Increased non-fatal overdose risk associated with involuntary drug treatment in a longitudinal study with people who inject drugs

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ABSTRACT

Aim To assess the effect of involuntary drug treatment (IDT) on non-fatal overdose among people who inject drugs (PWID). Design Longitudinal study. Setting Tijuana, Mexico. Participants Baseline sample of 671 PWID included 258 (38.4%) women and 413 (61.6%) men. Measurements Primary independent variables were reported recent (i.e. past 6 months) non-fatal overdose event (dependent variable) and IDT. Substance use the day of the non-fatal overdose was also examined. Findings From 2011 to 2017, 213 participants (31.7%) reported a recent non-fatal overdose and 103 (15.4%) reported recent IDT. Heroin, in combination with methamphetamine and tranquilizers, were the drugs most reported at the day of the event. IDT significantly increased the odds of reporting a non-fatal overdose event [adjusted odds ratio (aOR) = 1.76; 95% confidence interval (CI) = 1.04–2.96]. Odds of non-fatal overdose also increased independently for each additional injection per day (aOR = 1.05; 95% CI = 1.02–1.08), recent tranquilizer use (aOR = 1.92; 95% CI = 1.41–2.61) and using hit doctors (aOR = 1.68; 95% CI = 1.29–2.18) and decreased with age (aOR = 0.97 per year, 95% CI = 0.95–0.99). Conclusions Recent involuntary drug treatment in Mexico is a risk factor for non-fatal drug overdose.

Keywords Cohort study, generalized estimating equation, involuntary treatment, non-fatal overdose, people who inject drugs, Tijuana.

INTRODUCTION

Several countries have implemented some form of involuntary drug treatment (IDT), ranging from treatment administered within the civil commitment framework in the United States [1] to legally mandated and enforced drug treatment, such as forced labor camps in South-East Asia [2,3]. Although implemented widely, there is little evidence of the effectiveness of compulsory treatment in sustaining drug use remission [4]. Globally, IDT has also been associated with high rates of relapse at the individual level and with forced labor and corporal punishment at the structural level, conflicting with fundamental human rights principles [5,6].

Another potential detrimental effect of IDT is that it may increase the risk of overdose. Periods of involuntary drug abstinence (e.g. jail or prison [7]) among people with opioid use disorders have been associated with an increased risk for fatal opioid overdose [7]. This may be related to a loss of tolerance and untreated addiction [7]. Few studies have examined the relationship between drug treatment (voluntary and involuntary) and non-fatal overdose. There is inconclusive evidence for the association between overdose and drug treatment. For instance, with 1 year of follow-up after treatment, an English sample of people who use drugs (PWUD; injecting and non-injecting) from the National Treatment Outcome Research Study showed no association between rates of overdose with voluntary drug treatment [8]. In San Francisco, Ochoa and colleagues [9] found that last-year overdose among PWID was associated with a life-time history of drug treatment. Also in San Francisco, Seal and colleagues [10] found that...
recent non-fatal overdose among PWID was associated with having been imprisoned but was not associated with drug treatment. A national cohort study in Italy among PWUD showed that retention in any drug treatment was protective against fatal overdose, but also showed an excess mortality risk in the month following treatment [11]. A study among PWID in Vancouver, Canada found that being denied drug treatment was associated significantly with recent non-fatal overdose [12].

To our knowledge, only one study has addressed the association between IDT outside prison settings and overdose [13]. This study was conducted among a Thai cohort of PWID and found no association between history of forced treatment and overdose [13]. However, temporal understanding of the relationship between recent IDT and recent experiences of overdose among PWID is largely absent from the literature.

