clark et al., 2014; Darke and Hall, 2003; Hawk et al., 2015; Wheeler et al., 2015). In addition to how to recognize and manage an overdose and effectively administer naloxone, the education and training curricula delivered by these programs often cover established risk factors for overdose (Clark et al., 2014). Several studies have reported increases in knowledge of overdose risk factors among opioid-users following participation in community-based overdose prevention trainings (Bennett

and Holloway, 2012; McGregor et al., 2001; Strang et al., 2008); however, no recent study has assessed whether having or engaging in established overdose risk factors translates to higher perceived overdose risk among opioid users (McGregor et al., 1998).

We assess demographic and behavioral correlates of perceived overdose risk among a cross-sectional sample of individuals who use opioids illicitly (i.e., illicit opioid users) in San Francisco, CA. By examining our findings in the context of established overdose risk factors, we aim to assess whether characteristics and behaviors that have been associated with actual overdose risk correspond with higher perception of risk among opioid users.

2. Materials and Methods

2.1 Study sample

We conducted a convenience-based cross-sectional survey of opioid-users aged 18 and older in the San Francisco Bay Area from August, 2014 to August, 2015 as part of the screening phase of a randomized-controlled trial assessing the feasibility and acceptability of a behavioral intervention to reduce overdose and risk behaviors among naloxone recipients (REBOOT Study; ClinicalTrials.gov Identifier: NCT02093559). Participants were recruited through active outreach and print advertisements at syringe access programs in San Francisco, CA. All participants provided informed consent to participate and study procedures were approved by the Committee on Human Research, University of California, San Francisco.

2.2 Data collection

Trained staff administered structured telephone questionnaires to opioid-users willing to be screened for the REBOOT study. Demographic characteristics, substance use and injection frequency, experience with overdose and naloxone, self-reported HIV and HCV serostatus, and perception of personal overdose risk were collected.

Substance use and injection frequency were assessed in the last four months as seven categories: never, once per month or less, two to three days per month, once per week, two to three days per week, four to six days per week, and every day. For all analyses, substance use and injection frequency variables were converted from the initial seven categorical selections to continuous variables representing days of use of each substance or days of injection per month. Witnessing of an opioid overdose was assessed in the participant's lifetime and personal opioid overdose and receipt of a naloxone kit were assessed in the last five years. Due to small numbers of participants with unknown HIV and HCV serostatus (n=2 for HIV and n=14 for HCV), participants with unknown or negative status were combined into a single category for each infection. Perception of opioid overdose risk was assessed with the question “What do you feel your risk is for an opiate overdose?” and response options of “no risk”, “low risk”, “moderate risk”, and “high risk”, which were categorized as no/low risk (referred to as low risk) and moderate/high risk (referred to as high risk) for this analysis. Participants were given a definition for overdose prior to answering survey questions; the definition stated that an overdose is when an individual uses opioids and any of the following happens: “the person is unresponsive when shaken or their

name is called; the person can't be woken up without help (e.g., CPR or naloxone); the person's skin, lips, or fingers turn blue; the person stops breathing or breathes really slowly."

2.3 Statistical analysis

The primary outcome was participant self-report of being at high risk for opioid overdose. We assessed bivariate relationships between all demographic and behavioral characteristics and perception of being at either low risk or high risk of opioid overdose using Wilcoxon rank-sum and Fisher's exact tests, as appropriate.

We used a multivariable logistic regression model to identify independent predictors of perception of high risk for opioid overdose. All covariates assessed in bivariate analysis were included in the model as independent variables, with the exception of the binary measures of substance use in the last four months.

Because HIV and HCV serostatus were significantly correlated ($p < 0.05$), we conducted a sensitivity analysis in which we excluded HCV status from the multivariable logistic regression model.

To assess our overall model specification, we conducted a Hosmer-Lemeshow goodness of fit test using ten risk groups, which provided no evidence of a poor fit ($p = 0.72$).

