

Published in final edited form as:

Drug Alcohol Depend. 2013 February 1; 128(0): 104–110. doi:10.1016/j.drugalcdep.2012.08.014.

Factors associated with history of non-fatal overdose among young nonmedical users of prescription drugs

Karol Silva^{a,c,*}, Sheree M. Schragger^b, Aleksandar Kecojevic^a, and Stephen E. Lankenau^a

^aDrexel University, School of Public Health, Department of Community Health and Prevention, 1505 Race Street, 11th Floor, Philadelphia, PA 19102, USA

^bChildren's Hospital Los Angeles, Division of Adolescent Medicine, 5000 Sunset Boulevard, 7th Floor, Los Angeles, CA 90027, USA

^cTemple University, Department of Psychology, WeissHall, 1701 N. 13th Street, Philadelphia, PA 19122-6085, USA

Abstract

Objectives—The current study examines the prevalence and correlates of lifetime non-fatal overdose (OD) involving the nonmedical use of prescription opioids and tranquilizers among a sample of high-risk young adults in New York, NY and Los Angeles, CA.

Methods—Data were derived from a cross-sectional study of 16–25 year old nonmedical users of prescription drugs ($n = 596$). Unadjusted associations between OD history and socio-demographic and drug use variables were investigated in bivariate logistic regression models. Multivariate logistic regression models identified correlates of non-fatal OD.

Results—Lifetime prevalence of non-fatal overdose involving prescription opioids and/or tranquilizers was 23.6%. Factors associated with increased risk of non-fatal overdose included lower social class while growing up (OR: 1.81, 95% CI: [1.15, 2.83], $p < 0.01$), having ever received care at a psychiatric hospital (OR: 1.79, 95% CI: [1.12, 2.85], $p < 0.05$), ever witnessing a family member OD on drugs (OR: 1.59, 95% CI: [1.02, 2.50], $p < 0.05$), being prescribed tranquilizers (OR: 2.07, 95% CI: [1.29, 4.27], $p < 0.01$), ever snorting or sniffing opioids (OR: 2.51, 95% CI: [1.48, 4.27], $p < 0.001$), injecting tranquilizers (OR: 3.09, 95% CI: [1.61, 5.93], $p < 0.001$), and past 90-day injection drug use (OR: 1.68, 95% CI: [1.03, 2.74], $p < 0.05$). Participants who reported past 90-day stimulant misuse had lower odds of reporting OD compared to those who were not recent stimulant users (OR: 0.60, 95% CI: [0.38–0.96], $p < 0.05$).

*Corresponding author at: Temple University, Department of Psychology, Weiss Hall, 1701 N. 13th Street, Philadelphia, PA 19122-6085, USA. Tel.: +1 215 204 7321; fax: +1 215 204 5539, karol.silva@temple.edu (K. Silva).

Contributors: Karol Silva conducted literature searches, undertook the statistical analysis, and wrote the first draft of the manuscript. Dr. Sheree Schragger assisted with the statistical analysis, data interpretation, and development of the manuscript. Aleksandar Kecojevic assisted with the statistical analysis and editing of the manuscript. Dr. Stephen Lankenau designed the study, developed the survey, wrote the protocol, and assisted in data interpretation and manuscript development. All authors contributed to and approved the final version of the manuscript.

Conflict of interest: All authors declare they have no conflicts of interest.

Conclusions—This study documents the high prevalence of experiencing non-fatal overdose among young nonmedical users of prescription drugs. Results could inform overdose prevention efforts throughout the U.S.

Keywords

Non-fatal overdose; Prescription drug misuse; Nonmedical use of prescription drugs; Young drug users

1. Introduction

In the U.S., drug-related mortality and morbidity have increased significantly in the past decade, largely due to increases in the number of fatal and non-fatal overdoses (OD) involving nonmedical use of prescription drugs (Center for Disease Control and Prevention (CDC), 2010, 2011). Opioids and tranquilizers are the most commonly reported prescription drugs involved in both fatal and non-fatal ODs (Paulozzi and Xi, 2008; Xiang et al., 2012). Although most fatal ODs are observed among people over 35 years old (Bohnert et al., 2010), young adults aged 18–25 exhibit the highest rate of prescription drug misuse (Substance Abuse and Mental Health Service Administration (SAMHSA), 2010a) and account for nearly 20% of all emergency department visits for non-fatal poisonings involving prescription drugs (SAMHSA, 2010b).

Few studies have investigated the prevalence and risk factors associated with non-fatal OD among young drug users. Existing studies have focused primarily on heroin injection drug users (IDUs; Bohnert et al., 2011; Sherman et al., 2007; Evans et al., 2012), and thus mainly concentrated on heroin OD (Ochoa et al., 2005) or have generally defined drug overdose without specifying the drugs taken during the OD (Evans et al., 2012; Britton et al., 2010; Hakansson et al., 2008). Nonetheless, one study estimated the lifetime prevalence of non-fatal OD among young IDUs to be approximately 30% and found that risk of OD was associated with being White, homeless, using tranquilizers, and having a prolonged history of injection drug use (Sherman et al., 2007). Studies on older IDUs have described additional risk factors associated with non-fatal OD that include male gender (Bohnert et al., 2010), substance use disorders (Darke et al., 1996; Galea et al., 2006; Kaye and Darke, 2004; Maloney et al., 2009), history of drug treatment (Neale and Robertson, 2005; Darke et al., 2004), history of incarceration (Kinner et al., 2012; Britton et al., 2010; Havens et al., 2011; Wines et al., 2007), psychological distress (Tobin and Latkin, 2003; Havens et al., 2011; Bohnert et al., 2012; Latkin et al., 2004; Maloney et al., 2009), parental drug problems (Hakansson et al., 2008), injection of prescription opioids (Havens et al., 2011), and concurrent use of heroin and prescription drugs (Kerr et al., 2007).

