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# Patterns of non-prescribed buprenorphine and other opioid use among Individuals with opioid use disorder: a latent class analysis

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## Abstract

**Aim—**Non-prescribed buprenorphine (NPB) use increased in the US. This study aims to characterize heterogeneity in patterns of NPB and other opioid use among individuals with current opioid use disorder.

**Methods—**The study recruited 356 participants in Dayton (Montgomery County), Ohio, area in 2017–2018 using targeted and Respondent Driven Sampling. Participants met the following criteria: 1) 18 years or older, 2) current moderate/severe opioid use disorder (DSM-5), 3) past 6-month NPB use. Latent class analysis (LCA) was conducted to identify subgroups based on past 6-month (days of NPB and heroin/fentanyl use; use of NPB to get high; use of non-prescribed and prescribed pharmaceutical opioids; participation in formal treatment) and lifetime (years since first NPB and other illicit opioid use) characteristics. Selected auxiliary variables were compared across classes using Asparouhov and Muthén's 3-step approach.

**Results—**49.7% were female, and 88.8% were non-Hispanic whites. 89% used NPB to self-treat withdrawal. LCA resulted in three classes: "Heavy Heroin/Fentanyl Use" (61%), "More Formal Treatment Use" (29%) and "Intense NPB Use" (10%). After adjusting for multiple testing, the following past 6-month variables differed significantly between classes: injection as a primary

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Contributors

R. Daniulaityte, R. Nahhas, S. Martins, and R. Carlson designed the study. R. Daniulaityte reviewed the literature and wrote the first draft of the paper. R. Nahhas conducted statistical analyses. S. Silverstein, A. Moeller and A. Zaragozar contributed to data collection and refinement of conceptual design. S. Martins contributed to the analytical approach. All authors reviewed, commented, and edited the manuscript. All authors contributed to and have approved the final manuscript.

Author Disclosures

Conflict of Interest

All authors declare that there are no conflicts of interest.

route of heroin/fentanyl administration (p<0.001), cocaine use (p=0.044), unintentional drug overdose (p=0.023), and homelessness (p=0.044), with the “Intense NPB Use” class having the lowest prevalences.

**Conclusion—**Predominance of self-treatment goals and the association between more intense NPB use and lower risks of adverse consequences suggest potential harm minimization benefits of NPB use. More research is needed to understand consequences of NPB use over time.

### Keywords

Buprenorphine; Buprenorphine Diversion; Heroin; Non-Pharmaceutical Fentanyl; Illicit Opioids; Self-Treatment; Overdose

## 1. Introduction

Numerous clinical trials have established buprenorphine’s effectiveness in the treatment of opioid use disorder (Farrell et al., 2012; Fiellin et al., 2004; Gowing et al., 2009), and there has been a significant expansion of buprenorphine-based treatment in the U.S. (Arfken et al., 2010). From 2009 to 2015, the number of individuals in the U.S. who received buprenorphine as part of their substance use treatment increased nearly 400% (SAMHSA, 2015, 2017). However, the majority of people with an opioid use disorder still lack access to treatment (Jones et al., 2015).

There is also growing evidence of notable increases in diversion and use of non-prescribed buprenorphine (NPB) (Allen and Harocopos, 2016; Carroll et al., 2018; Cicero et al., 2018; Cicero et al., 2014; Daniulaityte et al., 2012; DEA, 2018; Fox et al., 2015; Lavonas et al., 2014; Lofwall and Walsh, 2014; Mitchell et al., 2009; Monte et al., 2009; Wish et al., 2012; Yokell et al., 2011). Concerns about diversion and potential harms associated with NPB use impact prescriber practices (Lin et al., 2018) and willingness to seek a waiver for buprenorphine prescription (Huhn and Dunn, 2017), even in the context of unprecedented increases in opioid-related harms.

Existing research suggests that NPB use is associated with insufficient access to appropriate substance abuse treatment services (Carroll et al., 2018; Cicero et al., 2018; Fox et al., 2015; Lofwall and Havens, 2012). Preliminary evidence indicates that experiences with NPB use could lead to more favorable treatment outcomes (Cunningham et al., 2013; Monico et al., 2015). Most prior studies have established that NPB use in the U.S. is commonly linked to self-treatment-related objectives, ranging from recovery-related goals to temporary substitution for preferred illicit opioids (Allen and Harocopos, 2016; Bazazi et al., 2011; Carroll et al., 2018; Cicero et al., 2018; Genberg et al., 2013; Mitchell et al., 2009; Monte et al., 2009; Schuman-Olivier et al., 2010). Prior studies have also noted greater levels of other drug use among individuals engaged in NPB use (Lofwall and Havens, 2012; Walker et al., 2018), but patterns of polydrug use practices are not yet well understood. To develop effective interventions and policy responses, more data are needed to better understand the complexity and diversity in patterns of NPB and other opioid use and associated social and health characteristics.

The goal of this study is to apply an inductive statistical technique, latent class analysis (LCA), to characterize heterogeneity in patterns of NPB and other opioid use among individuals with current severe or moderate opioid use disorder. We also examine how socio-demographics, other drug use characteristics, chronic pain and psychiatric comorbidity, and adverse experiences, such as overdose, homelessness, hospitalization and incarceration, relate to class membership.

