HHS Public Access

Author manuscript

Drug Alcohol Depend. Author manuscript; available in PMC 2021 June 01.

Published in final edited form as:

Drug Alcohol Depend. 2020 June 01; 211: 107932. doi:10.1016/j.drugalcdep.2020.107932.

Opioid withdrawal symptoms, frequency, and pain characteristics as correlates of health risk among people who inject drugs

Ricky N. Bluthenthal[1], **Kelsey Simpson**[1], **Rachel Carmen Ceasar**[1], **Johnathan Zhao**[1], **Lynn Wenger**[2], **Alex H. Kral**[2]

[1]Department of Preventive Medicine, Keck School of Medicine, University of Southern California, 2001 N. Soto Street, Los Angeles, CA, USA, 90032.

[2]Behavioral Health Research Division, RTI International, 2150 Shattuck Avenue, Suite 800, Berkeley, CA USA, 94704.

Abstract

Objective—Opioid withdrawal symptoms are widely understood to contribute to health risk but have rarely been measured in community samples of opioid using people who inject drugs (PWID).

Methods—Using targeted sampling methods, 814 PWID who reported regular opioid use (at least 12 uses in the last 30 days) were recruited and interviewed about demographics, drug use, health risk, and withdrawal symptoms, frequency, and pain. Multivariable regression models were developed to examine factors associated with any opioid withdrawal, withdrawal frequency, pain severity, and two important health risks (receptive syringe sharing and non-fatal overdose).

Results—Opioid withdrawal symptoms were reported by 85% of participants in the last 6 months, with 29% reporting at least monthly withdrawal symptoms and 35% reporting at least weekly withdrawal symptoms. Very or extremely painful symptoms were reported by 57%. In separate models, we found any opioid withdrawal (adjusted odds ratio [AOR]=2.75, 95% confidence interval [CI]=1.52, 5.00) and weekly or more opioid withdrawal frequency (AOR=1.94; 95% CI=1.26, 3.00) (as compared to less than monthly) to be independently associated with receptive syringe sharing while controlling for confounders. Any opioid withdrawal (AOR=1.96; 95% CI=1.14, 3.39) was independently associated with nonfatal overdose while controlling for confounders. In a separate model, weekly or more withdrawal frequency

Corresponding Author: Ricky N. Bluthenthal University of Southern California 2001 N. Soto Street, 3rd Floor Los Angeles, CA 90032, rbluthen@usc.edu, 323-442-8236.

Contributors: Ricky Bluthenthal designed the study (along with Alex Kral), conducted the statistical analysis and prepared drafts of the manuscript (along with Kelsey Simpson, Rachel Ceasar, and Johnathan Zhao). Lynn Wenger managed the study protocol. All authors contributed to and have approved the final manuscript.

Conflict of Interest: The authors have no conflict of interest to declare.

Data Statement: Data will be made available to other investigators 1 year following the completion of this study (July 2021).

(AOR=1.60; 95% CI=1.06, 2.42) and extreme or very painful withdrawal symptoms (AOR=1.47; 95% CI=1.04, 2.08) were associated with nonfatal overdose as well.

Conclusions—Withdrawal symptoms among PWID increase health risk. Treatment of withdrawal symptoms is urgently needed and should include buprenorphine dispensing.

Keywords

Risk factors; substance withdrawal syndrome/ prevention & control; heroin/adverse effects; HIV infections/complications; HCV infections/complications; drug overdose/epidemiology; heroin dependence/epidemiology

1. Introduction

1.1 U.S. trends in opioid and heroin use

Opioid use, including prescription opioids, heroin, and licitly and illicitly manufactured fentanyl, is a national crisis in the United States. In 2017, an estimated 11.4 million people misused opioids in the past year, including 11.1 million people who misused pain relievers and 886,000 people who used heroin (Administration, 2018). More than 130 people die each day in the United States from opioid-related overdose (Administration, 2018), with overdose now the leading cause of accidental death in the United States (Kochanek et al., 2019).

Along with increased overdose deaths, there is evidence of increased injection use of opioids. Epidemiological studies have documented HIV outbreaks, regional and national increases in HCV infection, injection-related infective endocarditis, and skin and soft tissue infections since 2000 (Campbell et al., 2017; CDC, 2014; Hedegaard et al., 2015; Keeshin and Feinberg, 2016; Longo et al., 2004; Mack et al., 2017; Unick and Ciccarone, 2017; Unick et al., 2013; Wurcel et al., 2016). Another common consequence of opioid use is opioid withdrawal.

1.2. Opioid withdrawal

Opioid withdrawal may occur if someone is physically dependent on opioids and then abruptly stops or substantially reduces their opioid dose, with the time of onset, peak symptoms, and duration of opioid withdrawal varying depending on the specific opioid being used. For example, symptoms of heroin withdrawal can begin as soon as 4 to 6 hours after last use, peak within approximately 24 to 48 hours, and may last for 7 to 14 days (O'Connor and Fiellin, 2000). The experience of opioid withdrawal is characterized by physical symptoms that may include muscle aches and bone pain, abdominal cramps, agitation and anxiety, nausea and vomiting, diarrhea, gastrointestinal upset, tachycardia, rhinorrhea, and chills (Donroe et al., 2016; Wesson and Ling, 2003).

As a person's opioid use increases and they become more involved in the moral economy of drug use exchanges and relationships (Wakeman, 2016), they may become more focused on obtaining opioids as an effective way to avoid withdrawal symptoms (i.e., "getting sick" and "staying well"), resulting in increased unsafe drug use contexts (Sherman and Latkin, 2002), socioeconomic marginalization, and related consequences such as incarceration and unemployment that may further increase risk (Richardson et al., 2019). Along these lines,

withdrawal has been found to be a common barrier to reducing the risk of unsafe drug contexts (Phillips, 2016) among people who inject drugs (PWID). This presents a cycle of increasing drug use to avoid withdrawal: a person develops an urgent need to avoid or alleviate withdrawal, they become anxious about withdrawal and/or getting well and will often seek injection as a route of administration to quickly alleviate being sick, which may lead to engaging in unsafe drug use behaviors (e.g., shared needles, using alone) with increased risk for infectious disease transmission and overdose, both nonfatal (Coffin et al., 2007; Pouget et al., 2017) and fatal (Fairbairn et al., 2017; Mars, Sarah G. et al., 2018). To break this cycle and related health risks, evidence points to interventions to reduce exposure to withdrawal episodes and risky injecting networks (Barnes et al., 2018; Mateu-Gelabert et al., 2014; O'Connor and Fiellin, 2000; Weiss et al., 2014).

Chronic opioid use can lead to withdrawal symptoms, yet withdrawal symptoms have rarely been measured in community samples of PWID. In the following, we describe the prevalence, demographic, and drug use factors associated with opioid withdrawal symptoms, frequency, and pain severity in a sample of street-recruited PWID and examine if opioid withdrawal symptoms are associated with receptive syringe sharing and non-fatal overdose.

2. Methods

2.1. Study sample

Data for these analyses come from the "Change the Cycle" efficacy trial study in Los Angeles and San Francisco, California (Strike et al., 2014) (NIDA grant #R01DA038965). For these analyses, we use data from the baseline interview. Participants were recruited using targeted sampling methods (Bluthenthal and Watters, 1995; Kral et al., 2010; Watters and Biernacki, 1989). Study inclusion criteria were self-reported injection drug use in the last 30 days (confirmed by visual inspection of injection stigmata or "track" marks) (Cagle et al., 2002), 18 years of age or older, and capacity to complete informed consent procedures. Participants completed a 45-minute computer-assisted personal interview using the Questionnaire Design System (NOVA Research, Bethesda, MD). All study procedures were reviewed and approved by the institutional review board at the University of Southern California. Participants received $20 for completing the interview.