3. Results

3.1 Demographic and behavioral characteristics

Our sample included 172 illicit opioid users in the San Francisco Bay Area. The original sample included 175 opioid users but 3 (1.7%) were excluded because they did not report any illicit substance use (i.e. heroin use, non-prescribed opioid analgesic use, or opioid injection). The majority of participants (65%) perceived themselves to be at high risk of opioid overdose (Table 1). Nearly two-thirds (64%) reported having an opioid overdose in the past five years and even more (88%) reported witnessing an opioid overdose in their lifetime. Heroin use was more prevalent than non-prescribed opioid analgesic use (94% vs. 84%). Mixing opioids with other substances with common; the most prevalent concurrently used substance was cocaine (70%), followed by benzodiazepines (67%) and alcohol (50%). On average, participants used heroin (18.5 days per month) more frequently than opioid analgesics (9.4 days per month) and mixed opioids with cocaine most frequently (8.6 days per month), followed by mixing with alcohol (7.4 days per month) and benzodiazepines (5.8 days per month). Participants reported injecting an average of 19.2 days per month. HIV and HCV seropositivity was reported by 14% and 51% of participants, respectively.

The results of our bivariate analyses are presented in Table 1. Those who perceived themselves as being at high overdose risk were more likely to have had an opioid overdose in the last five years, use heroin more frequently, and use opioids with benzodiazepines or alcohol more frequently ($p < 0.05$).

3.2 Multivariable analysis

In multivariable analysis controlling for all covariates, age (adjusted odds ratio = 0.96, 95%CI = 0.93-1.00) and number of injection days per month (0.91, 0.86-0.97) were associated with a lower odds of perceived high overdose risk (Table 2). Having overdosed in the last five years (2.90, 1.29-6.52), more days per month of heroin use (1.10, 1.03-1.16) and concurrent opioid and alcohol use (1.05, 1.01-1.09), and self-reported HCV-positive serostatus (2.38, 1.04-5.44) were all associated with an increased odds of perceived high overdose risk. Gender, having witnessed an overdose, use of opioid analgesics, concurrent use of opioids and benzodiazepines or cocaine, and self-reported HIV status were not independently associated with overdose risk perception.

In our sensitivity analysis excluding HCV status, self-reported positive HIV status was not independently associated with overdose risk perception (1.31, 0.45-3.82).

4. Discussion

We found that participants who were older and injected more frequently were less likely to perceive themselves as being at high risk for opioid overdose and participants who had experienced a past overdose, used heroin and mixed opioids and alcohol more frequently, and reported being HCV positive were more likely to perceive themselves as being at high risk. There were no independent associations between the use of opioid analgesics, concurrent use of opioids with cocaine or benzodiazepines, or self-reported HIV status and overdose risk perception. Examining these findings in the context of established overdose risk factors allows us to assess the overlap of actual and perceived overdose risk among opioid users, which can inform overdose prevention efforts.

Prior overdose is the strongest predictor of subsequent overdose and overdose death, which is reassuringly reflected in our finding that participants who had experienced a prior overdose were more likely to consider themselves as being at high risk of overdose (Coffin et al., 2007; Darke et al., 2011; Evans et al., 2012; Stoove et al., 2009; Wines et al., 2007). This finding is also consistent with a similar study conducted in Australia in the 1990's, prior to a more recent expansion of overdose awareness programs, and aligns with a broader tendency of individuals to derive perceptions of risk and vulnerability from personal experience (McGregor et al., 1998; Weinstein, 1989). The recognition of established linkages between prior overdose and subsequent overdose risk among opioid users highlights the suitability of this common traumatic event as a focus of motivational interventions aiming to discontinue opioid use or increase opioid safety. Experiencing an overdose has been shown to result in high rates of drug treatment enrollment and is a key motivational target in the intervention being assessed in the ongoing REBOOT study from which this sample was derived (Pollini et al., 2006).