Several studies have documented non-fatal OD among non-IDUs (Darke et al., 2004; Darke and Ross, 2000; Swift et al., 1999; Carpenter et al., 1998). While none have focused on young adults, these studies have estimated the prevalence of non-fatal OD to be between 3.5% and 13% among non-IDUs (Brugal et al., 2002; Darke et al., 2004), and found that prescription drug misuse, frequency of heroin use, and non-oral heroin administration were significant predictors of OD (Darke et al., 2004; Darke and Ross, 2000; Swift et al., 1999; Carpenter et al., 1998; Brugal et al., 2002).

Overall, there is consensus in the literature that nonmedical use of prescription drugs, along with other behavioral (e.g., heroin use or non-oral drug administration) and contextual factors (e.g., use of drugs following a period of abstinence due to incarceration or drug treatment) are associated with an increased risk of non-fatal OD among various samples of drug users. However, most studies on OD have not developed models to quantify the independent effects of different modes of prescription drug administration (e.g., inhalation vs. injection), particularly among young drug users. For instance, injection of prescription opioids has been associated with non-fatal OD in some studies (Havens et al, 2011), while non-injection opioid use is associated in others (Kerr et al., 2007). Moreover, several studies have reported tranquilizer use as a significant predictor of OD (Kinner et al., 2012; Hakansson et al., 2008; McGregor et al, 1998; Charlson et al, 2009; Gossop et al, 2002), but none have examined whether this association is related to mode of drug administration.

Given these gaps in the literature, this study explores risk factors associated with non-fatal OD resulting from nonmedical use of prescription opioids and/or tranquilizers among a diverse sample of high-risk young adults. In this study, we sought to investigate two general questions: (1) What is the prevalence of non-fatal OD involving prescription opioids and/or tranquilizers among a sample of young nonmedical users of prescription drugs? (2) What socio-demographic and behavioral characteristics are associated with non-fatal overdose on these substances?

2. Methods

2.1. Study sample

The analysis is based upon a sample of 596 young nonmedical users of prescription drugs interviewed in Los Angeles and New York between October 2009 and March 2011. Participants were between 16 and 25 years old and had engaged in misuse of a prescription drug, i.e., opioid, tranquilizer, stimulant, or any combination, at least three times in the past 90 days. "Misuse" or "nonmedical use" was defined and assessed as having used a prescription drug "when it was not prescribed for you or that you took only for the experience or feeling it caused" (SAMHSA, 2010a). Those who reported misuse of at least one of these medications, at least three times in the past 90 days, were eligible to participate in the study.

Sampling was stratified to enroll three groups of young adults with different risk profiles and access to prescription drugs. The first group was comprised of housed, non-IDU participants: who were neither homeless nor IDUs in the preceding 90 days ($n = 202$). The second group was comprised of homeless, non-IDUs participants: who described having inconsistent housing and/or sleeping on the street, in a park, or squat within the past 90 days, but had not injected drugs in the past 90 days ($n = 192$). The third group was comprised of IDUs, defined as having injected any drug within the past 90 days ($n = 202$). Many IDUs met the criteria for homelessness but were enrolled into the study as 'IDUs' based on their recent injection practices. Since many IDUs were also homeless, the total number of currently homeless young adults was 355.

Participants were located using a combination of sampling strategies and data sources. Interviewers employed both targeted (Watters and Biernacki, 1998) and chain-referral sampling (Biernacki and Waldorf, 1981) in combination with recruitment data from earlier project phases (Lankenau et al., 2012a) to recruit young adults in natural settings such as parks, streets, and neighborhoods. In New York, some participants were recruited from organizations serving homeless youth because homeless individuals meeting the enrollment criteria were more difficult to locate in natural settings. A brief screening tool was used to determine eligibility, and screened individuals received a \$3 gift card. Those consenting to participate were enrolled in the study and compensated \$25 for their time. The study was approved by the Institutional Review Boards (IRB) at Drexel University, Children's Hospital Los Angeles, and National Development and Research Institutes, Inc.

2.2. Measures

Data from the current study were gathered from a cross-sectional survey developed with Entryware Software (Techneos Systems, Inc., Vancouver, Canada) and loaded onto laptop computers. The instrument was administered during face-to-face interviews with enrolled participants by one of two interviewers at each recruitment site. Interviews were conducted in private offices or natural settings, such as fast food restaurants and parks. The instrument incorporated questions from standardized measures, previous studies (Lankenau et al., 2007), and topics that emerged during the formative qualitative phase of the study (Lankenau et al., 2012a). Participants were provided with written cards containing response options to facilitate standardization on some interview questions. Demographic indicators, such as age, gender, and race were assessed using conventional questions. Interview data were recorded on laptop computers and digital recorders.

The primary outcome of interest in this analysis was non-fatal OD resulting from nonmedical use of prescription opioids and/or tranquilizers. Opioids included opioid analgesics. Tranquilizers included benzodiazepines, as well as three related medications: Quaalude (Methaqualone), Catapres (Clonidine) and Seroquel (Quetiapine). Participants were asked, "Have you ever experienced an overdose from taking medications [opioids, tranquilizers] when they were not prescribed for you or only for the experience or feeling it caused?" A dichotomous variable was created to capture participants who answered "yes" to having overdosed on either, or both, of these prescription drugs (OD history =1, no OD history =0). Participants were also asked how long it had been since their last experienced OD. A simple descriptive analysis revealed that most ODs occurred more than 12 months prior to the time of interview. Therefore, this analysis is focused on lifetime non-fatal OD.

Predictor variables were selected based on previous literature identifying risk factors associated with non-fatal and fatal drug OD and other factors generally indicating inappropriate use of controlled medications, such as non-oral drug administration. Explanatory variables in this analysis included age, sex at birth (female = 0, male = 1), race (nonwhite = 0, white = 1), sexual identity (lesbian/gay/bisexual/transgender=0, heterosexual = 1), high school completion (no = 0, yes = 1), and social class while growing up (middle/upper = 0, poor/lower class = 1). To account for the two-city recruitment strategy and sampling methodology specific to the study design, we also investigated if site (NY = 0, LA

= 1), past 90-day homelessness (no = 0, yes = 1), and past 90-day injection drug use (no = 0, yes = 1) were associated with OD.