In Mexico, IDT may take the form of: (1) mandated treatment after a three-strike rule upon being presented to a judge for drug possession for personal consumption [14], (2) requests to a judge by a family member [15] and (3) requests made directly at a drug center by a family member (which is against the law, but common) [16]. There may be legal consequences (e.g. prison, fine, community service) only for those who, in addition to drug possession for personal consumption, have committed a crime. There are no exclusive centers for IDT; most of the voluntary and involuntary treatment is provided by abstinence-based residential centers run by small non-government agencies, often led by former drug users, their families and/or religious groups. Informal treatment centers exist due to lack of infrastructure and human resources needed to meet the demand for treatment in the city [17]. These centers operate outside government oversight and are run with minimal or no cost to families [18,19]. In Mexico, overdose surveillance is dismally poor. In 2015 there were only 134 deaths nation-wide that were registered as unintentional overdoses [20]. To overcome the under-registration of fatal overdoses, we focus upon non-fatal overdose events. Non-fatal overdose has been proved to be a predictor of overdose deaths [21,22].

The specific aim of the present study is to assess the impact of IDT experiences on non-fatal overdose among PWID within a framework of a longitudinal study in Tijuana, Baja California, Mexico. Due to its nexus as a drug-trafficking point with the United States, and subsequent drug availability, Tijuana is one of the cities with the highest prevalence of drug use; it is also located within Baja California, the state reporting the highest proportion of criminal justice mandated treatment nation-wide [23]. We hypothesized that PWID who have recently experienced IDT will be significantly more likely to also report recent non-fatal overdose events, compared to those with no IDT experience.

**METHODS**

**Sample**

PWID were recruited to the El Cuete Phase IV (Impact of Drug Policy Reform on the HIV Risk Environment Among PWID in Tijuana) cohort study in 2011 through targeted sampling, which consisted of street-based outreach in 10 neighborhoods throughout Tijuana. A full description of the cohort study is available elsewhere [24]. Briefly, inclusion criteria comprised being 18 years of age or older, having injected drugs in the past month, speaking English or Spanish, currently living in Tijuana with no plans to move over the next 18 months and not currently participating in an HIV intervention study. Participants completed interviewer-administered surveys at baseline and every 6 months (12 visits at the time of the analysis) and received US$20 per visit. Recruitment and data collection activities took place from 2011 to 2017. Of the 735 participants who completed baseline, for this analysis we included participants with at least two visits [n = 671; median = 6.50; interquartile range (IQR) = 3.50–9.50; standard deviation (SD) = 3.45] within the observation period (Supporting Information Table 1). The study protocol was approved by the Human Research Protections Program of the University of California, San Diego and by the Ethics Board at El Colegio de la Frontera Norte.

**Measures**

Data were collected by trained interviewers who administered surveys using computer-assisted participant interview (CAPI) technology. Survey items included socio-demographic characteristics, drug-using behaviors and contextual factors surrounding drug use and treatment. Most of the interviews were conducted at the study site; when participants were not able to attend, they were interviewed at a place of their choice close to where they live. Interviews lasted approximately 45 minutes. The outcome variable was defined as having recently (i.e. 6 months) suffered a non-fatal overdose. We used the following question: ‘In the last 6 months, how many times have you overdosed? This includes any situation where you passed out and couldn’t wake up or your lips turned blue’. For the analysis, a binary dummy variable was created for reporting at least one non-fatal overdose. The primary independent variable was recent IDT; a variable we created for this analysis based on participants’ reports of having been enrolled in a rehabilitation center during the past 6 months (‘In the last 6 months, have you enrolled in a rehabilitation center? By rehabilitation center, I mean a place where you went and stayed overnight for help with your drug or alcohol problems’), and to have been enrolled involuntarily at the rehabilitation center (‘The last time you enrolled in a drug rehab center over the last 6 months, did...')
you go voluntarily to this most recent rehab center?') or to have been forced by law enforcement officials ('I was forced by law enforcement officials' as answer to: 'What are all the reasons that you decided to enroll in this most recent rehab center?).