We had notable findings related to mixing of opioids with other substances; concurrent use of opioids and alcohol was associated with high-perceived overdose risk, whereas concurrent use of opioids and benzodiazepines or cocaine was not. Use of alcohol, benzodiazepines, and cocaine have been linked to opioid overdose (Coffin et al., 2003, 2007; White and Irvine, 1999). In San Francisco from 2010 to 2012, 35.3% of opioid

overdose deaths involved cocaine, 27.5% involved benzodiazepines, and 19.6% involved alcohol (Visconti et al., 2015). Nationally, involvement of benzodiazepines in opioid analgesic-related ED visits has more than tripled between 2004 and 2011 (Jones and McAninch, 2015). Our findings suggest that opioid users are more aware of the risk associated with mixing opioids with alcohol but may be less aware of the risks from benzodiazepines or cocaine, which highlights these latter two substances as potential focal points for efforts aiming to increase awareness of the dangers of polysubstance use among opioid users.

More frequent use of heroin, but not opioid analgesics, was associated with high perceived overdose risk. This difference in perceived risk may be related to differences in the transparency of dose and purity between heroin, manufactured and sold illicitly and often adulterated with other substances, and opioid analgesics (Muller et al., 2007; Turock et al., 2009). Indeed, the United States Drug Enforcement Agency (DEA) recently issued a nationwide alert in response to the combination and sale of heroin and fentanyl, an extremely potent, short-acting opioid, as a single product and rises in overdoses involving the mixture (DEA, 2015); locally, the San Francisco Department of Public Health also issued a health advisory in response to a spike in overdoses involving pure fentanyl marketed as heroin (San Francisco Department of Public Health, 2015). Moreover, opioid analgesics have been approved by the United States Food and Drug Administration (FDA) and are legitimately prescribed by licensed physicians for a variety of medical conditions, which results in a broad public perception of prescribed medications as being safer than illegal street drugs (Manchikanti, 2006). The elevated risk-perception among frequent heroin users and its absence from frequent opioid analgesic users is a public health concern given that nearly twice as many individuals in the U.S. in 2013 and ten times as many individuals in San Francisco from 2010 to 2012 died from opioid analgesic-related overdose compared to heroin-related overdose (Centers for Disease Control and Prevention National Center for Health Statistics, 2015; Visconti et al., 2015). Educational components of behavioral interventions may benefit from emphasizing overdose risk associated with opioid analgesics despite the greater knowledge of the dosage and contents and overall perceived safety of prescription drugs compared to illicit substances; indeed, wide variation in the potency of opioid analgesics make understanding strength and dosage extremely important to their safe use (Svendsen et al., 2011; Von Korff et al., 2008).

Our finding in regards to age, namely that age is inversely associated with high risk perception, is in accordance with several studies that have identified younger age as an independent risk factor for opioid overdose among people who inject drugs (PWID; Coffin et al., 2007; Kinner et al., 2012; Ochoa et al., 2005, 2001; Seal et al., 2001; Sherman et al., 2007). Although younger opioid users experience higher rates of overdose, those who are older are more likely to die from overdose (Pierce et al., 2015). Similarly, while more frequent heroin injection has been associated with higher rates of overdose (Brugal et al., 2002), participants who injected more frequently were less likely to perceive themselves as being at high risk for overdose. Notably, the combination of lower perceived risk of overdose and higher actual risk of overdose or death indicates the presence of a false sense of security among those who inject frequently or are older. These groups may benefit from behavioral interventions targeting this perception of relative safety.