History of ever being prescribed controlled medications was assessed with the following question: “Were you ever prescribed [opioids, tranquilizers, stimulants] by a doctor for any past injury or health condition?” The response scale was binary (no = 0, yes = 1). Participants were asked if they had ever been in drug treatment, been incarcerated, ever lived or received care in a psychiatric hospital, and ever lived in foster or group home(s). Participants were also asked, “Have any members of your family ever experienced an overdose after taking too large a dose of prescription or street drug?” The response scale for each of these predictors was binary (no = 0, yes = 1).

Behavioral variables pertaining to lifetime drug use activities included lifetime use of heroin, cocaine, and methamphetamine, as well as non-oral administration (intranasal and injection) of prescription opioids and tranquilizers, all of which were binary predictors (no = 0, yes = 1).

Binary variables (no = 0, yes = 1) describing past 90-day non-medical use of prescription drugs [opioids, tranquilizers, and/or stimulants] were included as independent variables. Frequency of recent drug use was assessed as continuous variables: mean number of days in the past 30 days that prescription drugs were misused, and mean number of days in the past 90 days that illicit drugs were used.

2.3. Statistical analyses

All analyses were conducted using the Predictive Analytics Software (PASW, formerly SPSS), version 18.0. Descriptive statistics were first calculated for OD history and all predictors of interest. Categorical variables were analyzed with chi-square comparisons, and age was analyzed in a t-test, with the a priori significance level set at $p < 0.05$. Due to the large number of comparisons, all p-values were adjusted using the false discovery rate controlling procedure (Benjamini and Hochberg, 1995; Brown and Russell, 1997). Unadjusted associations between OD history and each predictor variable were investigated in bivariate logistic regression models. All characteristics that were significant ($p < 0.05$) were entered into a stepwise backwards logistic regression to avoid potential biases of forward selection procedures (Field, 2000). We removed from the model those variables that were not significantly associated with OD history after adjustment and confirmed that we did not affect the fit of the model by conducting a change in log-likelihood test. To prevent over-fitting the model, collinearity between predictor variables was assessed using a correlation matrix procedure. Variables were considered collinear if the value of the correlation coefficient was greater than 0.6 (Tabachnick and Fidell, 2006). None of the variables demonstrated this degree of collinearity. Hosmer and Lemeshow tests confirmed that the predictors were a good fit for each model.

Of the 596 participants in the sample, 33 were excluded in the stepwise backwards logistic regression analyses due to missing data. Participants who were excluded in the final model did not significantly differ on drug use practices from participants who were included. They

were, however, more likely to be sexual minorities compared to participants who were included (57.7% vs. 31.3%, $\chi^2(1) = 7.87, p < 0.01$).

Associations between non-fatal OD history and all significant independent variables were expressed as odds ratios (OR) in the most parsimonious model. The explanatory power of the model estimating OD history was estimated using Nagelkerke's R^2 (Nagelkerke, 1991).

3. Results

Of the 596 study participants included in the study, the majority were male (7.6%) and white (5.9%), and the mean age was 21. In this sample, the lifetime prevalence of non-fatal overdose involving prescription opioids and/or tranquilizers was 23.6% ($n = 138$). Between sampled subgroups, housed-non-IDUs had the lowest prevalence of non-fatal OD (10.9%), followed by homeless-non-IDU respondents (20.3%), and IDUs (38.1%). Among the participants with a history of OD, 42% ($n = 58$) reported OD involving opioids, 37% ($n = 51$) reported OD involving tranquilizers, and 21% ($n = 29$) reported OD involving both opioids and tranquilizers. The majority of these reported OD experiences occurred more than 12 months prior to the time of study interview, while approximately 38% ($n = 52$) occurred in the past year (data not shown in tables).

Results from binary analyses examining correlates of OD history are displayed in Table 1. A number of statistically significant differences were found between participants who reported OD history compared to those who did not. These differences remained significant after adjusting for multiple comparisons. Participants who reported ever having overdosed were significantly more likely to grow up in a poor/working class environment (56.2% vs. 41.1%, $p < 0.01$), to be currently homeless (76.1% vs. 54.6%, $p < 0.001$), and to be current IDUs (55.8% vs. 27.3%, $p < 0.001$). In addition, compared to individuals without a history of OD, participants with OD history were more likely to report past 90-day opioid (89.1% vs. 77.2%, $p < 0.01$) and tranquilizer (82.6% vs. 67.5%, $p < 0.01$) misuse. By contrast, past 90-day stimulant misuse was higher in the non-overdose group (47.1%) compared to the OD history group (36.2%, $p < 0.05$). Important variables that were not statistically significant included site, age, sex, race, and sexual identity.

Several other characteristics were also significantly associated with non-fatal OD (Table 1). Compared to individuals without history of OD, those who reported lifetime OD were more likely to have ever been prescribed opioids (80.4% vs. 70.5%, $p < 0.05$), tranquilizers (68.1% vs. 38.6%, $p < 0.001$), and stimulants (53.6% vs. 42.6%, $p < 0.05$); to have ever been in drug treatment (58.7% vs. 36.9%, $p < 0.001$); to have been incarcerated (77.5% vs. 60.7%, $p < 0.001$); to have lived or received care in a psychiatric hospital (55.8% vs. 32.1%, $p < 0.001$); to report having lived in foster or group home (37.0% vs. 27.3%, $p < 0.05$); to have witnessed a family member OD on drugs (50.0% vs. 32.3%, $p < 0.001$); to have used heroin (67.4% vs. 43.4%, $p < 0.001$), cocaine (92.8% vs. 81.2%, $p < 0.01$), and/or methamphetamine (63.8% vs. 45.6%, $p < 0.001$); and to report non-oral modes of drug administration including inhalation of opioids (80.4% vs. 53.8%, $p < 0.001$) and tranquilizers (65.2% vs. 39.2%, $p < 0.001$), as well as injection of opioids (47.1% vs. 19.5%, $p < 0.001$) and tranquilizers (25.4% vs. 6.1%, $p < 0.001$). Lastly, individuals with OD history reported greater frequency of

opioid and tranquilizers misuse in the past 30 days, and greater frequency of heroin and methamphetamine use in the past 90 days.