Socio-demographic variables included were: age, sex, housing status (i.e. living in a house or apartment owned by participants, their parents, friends or partner versus other) and marital status (i.e. married versus other). Substance use-related variables included were: drug or drug combination injected most frequently (heroin, methamphetamine and heroin with methamphetamine), which are the main patterns of substance use among participants [25]; recent heroin ('In the last 6 months have you used heroin?'), methamphetamine, cocaine and tranquilizer use; hit doctor ('In the last 6 months, have you sought the help of a “hit doctor” to inject drugs?'), daily injection frequency and type of drug injected most frequently. Daily frequency of injection was a variable created based on injection drug use questions on the following drugs: heroin, cocaine, heroin and cocaine, methamphetamine, methamphetamine and cocaine, methamphetamine and heroin and methamphetamine and ketamine. For example, participants were asked: ‘During the last 6 months, have you injected heroin by itself?’ If the answer was positive, they were then asked: ‘During the last 6 months, how often have you injected heroin by itself?’ with the following possible answers: ‘one per month or less’, ‘2 or 3 days per month’, ‘once per week, 2 to 3 days per week’, ‘4 to 6 days per week’, ‘once per day’, and ‘more than one time per day every day’. If the answer was ‘more than one time per day every day’ then the value of ‘How many times a day do you inject heroin by itself?’ was used. Heroin was then coded as 0 for less than daily, and the number of times that participants reported injecting per day was entered. This was repeated for each of the drugs and drug combinations and summed.

Analyses

Descriptive summaries were performed for data on recent non-fatal overdose; $\chi^2$ tests were performed for categorical variables and Wilcoxon’s tests for continuous variables at baseline. Frequencies of type of substances the day of the non-fatal overdose event were also calculated. We also performed a sensitivity analysis to determine differences between participants with and without IDT at baseline (Supporting information Table 2).

Univariate and multivariable marginal models using generalized estimating equations (GEE) were also performed. This analytical technique models the outcome while taking into account the correlation between visits within subjects, and provides an estimation of standard errors. The outcome variable was reporting a recent non-fatal overdose event and our primary independent variable was IDT. The marginal models were fitted specifying an exchangeable working correlation structure [26]. First, univariate GEE analyses were generated to determine whether the main independent variable (i.e. recent IDT) and potential confounders (as listed above) were associated with recent non-fatal overdose. Secondly, based on the literature, the univariate and the sensitivity analysis, we entered variables into a multivariable logistic regression model in a manual forward stepwise fashion. Based on results from the variables that attained significance at $P < 0.05$ in univariate GEE models, we entered each variable manually one at a time into the model, starting with the variable with the lowest P-value and ending with the variable that was least significant. The proportion of non-used observations was 9.58%. Therefore, we only included observations with valid information for all the variables used in the analysis. All analyses were performed in SAS version 9.3 software [27].

RESULTS

The baseline sample of 671 PWID included 258 (38.4%) women and 413 (61.6%) men. The median age was 37 years [interquartile range (IQR) = 31–44] and the median number of injections per day was four (IQR = 3–6). There were 64 (9.5%) participants with at least one recent non-fatal overdose at baseline. The bivariate associations between recent overdose and socio-demographic characteristics are shown in Table 1. Those who reported a recent overdose were significantly younger than those with no recent overdose (median = 33.5 versus 37; $P \leq 0.001$). There were no significant differences by sex, marital and housing status. Regarding drug-related variables, there were no significant differences in recent non-fatal overdose reporting by recent IDT, recently requiring help to inject from a hit doctor and number of injections per day. Among those with recent tranquilizer and cocaine use there was a higher proportion of non-fatal overdose than among those with no tranquilizer and cocaine use (14.6 versus 8.4%; $P = 0.030$; 17.3 versus 8.6%; $P = 0.009$, respectively). There were no significant differences in recent methamphetamine and heroin use.

From March 2011 to July 2017, a total of 213 (31.7%) participants experienced at least one non-fatal overdose, 95 of whom (44.6%) suffered one event, 38 (17.8%) two events, 57 (26.8%) three to five events, 10 (4.7%) six events and 13 (6.1%) seven to 17 events. The median number of non-fatal overdoses among those who reported experiencing it at least once was two (IQR = 1–3). In addition, during the same period of observation, 103 participants (15.4%) reported recent IDT, 80 of whom (77.7%) were forced to enter once, 18 (17.5%) were forced twice, four (3.9%) were forced three times and one (1.0%) was
forced four times. All participants were taken to mutual aid/12-Step programs and religious-based groups, none of them run by the government. The median number of recent experiences with IDT among those who experienced it at least once was one (IQR = 1.0–1.0), and the median time spent at the drug center was 3 months (IQR = 1.61–5.00).