Following the work of Mateu-Gelabert on opioid withdrawal (Mateu-Gelabert et al., 2017), we only asked withdrawal items of participants who regularly used opioids, which we defined as at least 12 episodes of opioid use (i.e., heroin, prescription opioids, and opioids in combination with methamphetamine [goofball] or cocaine [speedball]) in the last 30 days (n=814). For analyses of opioid withdrawal symptom frequency and pain severity, only participants who reported any withdrawal were included (n=690).

2.2. Key variables

To determine if any opioid-related withdrawal symptoms were experienced in the last 6 months, we asked a single question comprised of DSM-5 diagnostic symptomatology for opioid withdrawal (Association, 2013; Shah and Huecker, 2019) with the exception of insomnia. Insomnia was excluded due to its strong association with homelessness (Léger et

al., 2017; Reitzel et al., 2017) and high prevalence of homelessness among participants (84%). The specific item was: “In the last 6 months, have you experienced restlessness, bone or muscle aches, runny nose, sweating, cold or hot flashes, anxiety, teary eyes, stomach cramps, nausea, diarrhea, vomiting, or other symptoms due to withdrawal from heroin or opiates?” Those responding “yes” were classified as having experienced opioid-related withdrawal. Participants with opioid withdrawal were also asked about the number of withdrawal episodes in the last 6 months and the pain severity of episodes (not painful, somewhat painful, moderately painful, very painful, extremely painful). Participants responding “don’t know” to frequency of withdrawal episodes (n=9) were recoded to 1 episode. Withdrawal frequency was not normally distributed, so we re-coded it using a natural break approach into the following categories: less than once a month, at least monthly to nearly weekly, at least weekly. The withdrawal pain severity variable was recoded into “extremely or very painful” versus “moderately to not painful” to facilitate data analysis. While clinical assessments of opioid withdrawal are available, those methods were inappropriate for use in our study because interviews were conducted by non-clinicians (Wesson and Ling, 2003).

Potential covariates included variables associated with withdrawal in prior literature (Mateu-Gelabert et al., 2010b; Michel et al., 2009), drug use patterns (drug use frequency, types) excluding opioids, demographic (race, gender, and age), and socioeconomic (income, housing, food insecurity) characteristics. Due to combined use of some substances (e.g., cocaine with heroin or methamphetamine with heroin), we calculated several summed variables that account for total use of a substance. In these analyses, we looked at total use of cocaine (including crack cocaine and in combination with heroin) and total use of methamphetamine (including use in combination with heroin).

We also considered whether withdrawal variables were associated with important health risks. Receptive syringe sharing was assessed as follows: “In the last 6 months, how many times did you inject using syringes/needles that had been used by someone else (including a close friend or lover)?” To facilitate analysis, we recoded this variable such that a response of zero times equaled “no,” and 1 or more equaled “yes.” Non-fatal overdose was assessed as follows: “In the last 6 months, have you overdosed?”

2.3 Statistical analysis

Descriptive statistics (e.g. frequencies, means, standard deviations, among others) were examined for all study variables. To examine factors associated with any opioid withdrawal, opioid withdrawal frequency, and opioid withdrawal symptom pain we used the following approach. Bivariate analysis was conducted to determine characteristics associated with these outcome variables. Variables significant (p <0.05) in bivariate analysis were assessed for collinearity. Collinear variables were removed from the final analysis based on strength of association with the outcome variable. Associations were assessed using multivariable logistic regression models or multinomial regression (for withdrawal frequency). Variables found to be significant at p <0.05 were considered to be independently associated with the outcome variable and were retained in the final models.

To examine receptive syringe sharing in the last 30 days and nonfatal overdose in the last 6 months, we constructed two models for each outcome following the methods described above. Model 1 included only any withdrawal (n=814), while model 2 includes withdrawal pain severity and frequency since these measures were only collected from participants who had at least one opioid withdrawal episode in the last 6 months (n=690).

3. Results

3.1 Sample characteristics

The sample was mostly male (75%) with an average age of 42 years (SD = 12.34; median = 42; Interquartile Range [IQR] = 31, 52)(Table 1). The plurality of subjects was White (41%), with meaningful proportions reporting being Latinx (25%), African American (21%), Native American (7%), and Mixed Race/Other Race (6%). Average number of years of drug injection was 20.36 (SD = 14.20; median = 19.00; IQR = 7, 32). Current homelessness was reported by 84% of our sample. Overall, the mean frequency of past 30-day drug use (non-injection and injection) was 231 times (SD = 224.08; median = 165; IQR = 96.75, 284). Average number of drug injections in the last 30 days was 144.14 (SD = 135.12; median = 106; IQR= 106, 180.25), and mean frequency of total past month opioid/heroin use was 129.80 times (SD = 116.14; median = 99.50; IQR = 60, 165).

Among regular opioid using PWID, opioid withdrawal symptoms (past 6 months) were reported by 85% (692/814). Withdrawal episodes occurred an average of 46.01 times (SD = 72.47, median = 12; IQR = 4, 58) in the last 6 months. Looking at withdrawal frequency categorically, we found that 36% reported withdrawal symptoms less than once a month, 29% reported monthly to almost weekly withdrawal symptoms, and 35% reported weekly to daily withdrawal symptoms. Very or extremely painful symptoms were reported by 57% of participants.

3.2 Factors associated with any recent opioid withdrawal

Results from bivariate analyses revealed the following variables to be associated with recent (past 6 month) opioid withdrawal: age; White race; past month non-injection prescription tranquilizer and buprenorphine use; injection powder cocaine use; social security income, illegal or possibly illegal activities, and panhandling income sources; 30-day total injection frequency and 30-day drug use frequency (Table 2a). In the multivariable analysis model (Table 3), being younger than 50 years of age was associated with higher odds of withdrawal as was having an illegal or possibly illegal income source in the last 30 days.

3.3 Factors associated with frequency of opioid withdrawal episodes and withdrawal pain severity

Key variables found to be associated with frequency of withdrawal symptoms were drug use frequency (including injection drug frequency, total methamphetamine use), drug use types (injection methamphetamine use, non-injection use of tranquilizers), years of injecting, demographics (age and race), and income sources (SSI, recycling, and illegal or possibly illegal sources) (Table 2b). In multinomial regression analysis (Table 4), younger age and methamphetamine injection in the last 30 days significantly increased odds of weekly or

more opioid withdrawal frequency as compared to participants that reported withdrawal symptoms less than once a month. African American race and lower injection frequency significantly reduced odds of having weekly or more opioid withdrawal symptoms.

Variables significantly associated with withdrawal pain severity (very or extremely severe pain versus moderate to no pain) are presented in Table 2a. In bivariate analysis, factors associated with withdrawal pain severity included being female, White race, 30-day non-injection crack cocaine use, and non-injection methadone use. In the multivariable logistic regression analysis, we found sex (female), race (African American and Mixed Race/Other Race), and 30-day non-prescribed methadone use to increase odds of experiencing very or extremely painful withdrawal within the prior 6 months. Non-injection crack cocaine use in the last 30 days reduced odds of experiencing very or extremely painful withdrawal symptoms in the last 6 months (Table 5).