All socio-demographic and behavioral characteristics significantly associated with OD history were entered in multivariate logistic regression using backwards elimination. We entered all variables and removed them one at a time, depending on their significance (p -value), to trim the model. The most parsimonious multivariate model provided adequate fit ($X^2(8) = 9.1, p = 0.334$) and showed good predictive value ($X^2(8) = 109.01, p < 0.001$, Nagelkerke $R^2 = 0.266$) (Table 2). Factors associated with increased risk of non-fatal overdose included lower social class while growing up (OR: 1.81, 95% CI: [1.15, 2.83], $p < 0.01$), injection drug use in the past 90 days (OR: 1.68, 95% CI: [1.03, 2.74], $p < 0.05$), having ever received care at a psychiatric hospital (OR: 1.79, 95% CI: [1.12, 2.85], $p < 0.05$), ever witnessing a family member OD on drugs (OR: 1.59, 95% CI: [1.02, 2.50], $p < 0.05$), having ever been prescribed tranquilizers (OR: 2.07, 95% CI: [1.29, 4.27], $p < 0.01$), ever snorting or sniffing opioids (OR: 2.51, 95% CI: [1.48, 4.27], $p < 0.001$), and having ever injected tranquilizers (OR: 3.09, 95% CI: [1.61, 5.93], $p < 0.001$). Participants who reported stimulant misuse in the past 90 days had lower odds of reporting overdose compared to those who were not recent stimulant users (OR: 0.60, 95% CI: [0.38, 0.96], $p < 0.05$).

We tested two-way interactions between IDU status and all other significant factors in the multivariate model to examine potential differences in risk factors between IDUs and non-IDUs that were associated with OD history on prescription drugs. None of the interactions tested were statistically significant and were thus excluded from the final model.

4. Discussion

To our knowledge, this is the first study to examine non-fatal OD resulting in part from nonmedical use prescription opioids and/or tranquilizers in a sample of young adults, a population that exhibits the highest rate of prescription drug misuse and highest percentage increase in emergency department visits for drug-related poisonings (SAMHSA, 2010a, 2010b). Previous studies have consistently found that misuse of prescription opioids and tranquilizers is a risk factor of fatal and non-fatal OD (Paulozzi et al., 2012; Kinner et al., 2012; Hakansson et al., 2008; McGregor et al., 1998; Charlson et al., 2009; Gossop et al., 2002). However, the present study's sampling strategy, which included various high-risk groups of young adults (e.g., IDUs and homeless, non-IDU), is an important development in this line of research because much of the prior research has exclusively focused on IDUs or older, drug-dependent heroin users.

In this sample, lifetime prevalence of non-fatal overdose was 23%, which is slightly lower than what has been found in previous studies of rural and urban populations of heroin users (25–68%; Havens et al., 2011; Fairbairn et al., 2008; Latkin et al., 2004; Pollini et al., 2006). Non-fatal OD involving prescription opioids and tranquilizers was independently associated with various socio-demographic factors including growing up in a lower socioeconomic social class, ever witnessing a family member OD, and being a current IDU. These findings corroborate previous studies indicating that poverty, injection behaviors, and drug environment play a role in drug overdose (Hakansson et al., 2008; Fleary et al., 2011).

Contextual stressors may increase negative mood and hopelessness, and result in greater risk-taking in terms of use and abuse of drugs, alcohol, and medications. Family drug problems were particularly high in this sample: over a third of participants reported witnessing a family member OD on illicit and/or prescription drugs. While some studies have reported that family substance abuse is associated with non-fatal OD (Hakansson et al., 2008) and others have investigated factors associated with witnessing ODs within drug users' social networks (Havens et al., 2011), this is the first study to identify that witnessing a family member overdose as predictive of experiencing non-fatal OD.

It should be acknowledged, however, that significant sociodemographic differences between individuals with OD history and those without were not necessarily very large. After adjusting for socio-demographics, the most significant findings were noted for differences related to history of prescribed tranquilizer use and non-oral prescription drug administration, most notably intranasal administration of prescription opioids and injection of tranquilizers. In summary, individuals with a history of being prescribed tranquilizers had twice the odds of non-fatal OD compared to individuals without a history of prescribed tranquilizer use. Moreover, individuals who reported inhalation of opioids and injection of tranquilizers had approximately three times the odds of experiencing OD compared to individuals who never engaged in these behaviors.

The association between non-fatal OD and history of being prescribed tranquilizers is a novel finding for this area of research. One study of overdose decedents in New Mexico found that having a history of prescription for tranquilizers was a stronger risk factor of OD death than having a history of prescribed opioids (Paulozzi et al, 2012). Taken together, our study findings support previous recommendations that medical practitioners be aware that prescription tranquilizers may be associated with an increased risk of OD (Paulozzi et al., 2012; Darke and Hall, 2003). While the important role of tranquilizers in fatal and non-fatal OD has been well documented in the literature, previous studies have generally addressed this important factor as 'tranquilizer use' or 'tranquilizer misuse'. The findings from the present study are novel in two ways. First, we find that prescribed use of tranquilizers is significant, thus distinguishing between medical use and misuse. Second, the present study distinguishes between non-oral modes of administration and concludes that inhalation of opioids and injection of tranquilizers are predictive of non-fatal OD, therefore adding to the OD literature the importance of method of drug administration.