Table 2 shows substances used on the day of the non-fatal overdose event. Heroin was the most frequently injected drug, either by itself (43.6%) or combined with other substances (46.9%). The most common combination was with methamphetamine and tranquilizers. Other drugs reported were alcohol, cocaine and a few cases of crocodile/krokodil (i.e. a mixture of several substances that is used as a cheap substitute for heroin), barbiturates, methadone, prescription opioids and phencyclidine (PCP).

Table 3 shows the GEE univariate and multivariable analyses. Non-fatal overdose was associated significantly with younger age, having experienced IDT and greater daily injection frequency. Having been taken involuntarily to drug treatment increased the odds of non-fatal overdose [odds ratio (OR) = 1.97; 95% confidence interval (CI) = 1.15–3.36]. The odds of non-fatal overdose also increased with recent cocaine (OR = 2.26; 95%


**DISCUSSION**

The study findings confirmed our hypothesis that PWID who have recently experienced IDT will be significantly more likely to also report recent non-fatal overdose events. Our study also highlights the common occurrence of non-fatal overdose among our sample of PWID in Tijuana. During a period of 6 years, we found that almost one-third suffered at least one non-fatal overdose, more than half of whom had had more than one event. Additionally, more than one-fifth experienced IDT.

Although we cannot determine conclusively a causal relationship between recent IDT and recent non-fatal overdose, qualitative analysis that we conducted simultaneously to this paper [28] reveals that most of the PWID in our sample are not prepared to stop using drugs when they are taken involuntarily to drug treatment. This, in turn, may increase the risk of non-fatal overdose.

A notable finding is the increased odds of non-fatal overdose associated with daily injection frequency, recent heroin use, and recent methamphetamine use. These findings underscore the importance of addressing these behaviors in intervention programs aimed at reducing non-fatal overdose.

**Table 2** Substances used at the day of the non-fatal overdose events among people who inject drugs. El Cuete Phase IV, Tijuana, Mexico, 2011–17 (n = 671).

<table>
<thead>
<tr>
<th>Substances</th>
<th>n = 326</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>One substance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroina</td>
<td>157</td>
<td>48.16</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>5</td>
<td>1.53</td>
</tr>
<tr>
<td>Crocodile/krokodil</td>
<td>2</td>
<td>0.61</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2</td>
<td>0.61</td>
</tr>
<tr>
<td>Two substances</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin and methamphetaminea</td>
<td>88</td>
<td>26.99</td>
</tr>
<tr>
<td>Heroin and tranquilizers</td>
<td>20</td>
<td>6.13</td>
</tr>
<tr>
<td>Heroin and cocaine</td>
<td>9</td>
<td>2.76</td>
</tr>
<tr>
<td>Heroin and alcohol</td>
<td>6</td>
<td>1.84</td>
</tr>
<tr>
<td>Heroin and methadone</td>
<td>1</td>
<td>0.31</td>
</tr>
<tr>
<td>Methamphetamine and crocodile/krokodil</td>
<td>1</td>
<td>0.31</td>
</tr>
<tr>
<td>Three or more substances</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin, methamphetamine and tranquilizersb</td>
<td>16</td>
<td>4.91</td>
</tr>
<tr>
<td>Heroin, methamphetamine and alcohol</td>
<td>7</td>
<td>2.15</td>
</tr>
<tr>
<td>Heroin, methamphetamine, tranquilizers and alcohol</td>
<td>4</td>
<td>1.23</td>
</tr>
<tr>
<td>Heroin, methamphetamine and cocaine</td>
<td>3</td>
<td>0.92</td>
</tr>
<tr>
<td>Heroin, cocaine and barbiturates</td>
<td>1</td>
<td>0.31</td>
</tr>
<tr>
<td>Heroin, cocaine and tranquilizers</td>
<td>1</td>
<td>0.31</td>
</tr>
<tr>
<td>Heroin, cocaine and alcohol</td>
<td>1</td>
<td>0.31</td>
</tr>
<tr>
<td>Heroin, tranquilizers and methadone</td>
<td>1</td>
<td>0.31</td>
</tr>
<tr>
<td>Heroin, methamphetamine, prescription opioids and PCP</td>
<td>1</td>
<td>0.31</td>
</tr>
</tbody>
</table>