3.4 Associations between withdrawal measures, receptive syringe sharing, and non-fatal overdose

Results from logistic regression analyses exploring the relationship between withdrawal measures and receptive syringe sharing and non-fatal overdose are shown in Table 6. In the first model of receptive syringe sharing, we found that PWID with any withdrawal in the last 6 months had significantly higher odds of sharing syringes (adjusted odds ratio [AOR]=2.75; 95% confidence interval [CI]=1.52, 5.00) while controlling for confounders. In the second model, weekly or more withdrawal frequency (AOR=1.94; 95% CI=1.26, 3.00) as compared to less than monthly withdrawal frequency was significantly associated with receptive syringe sharing while controlling for confounders. Withdrawal pain severity was not associated with receptive syringe sharing. In the first model of non-fatal overdose, we found any withdrawal (AOR=1.71; 95% CI=1.04, 2.81) was significantly associated with increased odds of non-fatal overdose. In the second model, both weekly opioid withdrawal frequency (AOR=1.69; 95% CI=1.12, 2.55) and having very or extremely severe levels of withdrawal pain (AOR=1.53; 95% CI= 1.08, 2.16) were significantly associated with increased odds of having a non-fatal overdose.

4. Discussion

To our knowledge, this is the first study to characterize opioid withdrawal symptoms among community recruited PWID on the West Coast. Opioid withdrawal symptoms were reported by the vast majority of opioid-using PWID (85%) making opioid withdrawal symptoms among the most common chronic health problem experienced by this population (by way of comparison, HCV infection was reported by 61% and HIV by 4% of this sample; other samples have found any mental health diagnosis as high as 82% in similar samples, but rates by diagnosis are lower) (Colledge et al., 2020; Goodhew et al., 2016). Nearly two-thirds had opioid withdrawal symptoms at least monthly and over one third reported them at least weekly. Most study participants characterized pain from opioid withdrawal as very or extremely painful (57%). This proportion is comparable to the only other report on opioid withdrawal pain among community sampled PWID; this report from New York found that 56% reported serious withdrawal symptoms in the last 2 months (Coffin et al., 2007).

Qualitative studies among participants who use opioids describe withdrawal symptoms as being debilitating (Summers et al., 2018). Given the high prevalence and pain severity of opioid withdrawal symptoms, there is a clear need for community-based strategies to assist opioid-using PWID with management of withdrawal symptoms.

We also found two of three measures of opioids withdrawal to be associated with increased odds of receptive syringe sharing. Qualitative studies have linked withdrawal to increased HIV/HCV risk through rushed injection and syringe sharing, along with delaying treatment and leaving hospitalization against medical advice for PWID with skin and soft tissue infections (Mateu-Gelabert et al., 2010a) (Connors, 1994; McNeil et al., 2014). Our findings confirm the qualitative reports that opioid withdrawal symptoms are correlated to injection-related risk. Research in the future needs to examine the association between withdrawal symptoms and rushed injections in particular. While other studies have found rushed injections to be associated with syringe sharing (Ti et al., 2015), withdrawal symptoms have not been examined quantitatively as a facilitator of rushed injection. In addition, in the context of fentanyl contamination of the heroin supply in many locales (Carroll et al., 2017; Ciccarone et al., 2017; Daniulaityte et al., 2019a; Park et al., 2018) and transitions to illicitly manufactured fentanyl use specifically (Mars, S. G. et al., 2018; Morales et al., 2019), rushing injection can be particularly dangerous. One common strategy for preventing fentanyl overdoses is to slow down the injection process (Mars, Sarah G. et al., 2018; Rouhani et al., 2019). If withdrawal symptoms are associated with rushed injection then this strategy will fail to prevent overdose episodes in areas where fentanyl has contaminated the heroin supply or replaced it. Investigating the connection between withdrawal symptoms and rushed injections is urgently needed. In addition, efforts to manage opioid withdrawal symptoms among regular opioid using PWID is warranted.

We also found that opioid withdrawal symptom attributes (any, frequency, and pain severity) were associated with nonfatal overdose in the last 6 months. Our finding that very or extremely painful opioid symptoms were associated with elevated overdose odds confirms findings from a New York city study from 2001 to 2004 that found nonfatal overdose in the last 6 months to be associated with having at least one episode of serious withdrawal symptoms in the last 2 months (Coffin et al., 2007). Our findings add to the literature by documenting any opioid withdrawal episode over a 6-month period increases odds of a nonfatal overdose among opioid using PWID. In addition, in looking at the subsample of participants who reported any opioid withdrawal, those with more frequent withdrawal symptoms (i.e. weekly or more) were significantly more likely to report elevated odds of nonfatal overdose in the last 6 months. The consistent association of opioid withdrawal symptom attributes with non-fatal overdose, underscores the value of responding to opioid withdrawal as a means of reducing nonfatal overdoses and, by extension, opioid overdose mortality.

At present, medications (specifically, buprenorphine, lofexidine, and clonidine) exist to provide opioid-using PWID with relief from withdrawal symptoms, but are primarily available in the context of medical tapers/detoxification programs, long-term treatment, or during hospitalization (Doughty et al., 2019; Gowing et al., 2017; Kenney et al., 2018; Pergolizzi et al., 2019). Consideration of providing some of these medications (and in

particular, buprenorphine) to people who use opioids under more flexible conditions has been advocated (Roy and Stein, 2019). In an opinion piece published in the *Journal of the American Medical Association*, Roy and Stein lay out the conditions for permitting emergency dispensing of buprenorphine for people experiencing opioid withdrawal symptoms. They argue that the modest euphoric properties of buprenorphine (if used by opioid naïve people) along with its rapid effect on symptoms for people who have opioid use disorder make it an ideal medication for this type of distribution. Likewise, protocols have been developed and implemented to provide buprenorphine to people presenting at emergency departments with acute opioid withdrawal (Cisewski et al., 2019; Dunkley et al., 2019; Mateu-Gelabert et al., 2015), typically following an opioid-related overdose. Additional community-oriented approaches have been piloted in San Francisco, CA and Baltimore, MD. In San Francisco, a street-medicine approach was used to engage nearly 100 homeless people with heroin use disorder in buprenorphine treatment (Carter et al., 2019), while a mobile unit was used to dispense buprenorphine in Baltimore (Krawczyk et al., 2019). The patient use patterns of these low threshold approaches matches what we might imagine a dedicated withdrawal symptom intervention would look like: early initial use with significant drop in renewed prescriptions (about half do not renew), and some (~20%) moving on to sustain use that would characterize treatment. Since withdrawal symptom management and related risk were not assessed, we do not know if improvements in injection-related HIV/HCV risk, skin and soft tissue care, and hospitalization were achieved, but studies that pair low threshold access to withdrawal medications should consider other health outcomes along with changes in heroin, opioid, or fentanyl use disorder in the future. Lastly, it is worth noting that we have multiple reports of PWID using diverted opioid medications (i.e., methadone and buprenorphine) for purposes of withdrawal management, underscoring the acceptability of these medications for managing this common ailment among people who use opioids (Bazazi et al., 2011; Carroll et al., 2018; Daniulaityte et al., 2019b; Harris and Rhodes, 2013; Monte et al., 2009). Increased access to opioid treatment medication for purposes of withdrawal management, opioid misuse reduction, and cessation is urgently needed.