We also found that participants who reported being HCV-positive were more likely to perceive themselves as being at high risk for overdose whereas there was no such association among those who reported being HIV-positive. On the contrary, HIV infection, but not HCV infection, has been shown to be associated with increased risk of overdose mortality (Green et al., 2012; Wang et al., 2005; Zaccarelli et al., 1994). However, abnormal liver function, a common sequela of chronic HCV infection, has been associated higher risk of overdose mortality (Wang et al., 2005). This link, in combination with the association between HCV infection and overdose risk perception among our participants, suggests that the relationship between HCV and overdose mortality may be worthy of further investigation. Regarding our null HIV-related findings, the small percentage (14%) of participants who reported being HIV-positive may limit our ability to identify an independent association between self-reported HIV status and perceived overdose risk; however, the results of our sensitivity analysis excluding HCV status from the multivariable model indicate that the null finding related to HIV is robust. An alternative explanation for these findings may be related to the fact that HCV infection among PWID is most likely a result of injection whereas HIV infection may result from sexual activity. Similar to the relationship between prior overdose and subsequent perceptions of vulnerability, HCV-positive PWID have already suffered a negative outcome as a result of injecting and may perceive themselves as less able to control other risks and outcomes related to their substance use. However, given that HIV serostatus is a risk factor for opioid overdose, our findings suggest a need to raise awareness of the intersection between HIV infection and overdose risk among opioid users while further exploring the link between HCV and overdose.

The gaps we identified in risk perception are not only relevant to community-based programs that have conventionally provided overdose prevention services (i.e., naloxone distribution programs, syringe access programs), but also to any service providers or public agencies that interact with individuals who use opioids and may be at risk of overdose. Healthcare and emergency medical service providers, drug treatment programs, and law enforcement and other criminal justice entities are well-positioned to utilize these findings to address gaps in overdose knowledge and perception and raise awareness of specific overdose risk factors. Furthermore, it is important to recognize that individual behavior and decision-making occur and are shaped within the context of complex individual conditions (e.g., addiction, chronic pain, economic hardship) and broader social, cultural and economic forces (e.g., social, legal, and economic marginalization of individuals who use drugs) (Moore, 2004; Rhodes, 2009). Thus, while overdose prevention programs that target individual behavior change, such as those aiming to raise awareness of overdose risk factors, are an important component of efforts to reduce overdose morbidity and mortality, it is essential that they be carried out in parallel with measures that address the broader risk environments that influence the individual behavior of opioid users.

Our study has several limitations. First, our convenience sample of opioid users may not be generalizable to the general population of opioid users within the San Francisco Bay Area or more broadly. Indeed, the majority of participants were recruited from syringe access programs and 85% had received a naloxone kit in their lifetime, making them likely to have received some form of overdose prevention training. Moreover, all participants lived in the

San Francisco Bay Area, which has a relatively long history of overdose prevention efforts and naloxone distribution (Enteen et al., 2010). This limitation highlights the need for future studies to explore similar issues among opioid users who have had less exposure to overdose prevention efforts such as naloxone distribution and who reside in other regions. Second, the self-reported data in this study may be subject to social desirability or recall bias. Third, because we analyzed limited phone screen data, we did not have access to other potential confounders that may be associated with both our predictors of interest and overdose risk perception, such as education, income, or baseline awareness of overdose risk factors. Finally, because of our relatively small sample size and the large number of correlates assessed in our multivariable analysis, it is possible that any null findings are a result of power limitations; however, this motivates future research to assess these relationships more extensively.

To conclude, we found that opioid users who injected more frequently and those who were older were *less* likely to perceive themselves as being at risk of overdose, notwithstanding that those who inject more are at higher risk of overdose and those who are older are at higher risk of overdose mortality. In addition, despite being established overdose risk factors, there was no relationship between the use of opioid analgesics, concurrent use of opioids and cocaine or benzodiazepines, or self-reported HIV status and overdose risk perception. These findings elucidate gaps between actual overdose risk factors and perceptions of overdose risk, highlighting key populations of opioid users and established risk factors that may merit focused attention as part of education-based overdose prevention and opioid management strategies.

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Highlights

- Some overdose risk factors were not associated with higher perceived overdose risk.
- Opioid users who injected more frequently had lower perceived overdose risk.
- Older opioid users had lower perceived overdose risk.
- Use of opioid analgesics was not associated with perceived overdose risk.
- Mixing opioids with cocaine/benzodiazepines was not associated with perceived risk.