aOne case with marijuana. bTwo cases with marijuana. Crocodile/krokodil is a mixture of several substances that is used as a cheap substitute for heroin. PCP = phencyclidine.

**Table 3** Univariate and multivariable generalized estimating equation analyses for factors related to reporting non-fatal overdose in the past 6 months among people who inject drugs. El Cuete Phase IV, Tijuana, Mexico, 2011–17 (n = 671).

<table>
<thead>
<tr>
<th></th>
<th>Univariate GEE</th>
<th>Multivariate GEE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>0.96</td>
<td>0.94</td>
</tr>
<tr>
<td>Women</td>
<td>1.15</td>
<td>0.86</td>
</tr>
<tr>
<td>Involuntary drug treatmenta</td>
<td>1.97</td>
<td>1.15</td>
</tr>
<tr>
<td>Hit doctora</td>
<td>1.82</td>
<td>1.41</td>
</tr>
<tr>
<td>Heroin usea</td>
<td>0.49</td>
<td>0.24</td>
</tr>
<tr>
<td>Cocaine usea</td>
<td>2.26</td>
<td>1.54</td>
</tr>
<tr>
<td>Methamphetamine usea</td>
<td>1.38</td>
<td>1.02</td>
</tr>
<tr>
<td>Heroin and methamphetamine combination usea</td>
<td>1.05</td>
<td>0.76</td>
</tr>
<tr>
<td>Tranquilizer usea</td>
<td>2.11</td>
<td>1.60</td>
</tr>
<tr>
<td>Daily injection frequencya</td>
<td>1.06</td>
<td>1.04</td>
</tr>
</tbody>
</table>

aPast 6 months. GEE = Generalized Estimating Equation; OR = odds ratio; aOR = adjusted odds ratio; CI = confidence interval. Significance at P < 0.05 shown in bold type.
addition to the loss of tolerance related to abstinence periods, probably puts them at a higher risk of overdose. Furthermore, drug treatment centers in Mexico do not typically adhere to evidence-based modalities and are focused on abstinence-only models [29]. In Tijuana, there are community organizations that distribute naloxone sporadically and train PWID to reverse overdoses. However, there is a lack of public programs that include overdose prevention protocols among public hospitals and first responders. Moreover, drug treatment centers do not provide any type of discharge plans through which PWID could be referred to health or social services.

The proportion of non-fatal overdose in our sample is similar to what was found during a 7-year period among PWID in Vancouver (32.7%) [12]. In contrast to that study, we found that more than half the events occurred with a single drug; however, tranquilizer use was associated significantly with non-fatal overdose and was reported in 13% of the events. As previous research has shown [30–32], we also found that younger users were more likely to suffer a non-fatal overdose compared to an older population. We also found that PWID who inject more and those who asked a hit doctor for help injecting were more at risk of a non-fatal overdose. Higher frequency of injection may be related to the type of drug injected, as stimulants have a shorter half-life [33]. However, stimulant use was not significant after adjusting for covariates. As such, frequency of injection may be related to drug dependence. Having to ask a hit doctor for help indicates less agency in the type and amount of drug injected, and that PWID may no longer be able to inject by themselves because of a long drug injection trajectory [34]. These findings suggest that overdose prevention efforts among this population should focus upon young PWID who have recently experienced IDT and address frequent injecting and tranquilizer use as a risk factor.