We also found that opioid withdrawal, pain, and frequency were associated with demographic, economic, and drug use patterns. Of particular note, we found that younger PWID had higher odds of reporting any withdrawal and reported more frequent withdrawal episodes. Qualitative research might be needed to explain this finding, but elevated withdrawal frequency suggests the value of making opioid treatment medications more easily available to younger opioid-using PWID as a way to diminish both drug use and other health ailments that typically occur the longer a person uses and injects opioids. We also found that African American PWID reported more severe pain associated with withdrawal and, perhaps as a consequence, reported lower frequency of withdrawal. There is not an existing explanation for greater pain related to withdrawal symptoms by race, but the lower frequency of withdrawal could be due to this experience and adaption of drug use patterns and collection of resources to avoid withdrawal symptoms (Mateu-Gelabert et al., 2010a). On the other hand, at least one study has found that African American respondents had significantly lower odds of reporting opioid withdrawal symptoms (Elliott and Jones, 2019). Elliot and Jones (2019) noted that this may be due to opioid metabolism differences between

Whites and African Americans (Smith, 2009). Lastly, we found that female PWID had higher odds of reporting very or extremely painful withdrawal symptoms. While there is little research assessing sex differences from withdrawal, our findings are consistent with the literature on the unique risks of withdrawal for women (Darnall et al., 2012; Epele, 2001; Knight, 2015). One recent study found similar results for women with chronic pain and self-reported prescription opioid misuse in the last 30 days (Huhn et al., 2019). The continued study of race and sex differences among people who use opioids and consequences from this use appears warranted.

Study results should be assessed with the following limitations in mind. First, the study design is cross-sectional, and therefore further examinations of whether observed associations persist longitudinally is worthy of additional study. Second, our measures are self-reported and are therefore potentially subject to both recall bias and socially desirable responding. However, on measures of drug use, the items used in this study have been found to be reliable and valid (Dowling-Guyer et al., 1994; Weatherby et al., 1994). Third, we used a single item to assess withdrawal symptoms. This approach has been used in samples of PWID on occasion (Michel et al., 2009). More common clinical measures of withdrawal symptoms typically ask about a longer time frame (12 months) and assess each symptom, with participants reporting 3 or more symptoms being classified as opioid/heroin withdrawal (Elliott and Jones, 2019). Our single item measure may lead to more reports of withdrawal, but our shorter observation period (6 months) may lead to fewer reports. Direct comparisons between our measure and others should not be made.

Nonetheless, this study is the first to report opioid withdrawal symptoms frequency in a large sample of opioid-using PWID. The high prevalence, frequency, and pain severity of opioid withdrawal indicates that this is a significant health challenge for PWID. To date, few intervention efforts have been made to mitigate the harms of withdrawal for PWID unless they are willing to initiate formal treatment. This needs to change. Treatment of withdrawal symptoms, in its own right, appears warranted. It is likely that using medications that are typically used for treatment, such as buprenorphine, would have the additional benefit of introducing this medication to PWID who have low access to medication-assisted opioid treatment.

Additional benefits might also be obtained within the context of the growing fentanyl overdose crisis in the United States. With heroin contaminated with fentanyl or fentanyl being sold as a standalone product, the risk of overdose (Lambdin et al., 2019; Spencer et al., 2019), overdose death, and injection-related HIV risk have increased significantly. In this context, use of non-prescribed buprenorphine or methadone serves the purpose of directly reducing immediate risk for overdose and reducing the probability of injection-related risk, such as HIV/HCV and skin and soft tissue infections.

The opioid crisis in the United States has revealed numerous gaps in services for PWID who are not in treatment. At the same time, we have highly efficacious medications for the treatment of opioid use disorder. Regulations, absence of political will, and indifference have contributed to the extension of this crisis, resulting in downstream health calamities such as overdose deaths, HIV outbreaks, nationwide epidemics of HCV and skin and soft tissue

infections, and an emerging epidemic of injection-related infective endocarditis (CDC, 2015; Unick et al., 2013; Wurcel et al., 2016; Zibbell et al., 2017). Tools to address these health risks continue to be underused, but in the case of buprenorphine, at least significant progress has been made with dramatic increases in physician training for prescribing this medication for opioid treatment. To address the frequent yet preventable health problem of opioid withdrawal among PWID, we should increase prescribing of buprenorphine (Rhee and Rosenheck, 2019) along with de-regulation of buprenorphine (Roy and Stein 2019) so that more providers and locations can make this valuable medication available to opioid-using PWID.

Acknowledgement

We would like to thank study participants for their time and effort in this project. We would also that the following individuals who meaningfully contributed to the study: Amin Afsahrezvani, Debra Allen, Letizia Alvarez, Julia Balboni, Joseph Becerra, Kacie Blackman, Guiseppe Cavaleri, Janae Chatmon, Fitsum Dejene, Karina Dominguez Gonzalez, Mohammed El-Farro, Brian Erwin, Sernah Essien, Allison Few, Hrant Gevorgian, Allessandra Gianino, Johnathan Hakakha, Jennifer Hernandez, Monika Howe, Alexander Ildaradashty, Cora Jenkins, Sasha Lasky, Joshua McKeever, Askia Mohammad, Rebecca Penn, Tasha Perdue, Jennifer Plumber, T'yana Taylor, Olivia Uhley, Jeffery Williams, David Wiss, Thomas Won, and Senem Yilmaz.

Role of funding source: Research reported in this publication was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number RO1 DA038965, Project Official, Richard Jenkins, Ph.D. and R01DA046049, Project Official, Heather Kimmel, Ph.D.

REFERENCES

American Psychiatric Association, 2013 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Ed. Arlington, VA.

Barnes DM, Des Jarlais DC, Wolff M, Feelemyer J, Tross S, 2018 A qualitative study of persons who inject drugs but who have never helped others with first injections: How their views on helping contrast with the views of persons who have helped with first injections, and implications for interventions. Harm Reduct J, 15, 43. [PubMed: 30153826]

Bazazi AR, Yokell M, Fu JJ, Rich JD, Zaller ND, 2011 Illicit use of buprenorphine/naloxone among injecting and noninjecting opioid users. J. Addict. Med 5, 175–180. [PubMed: 21844833]

Bluthenthal RN, Watters JK, 1995 Multimethod research from targeted sampling to HIV risk environments. NIDA Res. Monogr 157, 212–230. [PubMed: 8684438]

Cagle HH, Fisher DG, Senter TP, Thurmond RD, Kastar AJ, 2002 Classifying skin lesions of injection drug users: A method for corroborating disease risk. Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, Rockville, MD.

Campbell EM, Jia H, Shankar A, Hanson D, Luo W, Masciotra S, Owen SM, Oster AM, Galang RR, Spiller MW, Blosser SJ, Chapman E, Roseberry JC, Gentry J, Pontones P, Duwve J, Peyrani P, Kagan RM, Whitcomb JM, Peters PJ, Heneine W, Brooks JT, Switzer WM, 2017 Detailed transmission network analysis of a large opiate-driven outbreak of HIV infection in the United States. J. Infect. Dis 216, 1053–1062. [PubMed: 29029156]

Carroll JJ, Marshall BDL, Rich JD, Green TC, 2017 Exposure to fentanyl-contaminated heroin and overdose risk among illicit opioid users in Rhode Island: A mixed methods study. Int. J. Drug Policy 46, 136–145. [PubMed: 28578864]

Carroll JJ, Rich JD, Green TC, 2018 The more things change: Buprenorphine/naloxone diversion continues while treatment remains inaccessible. J. Addict. Med 12, 459–465. [PubMed: 30095563]

Carter J, Zevin B, Lum PJ, 2019 Low barrier buprenorphine treatment for persons experiencing homelessness and injecting heroin in San Francisco. Addict. Sci. Clin. Pract 14, 20. [PubMed: 31060600]

Centers for Disease Control and Prevention, 2014 *QuickStats:* Rates of drug poisoning deaths involving heorin,* by selected age and racial/ethnic groups - United States, 2002 and 2011. MMWR 63, 595.