Our study findings showed that receiving care in a psychiatric hospital was also a predictor of non-fatal OD. These findings corroborate previous literature indicating that poor psychological health is associated with drug OD (Bohnert et al., 2012; Toblin et al., 2010; Tobin and Latkin, 2003; Burns et al, 2004). People with higher levels of psychological distress, particularly those who have been treated in psychiatric institutions, may be inclined to take more of their medications than prescribed in an effort to reduce distress, or take their medications in combination with other drugs or alcohol (Farrell et al., 1996; Robinson et al., 2011; Sansone and Wiederman, 2009). More research is needed to better understand the role of psychological distress, psychiatric care, and prescribing patterns of tranquilizer medications in overdose risk.

Interestingly, recent stimulant misuse is the only variable that was inversely related to non-fatal OD on opioids and/or tranquilizers. Nonmedical users of prescription stimulants are likely to exhibit different drug use patterns and profiles than individuals who primarily use prescription opioids and tranquilizers. Stimulant misuse has generally been noted to be prevalent among student populations (Teter et al, 2010; McCabe et al., 2005; Hall et al., 2005), whereas opioids and tranquilizers have generally been noted among homeless IDUs or heroin users (Kerr et al., 2007; Lankenau et al., 2007, 2012a; Roy et al., 2011; Daniulaityte et al., 2009; Brugal et al., 2002; Darke et al., 2010; Ross and Darke, 2000). In this sample, most stimulants users were housed and non-injectors, and may therefore face less contextual stressors that increase the risks of OD.

There are several notable limitations to this study. The sampling methodology included recruitment of quota samples for three high-risk groups: housed-non-IDUs, homeless-non-IDU youth, and IDUs. Given this sampling stratification, the prevalence of non-fatal OD reported for the overall sample should be interpreted with caution, as the most accurate prevalence estimate is the one reported for each subgroup. Some of the lifetime events or behaviors considered in this study may have occurred after the OD, which limits causal inferences. Moreover, the definition of overdose is self-perceived, which can produce misclassification. Nevertheless, our low non-response rate and previous studies (Darke and Zador, 1996) suggest that users recognize ODs well. In addition, while the question specifically asks about ODs resulting from nonmedical use of prescription opioids and/or tranquilizer (a defining distinction that previous studies have not made), there was no elaboration regarding the intake of other substances at the time of the OD. Since it is widely acknowledged that most ODs typically involve multiple substances, including alcohol, illicit, and/or prescription drugs (Brugal et al, 2002), the findings from the present study must be interpreted with caution, as it is likely that other substances, not solely prescription opioids/tranquilizers, were involved in OD.

Despite these limitations, the current study adds to our understanding of the risk factors associated with the occurrence of non-fatal OD involving nonmedical use of prescription opioids and tranquilizers among high-risk young adults in two large U.S. cities. Study findings have important implications for prevention efforts aimed to reduce OD among young drug users. First, the continued development of abuse-deterrent opioid formulations would appear to be warranted (Katz et al, 2007), as well as considerations to develop tranquilizer formulations with less potential for misuse through tampering. Second, it is important that young nonmedical users of prescription drugs be targeted for appropriate harm reduction initiatives to prevent the progression of more intensive drug use practices, including inhalation and injection of opioids and tranquilizers, since such behaviors are associated with increased risk of morbidity. In particular, overdose prevention programs that prescribe naloxone, an opioid antagonist, have played an important role in reversing thousands of potentially fatal OD across the U.S. (CDC, 2012). However, these programs should emphasize the particular risks associated with misusing tranquilizers since there are no known antidotes that can reverse OD primarily attributed to tranquilizers.

Acknowledgments

The authors gratefully acknowledge Cesar Arauz-Cuadra, Meghan Treese, and Alex Harocopos for participant recruitment and interviews. We also would like to acknowledge the young adults who participated in this study.

Role of funding source: The development of this manuscript was supported by research grant (R01 DA021299) from the National Institute on Drug Abuse. NIDA had no further role in the study design; in the collection, analysis, or interpretation of data; in the writing of the report; or in the decision to submit the paper for publication. The content is solely the responsibility of the authors and does not necessarily reflect the official views of the National Institute on Drug Abuse or the National Institute of Health.

References

- Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Statist Soc B*. 1995; 57:289–300.
- Biernacki P, Waldorf D. Snowball sampling: problems and techniques of chain referral sampling. *Soc Meth Res*. 1981; 10:141–163.
- Bohnert AS, Fudalej S, Ilgen MA. Increasing poisoning mortality rates in the United States, 1999–2006. *Public Health Rep*. 2010; 125:542–547. [PubMed: 20597454]
- Bohnert AS, Roeder KM, Ilgen MA. Suicide attempts and overdoses among adults entering addictions treatment: comparing correlates in a U.S. national study. *Drug Alcohol Depend*. 2011; 119:106–112. [PubMed: 21715108]
- Bohnert AS, Ilgen MA, Ignacio RV, McCarthy JF, Valenstein M, Blow FC. Risk of death from accidental overdose associated with psychiatric and substance use disorders. *Am J Psychiatry*. 2012; 169:64–70. [PubMed: 21955932]
- Britton PC, Wines JD Jr, Conner KR. Non-fatal overdose in the 12 months following treatment for substance use disorders. *Drug Alcohol Depend*. 2010; 107:51–55. [PubMed: 19828263]
- Brown BW, Russell K. Methods correcting for multiple testing: operating characteristics. *Statist Med*. 1997; 16:2511–2528.
- Brugal MT, Barrio G, De LF, Regidor E, Royuela L, Suelves JM. Factors associated with non-fatal heroin overdose: assessing the effect of frequency and route of heroin administration. *Addiction*. 2002; 97:319–327. [PubMed: 11964108]
- Burns JM, Martyres RF, Clode D, Boldero JM. Overdose in young people using heroin: associations with mental health, prescription drug use and personal circumstances. *Med J Aust*. 2004; 181(Suppl. 7):S25–S28. [PubMed: 15462639]
- Carpenter MJ, Chutuape MA, Stitzer ML. Heroin snorters versus injectors: comparison on drug use and treatment outcome in age-matched samples. *Drug Alcohol Depend*. 1998; 53:11–15. [PubMed: 10933336]
- Center for Disease Control and Prevention (CDC). Emergency department visits involving nonmedical use of selected prescription drugs – United States, 2004–2008. *MMWR*. 2010; 59:705–709. [PubMed: 20559200]
- Center for Disease Control and Prevention (CDC). Drug-induced deaths – United States, 2003–2007. *MMWR*. 2011; (Suppl. 60):60–61. [PubMed: 21430623]
- Centers for Disease Control and Prevention (CDC). Community-based opioid overdose prevention programs providing naloxone – United States, 2010. *MMWR*. 2012; 61:101–105. Retrieved from <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6106a1.htm>. [PubMed: 22337174]
- Charlson F, Degenhardt L, McLaren J, Hall W, Lynskey M. A systematic review of research examining benzodiazepine-related mortality. *Pharmacoepidemiol Drug Saf*. 2009; 18:93–103. [PubMed: 19125401]
- Daniulaityte R, Falck RS, Wang J, Carlson RG. Illicit use of pharmaceutical opioids among young polydrug users in Ohio. *Addict Behav*. 2009; 34:649–653. [PubMed: 19398164]
- Darke S, Ross J. Fatal heroin overdoses resulting from non-injecting routes of administration, NSW, Australia, 1992–1996. *Addiction*. 2000; 95:569–573. [PubMed: 10829332]
- Darke S, Zador D. Fatal heroin ‘overdose’: a review. *Addiction*. 1996; 91:1765–1772. [PubMed: 8997759]