The spiraling opioid overdose crisis in North America is fueling increased policy and programmatic emphasis on coercive treatment modalities [35]. Although one study found that being denied access to drug treatment is associated significantly with an elevated risk of non-fatal overdose [12], our study extends this research by showing that experiencing IDT increases the odds of non-fatal overdose. Forced treatment is considered a type of low-security imprisonment or deprivation of basic human rights [36]. Accordingly, it is more adequate to compare our findings to those of imprisonment [12,30]. PWUD who are released from prison usually return to environments that trigger relapse to drug use and put them at risk of non-fatal and fatal overdose [37–40].

The limited resources available for drug treatment need to be allocated to voluntary, evidence-based drug treatment. In Mexico, the median years of delayed treatment since the onset of a substance use disorder is 10 years [41]. That is, the general population would benefit greatly from the institutional strengthening and expansion of treatment services for those who are aware of their treatment need and willing to engage in treatment. Public and private efforts would be needed for a successful transition from involuntary to voluntary service provision in terms of changing treatment centers’ protocols of admission, referrals and case management programs.

This study highlights several future research directions. First, future studies should analyze how IDT affects subsequent treatment seeking and whether, in fact, involuntary drug treatment is related causally to overdose risk. This may be addressed through mixed-methods research conducted specifically with people released from treatment centers. Secondly, we showed an association between IDT and non-fatal overdose; the next step is therefore to address fatal overdose after IDT. Indeed, there is sufficient evidence that non-fatal events are strong predictors of other non-fatal [42,43] and fatal events, including fatal overdose [21,22].

This study has several limitations. First, there is a possibility of residual confounding and a spurious association between the outcome and main independent variables. However, we controlled for the variables that, based on the sensitivity analysis, may be associated with IDT (i.e. age and substance use patterns) to limit it. Secondly, the definition provided to participants concerning overdose is more descriptive of opioid-related overdose, and may have missed cases of stimulant-related overdose [25]. Thirdly, this analysis may have not taken full advantage of the longitudinal data by using lagged variables as predictors. Nevertheless, research suggests that substance use behavior and loss of tolerance that is most proximal to overdose is probably the most predictive [7,11]. Fourthly, selection bias is possible due to attrition, but in the sensitivity analysis we did not find significant differences in the variables included in the analysis among those with more than one visit and those lost after baseline. Fifthly, as we used self-reported measures, there may be recall bias. Nevertheless, non-fatal overdoses and IDT are traumatic events that are unlikely to be forgotten. Finally, we grouped all the IDT experiences and it may be that differences exist depending on the nature of IDT (e.g. law enforcement, family or partner). However, people who are taken involuntarily to treatment by their relatives go to the same centers in which law enforcement officers detain users involuntarily [29]. It is also possible that some PWID who reported having been in drug treatment voluntarily may have been coerced into agreeing to go into treatment, and therefore we would be underestimating the proportion of PWID forced into treatment.

Overall, IDT, as other types of forced abstinence, reduces drug tolerance, putting PWID at risk of non-fatal
overdose. Policy implications include government and treatment centers’ respect for PWID and their right to choose the circumstances of treatment. Professionalization of treatment providers and oversight of addiction treatment agencies will reduce the potential consequences of being discharged into the same psychosocial context of previous drug use, and the need to include overdose prevention at drug treatment centers and upon release [38, 39, 44]. This study highlights the life-threatening risks PWID experience in relation to IDT.

Declaration of interests

None.

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References


Supporting Information
Additional Supporting Information may be found online in the supporting information tab for this article.

**Table S1** Sensitivity analysis of participants with baseline only and more than baseline. El Cuete Phase IV Tijuana (Impact of Drug Policy Reform on the HIV Risk Environment Among PWID in Tijuana), *n* = 735.

**Table S2** Sensitivity analysis of participants with and without involuntary drug treatment. El Cuete Phase IV Tijuana (Impact of Drug Policy Reform on the HIV Risk Environment Among PWID in Tijuana), *n* = 671.

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