Centers for Disease Control and Prevention, 2015 Community outbreak of HIV infection linked to injection drug use of oxymorphone - Indiana. MMWR 64, 443–444. [PubMed: 25928470]

Ciccarone D, Ondocsin J, Mars SG, 2017 Heroin uncertainties: Exploring users' perceptions of fentanyl-adulterated and -substituted 'heroin'. Int. J. Drug Policy 46, 146–155. [PubMed: 28735775]

Cisewski DH, Santos C, Koyfman A, Long B, 2019 Approach to buprenorphine use for opioid withdrawal treatment in the emergency setting. Am. J. Emerg. Med 37, 143–150. [PubMed: 30355476]

Coffin PO, Tracy M, Bucciarelli A, Ompad D, Vlahov D, Galea S, 2007 Identifying injection drug users at risk of nonfatal overdose. Acad. Emerg. Med 14, 616–623. [PubMed: 17554010]

Colledge S, Larney S, Peacock A, Leung J, Hickman M, Grebely J, Farrell M, Degenhardt L, 2020 Depression, post-traumatic stress disorder, suicidality and self-harm among people who inject drugs: A systematic review and meta-analysis. Drug Alcohol Depend. 207, 107793. [PubMed: 31874449]

Connors MM, 1994 Stories of pain and the problem of AIDS prevention: Injection drug withdrawal and its effect on risk behavior. Med. Anthropol. Q 8, 47–68.

Daniulaityte R, Carlson RR, Juhascik MP, Strayer KE, Sizemore IE, 2019 Street fentanyl use: Experiences, preferences, and concordance between self-reports and urine toxicology. Int. J. Drug. Policy 71, 3–9. [PubMed: 31146200]

Daniulaityte R, Nahhas RW, Silverstein S, Martins S, Zaragoza A, Moeller A, Carlson RG, 2019 Patterns of non-prescribed buprenorphine and other opioid use among individuals with opioid use disorder: A latent class analysis. Drug Alcohol Depend. 204, 107574. [PubMed: 31568934]

Darnall BD, Stacey BR, Chou R, 2012 Medical and psychological risks and consequences of long-term opioid therapy in women. Pain Med. 13, 1181–1211. [PubMed: 22905834]

Donroe JH, Holt SR, Tetrault JM, 2016 Caring for patients with opioid use disorder in the hospital. CMAJ. 188, 1232–1239. [PubMed: 27647616]

Doughty B, Morgenson D, Brooks T, 2019 Lofexidine: A newly FDA-approved, nonopioid treatment for opioid withdrawal. Ann. Pharmacother 53, 746–753. [PubMed: 30724094]

Dowling-Guyer S, Johnson ME, Fisher DG, Needle R, Watters J, Andersen M, Williams M, Kotranski L, Booth R, Rhodes F, Weatherby N, Estrada AL, Fleming D, Deren S, Tortu S, 1994 Reliability of drug users' self-reported HIV risk behaviors and validity of self-reported recent drug use. ASM. 1, 383–392.

Dunkley CA, Carpenter JE, Murray BP, Sizemore E, Wheatley M, Morgan BW, Moran TP, Steck A, 2019 Retrospective review of a novel approach to buprenorphine induction in the emergency department. J. Emerg. Med 57, 181–186. [PubMed: 31060846]

Elliott KR, Jones E, 2019 The association between frequency of opioid misuse and opioid use disorder among youth and adults in the United States. Drug Alcohol Depend. 197, 73–77. [PubMed: 30784951]

Epele ME, 2001 Scars, harm and pain. J. Ethn. Subst. Abuse 1, 47–69.

Fairbairn N, Coffin PO, Walley AY, 2017 Naloxone for heroin, prescription opioid, and illicitly made fentanyl overdoses: Challenges and innovations responding to a dynamic epidemic. Int. J. Drug Policy 46, 172–179. [PubMed: 28687187]

Goodhew M, Salmon AM, Marel C, Mills KL, Jauncey M, 2016 Mental health among clients of the Sydney Medically Supervised Injecting Centre (MSIC). Harm Reduct. J 13, 29. [PubMed: 27733167]

Gowing L, Ali R, White JM, Mbewe D, 2017 Buprenorphine for managing opioid withdrawal. The Cochrane database of systematic reviews 2, Cd002025. [PubMed: 28220474]

Harris M, Rhodes T, 2013 Methadone diversion as a protective strategy: the harm reduction potential of 'generous constraints'. Int. J. Drug Policy 24, e43–50. [PubMed: 23199896]

Hedegaard H, Chen L, Warner M, 2015 Drug-poisoning deaths involving heroin: United States, 2000–2013, NCHS data brief. National Center for Health Statistics, Hyattsville, MD.

Huhn AS, Tompkins DA, Campbell CM, Dunn KE, 2019 Individuals with chronic pain who misuse prescription opioids report sex-based differences in pain and opioid withdrawal. Pain Med.

Keeshin SW, Feinberg J, 2016 Endocarditis as a marker for new epidemics of injection drug use. Am. J. Med. Sci 352, 609–614. [PubMed: 27916216]

Kenney SR, Anderson BJ, Bailey GL, Stein MD, 2018 Buprenorphine treatment formulations: Preferences among persons in opioid withdrawal management. J. Subst. Abuse Treat 94, 55–59. [PubMed: 30243418]

Knight K, 2015 addicted.pregnant.poor. Duke University Press, Durham, NC.

Kochanek K, Murphy S, Xu J, Arias E, 2019 Deaths: Final data for 2017, National Vital Statistics Reports. National Center for Health Statistics, Hyattsville, MD.

Kral AH, Malekinejad M, Vaudrey J, Martinez AN, Lorvick J, McFarland W, Raymond HF, 2010 Comparing respondent-driven sampling and targeted sampling methods of recruiting injection drug users in San Francisco. J. Urban Health 87, 839–850. [PubMed: 20582573]

Krawczyk N, Buresh M, Gordon MS, Blue TR, Fingerhood MI, Agus D, 2019 Expanding low-threshold buprenorphine to justice-involved individuals through mobile treatment: Addressing a critical care gap. J. Subst. Abuse Treat 103, 1–8. [PubMed: 31229187]

Lambdin BH, Bluthenthal RN, Zibbell JE, Wenger L, Simpson K, Kral AH, 2019 Associations between perceived illicit fentanyl use and infectious disease risks among people who inject drugs. Int. J. Drug Policy 74, 299–304. [PubMed: 31733979]

Longo MC, Henry-Edwards SM, Humeniuk RE, Christie P, Ali RL, 2004 Impact of the heroin 'drought' on patterns of drug use and drug-related harms. Drug Alcohol Rev. 23, 143–150. [PubMed: 15370019]

Léger D, Beck F, Richard JB, 2017 Sleep loss in the homeless—An additional factor of precariousness: Survey in a group of homeless people. JAMA. Intern. Med 177, 278–279.