- Darke S, Ross J, Hall W. Overdose among heroin users in Sydney, Australia. I: Prevalence and correlates of non-fatal overdose. *Addiction*. 1996; 91:405–411. [PubMed: 8867202]
- Darke S, Hall W. Heroin overdose: research and evidence-based intervention. *J Urban Health*. 2003; 80:189–200. [PubMed: 12791795]
- Darke S, Hetherington K, Ross J, Lynskey M, Teesson M. Non-injecting route of administration among entrants to three treatment modalities for heroin dependence. *Drug Alcohol Rev*. 2004; 23:177–183. [PubMed: 15370024]
- Darke S, Ross J, Mills K, Teesson M, Williamson A, Havard A. Benzodiazepine use among heroin users: baseline use, current use and clinical outcome. *Drug Alcohol Rev*. 2010; 29:250–255. [PubMed: 20565516]
- Evans JL, Tsui JI, Hahn JA, Davidson PJ, Lum PJ, Page K. Mortality among young injection drug users in San Francisco: a 10-year follow-up of the UFO study. *Am J Epidemiol*. 2012; 175:302–308. [PubMed: 22227793]
- Fairbairn N, Wood E, Stoltz JA, Li K, Montaner J, Kerr T. Crystal methamphetamine use associated with non-fatal overdose among a cohort of injection drug users in Vancouver. *Public Health*. 2008; 122:70–78. [PubMed: 17645904]
- Farrell M, Neeleman J, Griffiths P, Strang J. Suicide and overdose among opiate addicts. *Addiction*. 1996; 91:321–323. [PubMed: 8867195]
- Field, A. *Discovering Statistics Using SPSS for Windows*. Sage Publications; Thousand Oaks, CA: 2000.
- Fleary SA, Heffer RW, McKyer EL. Dispositional, ecological and biological influences on adolescent tranquilizer, Ritalin, and narcotics misuse. *J Adolesc*. 2011; 34:653–663. [PubMed: 20971501]
- Galea S, Nandi A, Coffin PO, Tracy M, Markham Piper T, Ompad D, Vlahov D. Heroin and cocaine dependence and the risk of accidental non-fatal drug overdose. *J Addict Dis*. 2006; 25:79–87. [PubMed: 16956872]
- Gossop M, Stewart D, Treacy S, Marsden J. A prospective study of mortality among drug misusers during a 4-year period after seeking treatment. *Addiction*. 2002; 97:39–47. [PubMed: 11895269]
- Hakansson A, Schlyter F, Berglund M. Factors associated with history of non-fatal overdose among opioid users in the Swedish criminal justice system. *Drug Alcohol Depend*. 2008; 94:48–55. [PubMed: 18082338]
- Hall KM, Irwin MM, Bowman KA, Frankenberger W, Jewett DC. Illicit use of prescribed stimulant medication among college students. *J Am Coll Health*. 2005; 53:167–174. [PubMed: 15663065]
- Havens JR, Oser CB, Knudsen HK, Lofwall M, Stoops WW, Walsh SL, Leukefeld CG, Kral AH. Individual and network factors associated with non-fatal overdose among rural Appalachian drug users. *Drug Alcohol Depend*. 2011; 115:107–112. [PubMed: 21126831]
- Katz NP, Adams EH, Chilcoat H, Colucci RD, Comer SD, Goliber P, Grudzinskas C, Jasinski D, Lande SD, Passik SD, Schnoll SH, Sellers E, Travers D, Weiss R. Challenges in the development of prescription opioid abuse-deterrent formulations. *Clin J Pain*. 2007; 23:648–660. [PubMed: 17885342]
- Kaye S, Darke S. Non-fatal cocaine overdose among injecting and non-injecting cocaine users in Sydney, Australia. *Addiction*. 2004; 99:1315–1322. [PubMed: 15369570]
- Kerr T, Fairbairn N, Tyndall M, Marsh D, Li K, Montaner J, Wood E. Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. *Drug Alcohol Depend*. 2007; 87:39–45. [PubMed: 16959438]
- Kinner SA, Milloy MJ, Wood E, Qi J, Zhang R, Kerr T. Incidence and risk factors for non-fatal overdose among a cohort of recently incarcerated illicit drug users. *Addict Behav*. 2012; 37:691–696. [PubMed: 22385733]
- Lankenau SE, Teti M, Silva K, Bloom JJ, Harocopos A, Treese M. Initiation into prescription opioid misuse amongst young injection drug users. *Int J Drug Policy*. 2012a; 23:37–44. [PubMed: 21689917]
- Lankenau SE, Sanders B, Bloom JJ, Hathazi DS, Alarcon E, Tortu S, Clatts M. Prevalence and patterns of prescription drug misuse among young ketamine injectors. *J Drug Issues*. 2007; 37:717–736. [PubMed: 18612374]