Table 1

Demographic and Behavior Characteristics by Perceived Overdose Risk (n=172)

	Entire Sample		No or Low Overdose Risk		Moderate or High Overdose Risk		
Demographic and Behavioral Characteristics	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**P-Value**
Total	172	(100)	60	(35)	112	(65)	
Age, *mean (SD)*	42.8	(11.9)	44	(12.8)	42.2	(11.3)	0.339
Gender							
Male	104	(60)	35	(34)	69	(66)	
Female	68	(40)	25	(37)	43	(63)	0.744
Had Opioid Overdose in Last Five Years	110	(64)	30	(27)	80	(73)	0.007
Ever Witnessed Opioid Overdose	151	(88)	53	(35)	98	(65)	1.000
Substance Use in the Last Four Months							
Heroin	161	(94)	54	(34)	107	(66)	0.195
Non-Prescribed Opioid Analgesics	144	(84)	49	(34)	95	(66)	0.666
Concurrent Opioids and Benzodiazepines	115	(67)	36	(31)	79	(69)	0.177
Concurrent Opioids and Alcohol	86	(50)	16	(19)	70	(81)	<0.001
Concurrent Use of Opioids and Cocaine	121	(70)	39	(32)	82	(68)	0.295
Days of Substance Use Per Month							
Heroin, *mean (SD)*	18.5	(12.1)	15.2	(12.9)	20.2	(11.3)	0.015
Non-Prescribed Opioid Analgesics, *mean (SD)*	9.4	(10.5)	8.4	(10.8)	10	(10.3)	0.177
Concurrent Opioids and Benzodiazepines, *mean (SD)*	5.8	(8.8)	4	(7.5)	6.8	(9.3)	0.029
Concurrent Opioids and Alcohol, *mean (SD)*	7.4	(11.1)	4.1	(9.0)	9.1	(11.7)	<0.001
Concurrent Use of Opioids and Cocaine, *mean (SD)*	8.6	(11.1)	6.7	(10.1)	9.5	(11.5)	0.116
Any Injection of Opioids in the Last Four Months	151	(88)	54	(36)	(64)	0.629	
Injection Days Per Month, *mean (SD)*	19.2	(12.3)	18.9	(12.4)	19.3	(12.3)	0.909
Ever Received Take-Home Naloxone Kit	149	(85)	53	(36)	96	(64)	0.815
HIV Status							
Positive	24	(14)	9	(38)	15	(63)	
Negative/Unknown	148	(86)	51	(34)	97	(66)	0.819
HCV Status							

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	Entire Sample		No or Low Overdose Risk		Moderate or High Overdose Risk		
Demographic and Behavioral Characteristics	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**P-Value**
Positive	90	(52)	27	(30)	63	(70)	0.200
Negative/Unknown	82	(48)	33	(40)	49	(60)	

Table 2

Multivariable logistic regression model assessing odds of perception of high overdose risk (n=172)

Covariates	aOR*	(95% CI)	P-Value
Age	0.96	(0.93-1.00)	0.026
Gender			
Male	Reference		
Female	0.94	(0.44-2.03)	0.880
Overdosed in last 5 years	2.90	(1.29-6.52)	0.010
Ever Witnessed an Overdose	0.59	(0.19-1.90)	0.380
Days of Heroin Use per Month	1.10	(1.03-1.16)	0.002
Days of Opioid Analgesic Use per Month	1.03	(0.99-1.07)	0.132
Days of Concurrent Use of Opioids and Benzodiazepines per Month	1.04	(0.99-1.09)	0.129
Days of Concurrent Use of Opioids and Alcohol per Month	1.05	(1.01-1.09)	0.011
Days of Concurrent Use of Opioids and Cocaine per Month	1.01	(0.98-1.05)	0.501
Injection Days per Month	0.91	(0.86-0.97)	0.004
HIV Status			
Negative	Reference		
Positive	1.11	(0.36-3.38)	0.855
HCV Status			
Negative	Reference		
Positive	2.38	(1.04-5.44)	0.040
Received Naloxone in Last 5 Years	0.69	(0.21-2.25)	0.540

* Adjusted odds ratio