Mack KA, Jones CM, Ballesteros MF, 2017 Illicit drug use, illicit drug use disorders, and drug overdose deaths in metropolitan and nonmetropolitan areas—United States. Am. J. Transplant 17, 3241–3252. [PubMed: 29145698]

Mars SG, Ondocsin J, Ciccarone D, 2018 Toots, tastes and tester shots: User accounts of drug sampling methods for gauging heroin potency. Harm Reduct. J 15, 26. [PubMed: 29769132]

Mars SG, Rosenblum D, Ciccarone D, 2018 Illicit fentanyls in the opioid street market: desired or imposed? Addiction 114, 774–780. [PubMed: 30512204]

Mateu-Gelabert P, Guarino H, Jessell L, Teper A, 2015 Injection and sexual HIV/HCV risk behaviors associated with nonmedical use of prescription opioids among young adults in New York City. J. Subst. Abuse Treat 48, 13–20. [PubMed: 25124258]

Mateu-Gelabert P, Gwadz MV, Guarino H, Sandoval M, Cleland CM, Jordan A, Hagan H, Lune H, Friedman SR, 2014 The Staying Safe Intervention: Training people who inject drugs in strategies to avoid injection-related HCV and HIV infection. AIDS Educ. Prev 26, 144–157. [PubMed: 24694328]

Mateu-Gelabert P, Jessell L, Goodbody E, Kim D, Gile K, Teubl J, Syckes C, Ruggles K, Lazar J, Friedman S, Guarino H, 2017 High enhancer, downer, withdrawal helper: Multifunctional nonmedical benzodiazepine use among young adult opioid users in New York City. Int. J. Drug Policy 46, 17–27. [PubMed: 28577506]

Mateu-Gelabert P, Sandoval M, Meylakhs P, Wendel T, Friedman SR, 2010 Strategies to avoid opiate withdrawal: Implications for HCV and HIV risks. Int. J. Drug Policy 21, 179–185. [PubMed: 19786343]

McNeil R, Small W, Wood E, Kerr T, 2014 Hospitals as a 'risk environment': an ethno-epidemiological study of voluntary and involuntary discharge from hospital against medical advice among people who inject drugs. Soc. Sci. Med 105, 59–66. [PubMed: 24508718]

Michel L, Giorgi R, Villes V, Poizot-Martin I, Dellamonica P, Spire B, Protopopescu C, Carrieri MP, 2009 Withdrawal symptoms as a predictor of mortality in patients HIV-infected through drug use and receiving highly active antiretroviral therapy (HAART). Drug Alcohol Depend. 99, 96–104. [PubMed: 18774237]

Monte AA, Mandell T, Wilford BB, Tennyson J, Boyer EW, 2009 Diversion of buprenorphine/naloxone coformulated tablets in a region with high prescribing prevalence. J. Addict. Dis 28, 226–231. [PubMed: 20155591]

Morales KB, Park JN, Glick JL, Rouhani S, Green TC, Sherman SG, 2019 Preference for drugs containing fentanyl from a cross-sectional survey of people who use illicit opioids in three United States cities. Drug Alcohol Depend. 204, 107547. [PubMed: 31536877]

O'Connor PG, Fiellin DA, 2000 Pharmacologic treatment of heroin-dependent patients. Ann. Intern. Med 133, 40–54. [PubMed: 10877739]

Park JN, Weir BW, Allen ST, Chaulk P, Sherman SG, 2018 Fentanyl-contaminated drugs and non-fatal overdose among people who inject drugs in Baltimore, MD. Harm Reduct. J 15, 34. [PubMed: 29976195]

Pergolizzi JV, Annabi H, Gharibo C, LeQuang JA, 2019 The role of lofexidine in management of opioid withdrawal. Pain Ther. 8, 67–78. [PubMed: 30565033]

Phillips KT, 2016 Barriers to practicing risk reduction strategies among people who inject drugs. Addict. Res. Theory 24, 62–68. [PubMed: 27499724]

Pouget ER, Bennett AS, Elliott L, Rosenblum A, Britton PC, 2017 Recent overdose wxperiences in a community sample of military veterans who use opioids. J. Drug. Issues 47, 479–491. [PubMed: 28845055]

Reitzel LR, Short NA, Schmidt NB, Garey L, Zvolensky MJ, Moisiuc A, Reddick C, Kendzor DE, Businelle MS, 2017 Distress tolerance links sleep problems with stress and health in homeless. Am. J. Health Behav 41, 760–774. [PubMed: 29025504]

Rhee TG, Rosenheck RA, 2019 Buprenorphine prescribing for opioid use disorder in medical practices: Can office-based out-patient care address the opiate crisis in the United States? Addiction 114, 1992–1999. [PubMed: 31307111]

Richardson L, Mammel M, Milloy M-J, Hayashi K, 2019 Employment cessation, long term labour market engagement and HIV infection risk among people who inject drugs in an urban Canadian setting. AIDS Behav. 23, 3267–3276. [PubMed: 30924066]

Rouhani S, Park JN, Morales KB, Green TC, Sherman SG, 2019 Harm reduction measures employed by people using opioids with suspected fentanyl exposure in Boston, Baltimore, and Providence. Harm Reduct. J 16, 39. [PubMed: 31234942]

Roy PJ, Stein MD, 2019 Offering emergency buprenorphine without a prescription. JAMA.

Shah M, Huecker MR, 2019 Opioid withdrawal. StatPearls Publishing LLC, Treasure Island, FL.

Sherman SG, Latkin CA, 2002 Drug users' involvement in the drug economy: implications for harm reduction and HIV prevention programs. J. Urban Health 79, 266–277. [PubMed: 12023502]

Smith HS, 2009 Opioid metabolism. Mayo Clin. Proc 84, 613–624. [PubMed: 19567715]

Spencer MR, Warner M, Bastian BA, Trinidad JP, Hedegaard H, 2019 Drug overdose deaths involving fentanyl, 2011–2016. Natl. Vital Stat. Rep 68, 1–19.

Strike C, Rotondi M, Kolla G, Roy É, Rotondi NK, Rudzinski K, Balian R, Guimond T, Penn R, Silver RB, Millson M, Sirois K, Altenberg J, Hunt N, 2014 Interrupting the social processes linked with initiation of injection drug use: Results from a pilot study. Drug Alcohol Depend. 137, 48–54. [PubMed: 24529687]

Substance Abuse and Mental Health Services Administration, 2018 Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Rockville, MD.

Summers PJ, Hellman JL, MacLean MR, Rees VW, Wilkes MS, 2018 Negative experiences of pain and withdrawal create barriers to abscess care for people who inject heroin: A mixed methods analysis. Drug Alcohol Depend. 190, 200–208. [PubMed: 30055424]

Ti L, Milloy MJ, Buxton J, McNeil R, Dobrer S, Hayashi K, Wood E, Kerr T, 2015 Factors associated with leaving hospital against medical advice among people who use illicit frugs in Vancouver, Canada. PLoS One 10, e0141594. [PubMed: 26509447]

Unick GJ, Ciccarone D, 2017 US regional and demographic differences in prescription opioid and heroin-related overdose hospitalizations. Int. J. Drug Policy 46, 112–119. [PubMed: 28688539]

Unick GJ, Rosenblum D, Mars S, Ciccarone D, 2013 Intertwined epidemics: national demographic trends in hospitalizations for heroin- and opioid-related overdoses, 1993–2009. PLoS One 8, e54496. [PubMed: 23405084]

Wakeman S, 2016 The Moral Economy of Heroin in 'Austerity Britain'. Crit. Crim 24, 363–377.

Watters JK, Biernacki P, 1989 Targeted sampling: Options for the study of hidden populations. Social Problems 36, 416–430.

Weatherby N, Needle RH, Cesari H, Booth R, McCoy CB, Watters JK, Williams M, Chitwood DD, 1994 Validity of self-reported drug use among injection drug users recruited through street outreach. Eval. Program Plann 17, 347–355.