- Latkin CA, Hua W, Tobin K. Social network correlates of self-reported non-fatal overdose. *Drug Alcohol Depend.* 2004; 73:61–67. [PubMed: 14687960]
- Maloney E, Degenhardt L, Darke S, Nelson EC. Are non-fatal opioid overdoses misclassified suicide attempts? Comparing the associated correlates. *Addict Behav.* 2009; 34:723–729. [PubMed: 19447563]
- McCabe SE, Knight JR, Teter CJ, Wechsler H. Non-medical use of prescription stimulants among US college students: prevalence and correlates from a national survey. *Addiction.* 2005; 100:96–106. [PubMed: 15598197]
- McGregor C, Darke S, Ali R, Christie R. Experience of non-fatal overdose among heroin users in Adelaide, Australia: circumstances and risk perceptions. *Addiction.* 1998; 93:701–711. [PubMed: 9692269]
- Nagelkerke NJD. A note on a general definition of the coefficient of determination. *Biometrika.* 1991; 78:691–692.
- Neale J, Robertson M. Recent life problems and non-fatal overdose among heroin users entering treatment. *Addiction.* 2005; 100:168–175. [PubMed: 15679746]
- Ochoa KC, Davidson PJ, Evans JL, Hahn JA, Page-Shafer K, Moss AR. Heroin overdose among young injection drug users in San Francisco. *Drug Alcohol Depend.* 2005; 80:297–302. [PubMed: 15961257]
- Paulozzi LJ, Xi Y. Recent changes in drug poisoning mortality in the United States by urban-rural status and by drug type. *Pharmacoepidemiol Drug Saf.* 2008; 17:997–1005. [PubMed: 18512264]
- Paulozzi LJ, Kilbourne EM, Shah NG, Nolte KB, Desai HA, Landen MG, Harvey W, Loring LD. A history of being prescribed controlled substances and risk of drug overdose death. *Pain Med.* 2012; 13:87–95. [PubMed: 22026451]
- Pollini RA, McCall L, Mehta SH, Vlahov D, Strathdee SA. Non-fatal overdose and subsequent drug treatment among injection drug users. *Drug Alcohol Depend.* 2006; 83:104–110. [PubMed: 16310322]
- Roy E, Arruda N, Bourgois P. The growing popularity of prescription opioid injection in downtown Montreal: new challenges for harm reduction. *Subst Use Misuse.* 2011; 46:1142–1150. [PubMed: 21370963]
- Robinson J, Sareen J, Cox BJ, Bolton JM. Role of self-medication in the development of comorbid anxiety and substance use disorders: a longitudinal investigation. *Arch Gen Psychiatry.* 2011; 68:800–807. [PubMed: 21810645]
- Ross J, Darke S. The nature of benzodiazepine dependence among heroin users in Sydney, Australia. *Addiction.* 2000; 95:1785–1793. [PubMed: 11177494]
- Sansone RA, Wiederman MW. The abuse of prescription medications: borderline personality patients in psychiatric versus non-psychiatric settings. *Int J Psychiatry Med.* 2009; 39:147–154. [PubMed: 19860073]
- Sherman SG, Cheng Y, Kral AH. Prevalence and correlates of opiate overdose among young injection drug users in a large U.S. city. *Drug Alcohol Depend.* 2007; 88:182–187. [PubMed: 17110058]
- Substance Abuse Mental Health Services Administration (SAMHSA). Results from the 2009 National Survey on Drug Use and Health Vol I: Summary of National Findings. Office of Applied Studies; Rockville, MD, USA: 2010a. NSDUH Series H-38A, HHS Publication No. SMA 10-4856 Available at: <http://www.samhsa.gov/data/NSDUH/2k9NSDUH/2k9Results.htm> (accessed 22.05.12)
- Substance Abuse and Mental Health Services Administration (SAMHSA). The DAWN Report: Highlights of the 2009 Drug Abuse Warning Network (DAWN) Findings on Drug-related Emergency Department Visits. Rockville, MD: 2010b. Available at: <http://www.samhsa.gov/data/2k10/dawnsr034edhighlights/edhighlights.htm> (accessed 22.05.12)
- Swift W, Maher L, Sunjic S. Transitions between routes of heroin administration: a study of Caucasian and Indochinese heroin users in South-western Sydney, Australia. *Addiction.* 1999; 94:71–82. [PubMed: 10665099]
- Tabachnick, BG.; Fidell, LS. *Using Multivariate Statistics.* 5. Needham Heights, MA: Allyn and Bacon; 2006.

- Teter CJ, Falone AE, Cranford JA, Boyd CJ, McCabe SE. Nonmedical use of prescription stimulants and depressed mood among college students: frequency and routes of administration. *J Subst Abuse Treat.* 2010; 38:292–298. [PubMed: 20129754]
- Tobin KE, Latkin CA. The relationship between depressive symptoms and nonfatal overdose among a sample of drug users in Baltimore. *J Urban Health.* 2003; 80:220–229. [PubMed: 12791798]
- Toblin RL, Paulozzi LJ, Logan JE, Hall AJ, Kaplan JA. Mental illness and psychotropic drugs use among prescription drug overdose deaths: a medical examiner chart review. *J Clin Psychiatry.* 2010; 71:491–496. [PubMed: 20409446]
- Watters JK, Biernacki P. Targeted sampling: options for the study of hidden populations. *Soc Probl.* 1998; 36:416–430.
- Wines JD Jr, Saitz R, Horton NJ, Lloyd-Travaglini C, Samet JH. Overdose after detoxification: a prospective study. *Drug Alcohol Depend.* 2007; 89:161–169. [PubMed: 17280803]
- Xiang Y, Zhao W, Xiang H, Smith GA. ED visits for drug-related poisoning in the United States, 2007. *Am J Emerg Med.* 2012; 30:293–301. [PubMed: 21367556]

Table 1

Bivariate associations between socio-demographic and behavioral characteristics and history of non-fatal overdose (OD) on prescription opioids and/or tranquilizers in a sample of 596 high-risk young adults.