Weiss RD, Potter JS, Griffin ML, McHugh RK, Haller D, Jacobs P, Gardin J 2nd, Fischer D, Rosen KD, 2014 Reasons for opioid use among patients with dependence on prescription opioids: the role of chronic pain. J. Subst. Abuse Treat 47, 140–145. [PubMed: 24814051]

Wesson DR, Ling W, 2003 The Clinical Opiate Withdrawal Scale (COWS). J. Psychoactive Drugs 35, 253–259. [PubMed: 12924748]

Wurcel AG, Anderson JE, Chui KKH, Skinner S, Knox TA, Snydman DR, Stopka TJ, 2016 Increasing infectious endocarditis admissions among young people who inject drugs. Open Forum Infect. Dis 3, ofw157. [PubMed: 27800528]

Zibbell JE, Asher AK, Patel RC, Kupronis B, Iqbal K, Ward JW, Holtzman D, 2017 Increases in acute hepatitis C virus infection related to a growing opioid epidemic and associated injection drug use, United States, 2004 to 2014. Am. J. Public Health, e1–e7.

Highlights

- 85% of opioid-using people who inject drugs (PWID) reported opioid withdrawal.
- The majority of PWID reported very/extremely painful opioid withdrawal symptoms. were common among opioid-using PWID.
- Opioid withdrawal was associated with risk for non-fatal overdose among PWID.
- Opioid withdrawal was associated with receptive syringe sharing among PWID.

Table 1:

Demographic, socioeconomic, and drug use characteristics of regular opioid-using people who inject drugs in Los Angeles and San Francisco, CA, 2016–2017 (n=814).

Characteristic	n (%)
Site	
Los Angeles	390 (48%)
San Francisco	424 (52%)
Gender	
Female	193 (24%)
Male	611 (75%)
Transgender	6 (1%)
Other	4 (<1%)
Race	
White	331 (41%)
Latinx	202 (25%)
African American	168 (21%)
Asian/Pacific Islander	6 (1%)
Native American	55 (6.8%)
Mixed Race	52 (6.4%)
Age (years)	
<30	164 (20%)
30–39	206 (25%)
40–49	193 (24%)
≥50	251 (31%)
High school education or more	
Yes	584 (72%)
Homeless	
Yes	683 (84%)
Gay, lesbian, or bisexual	
Yes	133 (16%)
Sexual partner types	
Steady	382 (47%)
Casual	268 (33%)
Paid	96 (12%)
HIV positive	
Yes	36 (4%)
Monthly income	

Characteristic	n (%)
<$1,401	558 (69%)
$1,401 plus	254 (31%)
Selected income source, last 6 months	
Job	104 (13%)
Welfare, general relief	336 (41%)
SSI	143 (18%)
Family/spouse	104 (13%)
Recycling	178 (22%)
Illegal or possibly illegal source	351 (43%)
Panhandling	225 (28%)
Years of drug injection	
<10 years	243 (30%)
10–19 years	178 (22%)
≥20 years	392 (48%)
Injection drug use, last 30 days	
Crack cocaine	113 (14%)
Powder cocaine	133 (l6%)
Methamphetamine	459 (56%)
Heroin	789 (97%)
Non-prescribed Opioid medication	101 (12%)
Speedball	302 (37%)
Goofball	500 (61%)
Non-injection drug use in the last 30 days	
Crack cocaine	351 (43%)
Powder cocaine	113 (14%)
Methamphetamine	381 (47%)
Heroin	193 (24%)
Non-prescribed Opioid medication	200 (25%)
Non-prescribed Tranquilizer medication	261 (32%)
Goofball	68 (8%)
Non-prescribed Methadone	137 (17%)
Non-prescribed Buprenorphine	67 (8%)
Marijuana	534 (66%)
Injection frequency, last 30 days	
Less than once a day (<30 injections)	69 (9%)
Once or twice a day (30–89 injections)	231 (28%)
Three times or more a day (≥90 injections)	514 (63%)
Opioid use frequency, last 30 days	
Less than once a day (<30 times)	71 (9%)

Characteristic	n (%)
Once or twice a day (30–89 times)	245 (30%)
Three times or more a day (≥90 times)	498 (61%)
Drug use frequency, last 30 days	
Less than once a day (<30 times)	14 (2%)
Once or twice a day (30–89 times)	143 (18%)
Three times or more a day (≥90 times)	657 (81%)
Drug treatment in the last 6 months	
Detoxification	131 (16%)
Methadone maintenance	242 (30%)
Buprenorphine	74 (9%)
Outpatient	149 (18%)
Inpatient	100 (12%)
Residential	99 (12%)
Receptive syringe sharing in the last 6 months – Yes	218 (27%)
Overdose in the last 6 months - Yes	226 (28%)
Withdrawal measures	
Any withdrawal last 6 months	692 (85%)
Withdrawal times mean (standard deviation [SD]) median	46.01(SD =72.47) 12.00
Withdrawal frequency	
Less than once a month	250 (36%)
Monthly to less than once a week	200 (29%)
Weekly or more	242 (35%)
Withdrawal pain	690 (85%)
Very or extremely painful	391 (57%)
Moderate to no pain	299 (43%)

Table 2a:

Bivariate analysis of factors associated with opioid withdrawal symptoms among regular opioid using people who inject drugs in Los Angeles and San Francisco, CA, 2016–2017 (n=814).

Characteristic	Yes, withdrawal in the last 6 months N (%)	No, withdrawal in the last 6 months N (%)
Race		
White	**296 (89%)**	**35 (11%)**
Non-white	**396 (82%)**	**87 (18%)**
Age (years)		
<30	*145 (88%)*	*19 (12%)*
30–39	*188 (91%)*	*18 (9%)*
40–49	*168 (87%)*	*25 (13%)*
≥50	*191 (76%)*	*60 (24%)*
Income source, last 6 months		
SSI	**113 (79%)**	**30 (21%)**
Illegal or possibly illegal source	*321 (92%)*	*30 (8%)*
Panhandling	**203 (90%)**	**22 (10%)**
Injection drug use, last 30 days		
Powder cocaine	**125 (94%)**	**8 (6%)**
Non-injection drug use in the last 30 days		
Tranquilizer prescription medication	**239 (92%)**	**22 (8%)**
Buprenorphine	*64 (96%)*	*3 (4%)*
Injection frequency, last 30 days		
Less than once a day	**49 (71%)**	**20 (29%)**
Once or twice a day	**189 (82%)**	**42 (18%)**
Three times or more a day	**454 (88%)**	**60 (12%)**
Total drug use frequency, last 30 days		
Less than once a day (<30 times)	**7 (50%)**	**7 (50%)**
Once or twice a day (30–89 times)	**121 (85%)**	**22 (15%)**
Three times or more a day (≥90 times)	**564 (86%)**	**93 (14%)**

P<0.05 are noted in **BOLD**: P<0.001 are noted in *ITALICS*

Table 2b:

Bivariate factors associated with opioid withdrawal frequency and pain severity in the last 6 months among regular opioid using people who inject drugs in Los Angeles and San Francisco, CA, 2016–2017.