	Total sample n = 596 n (%)	OD history n = 138 n (%)	No OD history n = 458 n (%)	Unadjusted OR (95% CI)
Socio-demographic characteristics				
Site (LA)	303(50.8)	71 (51.4)	232(50.7)	1.03 (0.71,1.51)
Mean age (years)	20.86	21.02	20.81	1.05 (0.96,1.15)
Sex at birth (male)	403(67.6)	96(69.6)	307(67.2)	1.12(0.74,1.69)
Race (white)	333(55.9)	78(56.5)	255(56.0)	1.02(0.69,1.50)
Sexual identity (heterosexual)	401 (67.3)	91 (66.4)	310(67.8)	0.94(0.63,1.41)
Completed high school	445(74.7)	99(71.7)	346(75.5)	0.82(0.54,1.26)
Lower social class growing up	264(44.3)	77(56.2)	187(41.1)	1.84(1.25, 2.71)**
Past 90-day homelessness	355(59.6)	105(76.1)	250(54.6)	2.65 (1.72, 4.08)***
Past 90-day injection drug use	202(33.9)	77(55.8)	125(27.3)	3.36(2.27, 4.99)***
Lifetime prescribed use of				
Opioids	434(72.8)	111 (80.4)	323(70.5)	1.72(1.08, 2.74)*
Tranquilizers	271 (45.5)	94(68.1)	177(38.6)	3.39(2.26, 5.08)***
Stimulants	269(45.1)	74(53.6)	195(42.6)	1.56(1.06, 2.29)*
Lifetime history of institutionalization and family problems				
Drug treatment	250(41.9)	81 (58.7)	164(36.9)	2.43 (1.65, 3.58)***
Incarceration	385(64.6)	107(77.5)	278(60.7)	2.24(1.44, 3.48)***
Care in psychiatric hospital	224(37.6)	77(55.8)	147(32.1)	2.67 (1.81, 3.94)***
Lived in foster/group home	176(29.5)	51 (37.0)	125(27.3)	1.56(1.04, 2.34)*
Witness family member OD	207(34.7)	65(50.0)	142(32.3)	2.09(1.41,3.11)***
Lifetime drug use practices				
Heroin	292(49.0)	93(67.4)	199(43.4)	2.69(1.80, 4.02)***
Cocaine	500(83.9)	128(92.8)	372(81.2)	2.96(1.49, 2.87)**
Methamphetamine	297(49.8)	88(63.8)	209(45.6)	2.10(1.42,3.11)***
Sniff or snort Rx opioids	357(59.9)	111 (80.4)	246(53.8)	3.53 (2.23, 5.58)***
Sniff or snort Rx tranquilizers	270(45.3)	90(65.2)	180(39.3)	2.90(1.95, 4.31)***
Injection of Rx opioids	154(25.8)	65(47.1)	89(19.5)	3.68 (2.45, 5.53)***
Injection of Rx tranquilizers	63(10.8)	35(25.4)	28(6.1)	5.22(3.04, 8.97)***
Past 90-day misuse of Rx				
Opioids	475(79.7)	123(89.1)	352(77.2)	2.47 (1.39, 4.40)**
Tranquilizers	422(70.8)	114(82.6)	308(67.5)	2.31 (1.43, 3.74)**
Stimulants	265(44.5)	50(36.2)	215(47.1)	0.64(0.43, 0.95)*
Frequency of misuse in past 30 days, mean # of days (SD)				

	Total sample <i>n</i> = 596 <i>n</i> (%)	OD history <i>n</i> = 138 <i>n</i> (%)	No OD history <i>n</i> = 458 <i>n</i> (%)	Unadjusted OR (95% CI)
Opioids	4.55 (7.2)	6.55 (8.6)	3.95 (6.5)	1.05 (1.02,1.07) ***
Tranquilizers	4.09 (7.2)	6.54 (8.8)	3.35 (6.4)	1.06(1.03,1.08) ***
Stimulants	2.07 (5.5)	1.64 (5.1)	2.19(5.6)	0.98 (0.94,1.02)
Frequency of use in past 90 days, mean # of days(SD)				
Heroin	12.84 (25.5)	21.57 (31.4)	10.21 (22.9)	1.02(1.01,1.03) ***
Cocaine	5.44 (12.9)	6.83 (15.3)	5.02(12.1)	1.01 (0.99,1.02)
Methamphetamine	5.86 (17.1)	9.55 (20.7)	4.75 (15.7)	1.01 (1.00,1.02) **

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$.

Table 2

Final regression model predicting history of non-fatal overdose (OD) on prescription opioids and/or tranquilizers.

	Final model Odds ratio (95% CI)
Lower social class growing up	1.81 (1.15, 2.83)**
Past 90-day injection drug use	1.68 (1.03, 2.74)*
Past 90-day misuse of Rx stimulants	0.60(0.38, 0.96)*
Lifetime care in psychiatric hospital	1.79(1.12, 2.85)*
Ever witnessing family member OD	1.59(1.02, 2.50)*
Lifetime prescribed tranquilizers	2.07 (1.29,3.32)**
Lifetime snort opioids	2.51 (1.48, 4.27)***
Lifetime injection of tranquilizers	3.09(1.61, 5.93)***
Model statistics	Chi Square $\chi^2 = 109.01$ ***
	Nagelkerke's $R^2 = 0.266$

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$.