Variable	Opioid withdrawal < Monthly (n=250) n (%)	Opioid withdrawal Monthly (n=200) n (%)	Opioid withdrawal Weekly (n=242) n (%)	Extremely or very painful (N=391) n (%)	Moderately or not painful (N=299) n (%)
Sex					
Male	182 (35%)	153 (30%)	180 (35%)	**279 (54%)**	**234 (46%)**
Female	64 (38%)	43 (26%)	60 (36%)	**106 (64%)**	**61 (36%)**
Age					
<30	*39 (27%)*	*44 (30%)*	*62(43%)*	86 (59%)	60 (41%)
30–39	*52 (28%)*	*58 (31%)*	*78 (42%)*	105 (56%)	83 (44%)
40–49	*57 (34%)*	*41 (24%)*	*70 (42%)*	86 (52%)	80 (48%)
50 or older	*102 (53%)*	*57 (30%)*	*32 (17%)*	115 (60%)	76 (40%)
Race					
White	*80 (27%)*	*88 (30%)*	*128 (43%)*	**153 (52%)**	**142 (48%)**
Latinx	*65 (40%)*	*45 (27%)*	*54 (33%)*	92 (56%)	72 (44%)
African American	*72 (52%)*	*36 (26%)*	*30 (22%)*	88 (64%)	50 (36%)
Native American	*15 (33%)*	*13 (29%)*	*17 (38%)*	34 (55%)	20 (45%)
Asian/Pacific Islander	*2 (33%)*	*4 (67%)*	*0 (0%)*	4 (67%)	2 (33%)
Mixed Race/Other	*16 (37%)*	*14 (33%)*	*13 (30%)*	30 (70%)	13 (30%)
Income source					
SSI or retirement	*58 (51%)*	*25 (22%)*	*30 (27%)*	24 (67%)	12 (33%)
Recycling income	**64 (42%)**	**50 (32%)**	**40 (26%)**	87 (56%)	67 (44%)
Illegal or possibly illegal source	**98 (30%)**	**102 (32%)**	**121 (38%)**	178 (56%)	142 (44%)
Years of injection					
<10 years	*65 (31%)*	58 *(28%)*	*86 (41%)*	25 (52%)	23 (48%)
10–19 years	*42 (26%)*	*61 (38%)*	*59 (36%)*	102 (54%)	87 (46%)
20 or more	*142 (44%)*	*81 (25%)*	*97 (30%)*	264 (58%)	189 (42%)
Injection drug use, last 30 days					
Methamphetamine	*118 (30%)*	*117 (30%)*	*162 (41%)*	227 (57%)	169 (43%)
Non-injection drug use, last 30 days					
Crack	106 (35%)	92 (30%)	105 (35%)	**159 (53%)**	**144 (48%)**
Tranquilizer	**72 (30%)**	**70 (29%)**	**97 (41%)**	138 (58%)	100 (42%)
Methadone	50 (41%)	37 (30%)	35 (29%)	**80 (66%)**	**41 (34%)**
Total methamphetamine use, last 30 days					
<30	**156 (42%)**	**107 (29%)**	**108 (29%)**	208 (56%)	162 (44%)

Variable	Opioid withdrawal < Monthly (n=250) n (%)	Opioid withdrawal Monthly (n=200) n (%)	Opioid withdrawal Weekly (n=242) n (%)	Extremely or very painful (N=391) n (%)	Moderately or not painful (N=299) n (%)
30–89	**49 (31%)**	**49 (31%)**	**62 (39%)**	83 (52%)	77 (48%)
90 or more	**45 (28%)**	**44 (27%)**	**72 (45%)**	100 (63%)	60 (38%)
Injection frequency					
<30	*29 (59%)*	*11 (22%)*	*9 (18%)*	25 (52%)	23 (48%)
30–89	*75 (40%)*	*63 (33%)*	*51 (27%)*	102 (54%)	87 (46%)
90 or more	*146 (32%)*	*126 (28%)*	*182 (40%)*	264 (58%)	189 (42%)

P<0.05 are noted in **BOLD**: P<0.001 are noted in *ITALICS*

Table 3:

Multivariable logistic regression models of opioid withdrawal among PWID in Los Angeles and San Francisco, CA, 2016–2017 (n=814).

	Any withdrawal in the last 6 months Adjusted odds ratio (95% Confidence Interval)
Age	
<30	2.01 (1.14, 3.55) *
30–39	2.85 (1.61, 5.05) **
40–49	2.08 (1.24, 3.48) *
50 or more	Referent
Any illegal income, last 30 days – Yes	2.37 (1.51, 3.70) **

* p< 0.05

** p<0.001

Table 4:

Multinomial regression analysis of opioid withdrawal frequency among regular opioid using people who inject drugs, Los Angeles and San Francisco, California, 2016–17, (n=692).

Variable	Opioid withdrawal frequency Less than monthly	Monthly or more AOR (95% CI)	Weekly or more AOR (95% CI)
African American			
Yes	Referent	0.63 (0.39, 1.02)	0.50 (0.30, 0.83) *
Age			
<30		1.64 (0.94, 2.87)	3.95 (2.19, 7.10) **
30–39		1.55 (0.92, 2.63)	3.23 (1.84, 5.66) **
40–49		1.08 (0.63, 1.84)	3.08 (1.78, 5.34) **
50 or more	Referent	Referent	Referent
Any methamphetamine injection, last 30 days			
Yes	Referent	1.36 (0.92, 2.04)	1.59 (1.08, 2.38) *
Injection frequency			
<30		0.55 (0.26, 1.17)	0.37 (0.16, 0.85) *
30–89		1.03 (0.68, 1.57)	0.58 (0.37, 0.89) *
90 or more	Referent	Referent	Referent

* $p < 0.05$

** $p<0.001$

Table 5:

Multivariable logistic regression models of very or extremely painful withdrawal symptoms among regular opioid using people who inject drugs and use opioids in Los Angeles and San Francisco, CA, 2016–2017 (n=690).

	Very or extremely painful withdrawal symptoms Adjusted odds ratio (95% Confidence Interval)
Gender	
Male	Referent
Female	1.53 (1.06, 2.21) *
Race	
White	Referent
Latinx	1.11 (0.75, 1.65)
African American	1.70 (1.11, 2.61) *
Native American	0.98 (0.51, 1.88)
Asian or Pacific Islander	1.57 (0.28, 8.84)
Mixed or other	2.08 (1.03, 4.17) *
Non-injection crack use in the last 30 days – Yes	0.66 (0.48, 0.91) *
Non-prescribed, non-injection methadone use in the last 30 days -Yes	1.57 (1.03, 2.40) *

* $p < 0.05$

Table 6:

Multivariate logistic regression models of receptive syringe sharing and nonfatal overdose among regular opioid using people who inject drugs in Los Angeles and San Francisco, CA 2016–2017.

	Model 1 ***Opioid withdrawal in the last 6 mos.*** **AOR (95% CI)**	**Model 2** ***Extreme or very painful opioid withdrawal*** **AOR (95% CI)**	***Opioid withdrawal frequency*** **Less than monthly**	**Monthly to almost weekly AOR (95% CI)**	**Weekly or more AOR (95% CI)**
Receptive syringe sharing in the last 30 days (1)	2.75 * (1.52, 5.00)	0.86 (0.60, 1.23)	Referent	1.30 (0.82, 2.06)	1.94 * (1.26, 3.00)
Nonfatal overdose in the Last 6 months (2)	1.71 * (1.04, 2.81)	1.53 * (1.08, 2.16)	Referent	1.46 (0.95, 2.24)	1.69 * (1.12, 2.55)

(1) Controlling for race/ethnicity, sex work, gay, lesbian, bisexual, on parole, study site, non-injection methamphetamine use, non-injection tranquilizer use, and inpatient treatment in the last 6 months. (n=814)

(2) Controlling for race/ethnicity. (n=690)

* $p < 0.05$