## 2. Methods

### 2.1. Study Design

This study presents cross-sectional data collected at baseline from a 24-month natural history study on NPB use among individuals with moderate/severe opioid use disorder (DSM-5). A community-based sample of 357 (one person was excluded from LCA analyses because of missing data) individuals was recruited in Dayton (Montgomery County) area (Ohio, U.S.) between May 2017-October 2018. The study was approved by the Institutional Review Boards at Wright State and Columbia Universities.

### 2.2. Sample Recruitment and Eligibility

The recruitment strategy built on a combination of targeted recruitment (Korf et al., 2010; Sifaneck and Neaigus, 2001) and respondent-driven sampling (RDS) (Daniulaityte et al., 2012b; Heckathorn, 1997). RDS is a network-based referral methodology that begins with initial non-randomly selected “seed” participants and provides financial rewards for participation in the study ($50 for baseline interview) and for the referral of other participants ($15).

Out of our final sample of 357 individuals, 104 were the initial participants or “seeds.” They were recruited via targeted recruitment through multiple venues, including web-based ads (craigslist.com, Facebook) and flyers that were placed in diverse locations (pawn shops, convenience stores, gas stations, Laundromats, public transportation hubs, etc.) or distributed through support groups and service providers. This likely increased the diversity of social networks represented in the sample.

Participants were given instructions to recruit up to 3 eligible individuals. However, the pace of recruitment was very slow, as many individuals did not refer any eligible participants. To improve recruitment, participants were instructed to recruit additional individuals even if they reached initially set limit of 3 eligible recruits. Out of the total sample, 226 individuals (63.3%) did not refer any eligible individuals, 78 (21.9%) referred only one participant, 37 (10.4%) referred 2–3 participants, 10 (2.8%) referred 4–5 participants, and 3 (0.8%) persons referred more than 6 participants. We are not certain why so many individuals did not refer any eligible recruits. Potentially, some individuals became discouraged when the persons they referred to the study did not qualify for the very specific eligibility requirements. In addition, study recruitment occurred in 2017–2018, when opioid-related overdose mortality increased to unprecedented levels in the Dayton area (Public Health Dayton & Montgomery County, 2018). Our study participants reported knowing on average about 12 individuals (SD 16.0) from their close personal social networks who had died from unintentional drug

overdoses. It is possible that high mortality rates contributed to disrupted social networks and made RDS-based recruitment less efficient.

Eligibility requirements included: 1) being at least 18 years old; 2) residence in the Dayton, Ohio, metro area or surrounding counties; 3) current opioid use disorder (moderate or severe); and 4) self-reported use of non-prescribed buprenorphine at least once in the past six months. Eligibility determination was a two-stage process that used phone-based pre-screening followed by office-based assessment. Upon calling the project site office, the study was described to individuals who were asked a number of questions to assess if they met eligibility criteria. Those who passed the brief telephone screen were scheduled for an office-based visit. Upon presentation at the office, individuals were first engaged in an informed consent process, followed by the final eligibility assessment. Opioid use disorder was assessed using the DSM-5 Checklist (Forman et al., 2004).

There were a total of 1,155 phone-based eligibility assessments performed, and 505 individuals passed the phone-based eligibility screen and were scheduled for an office-based screening. Out of 505 scheduled, 404 kept their office appointments and completed an office-based eligibility screen. 374 passed the office eligibility and completed the baseline assessment. However, the final sample consisted of 357 individuals because 17 additional participants were disqualified after baseline assessment when the research team reviewed their baseline and follow-up interview records and identified significant inconsistencies suggesting intentional misrepresentation.

Participants were requested to show a picture ID to assure that they were not under 18 years of age. If they did not have a valid ID, they were allowed to bring in other forms of documentation (expired ID, student identification etc.). Close to 90% of all participants were able to produce some kind of document confirming their identity and age. Individuals who were not able to produce some form of ID were not automatically excluded from participation unless they reported and/or appeared of a very young age (younger than 25). The ID check helped identify and disqualify a few individuals who attempted to enter the study more than once.

To enhance the veracity of self-reported drug use, specific eligibility criteria were not revealed during the screening process and subsequent interviews, and screening included seemingly “irrelevant” question to mask true eligibility criteria. Individuals were also asked to submit an unobserved urine sample for drug testing. Request to participate in drug screening before the start of data collection is recognized as a useful method to increase the accuracy of self-reports (Donovan et al., 2012). All urine specimens were analyzed using the One Step Drug Screen Test Card (Redwood Toxicology Laboratory), an immunoassay-based method that tested for buprenorphine and other drugs (e.g., oxycodone, methadone, opioids (morphine), benzodiazepines). Results of urine testing were not used to exclude people from the study participation because the eligibility window was much broader than the buprenorphine detection window available with urine toxicology. Agreement between self-reported use of buprenorphine and urine testing results was high: 89% of those who tested positive for buprenorphine reported use in the past seven days, and Cohen’s kappa value was 0.76.

### 2.3. Structured Interviews and Variables

Baseline structured interviews were conducted in private offices by trained interviewers and lasted about 1.5–2 hours. The study relied on REDCap (Harris et al., 2009) system for data storage and direct computer-based data entry used by the trained interviewers to record participant responses to questions on socio-demographic and drug-related characteristics. The questionnaires were developed building on prior research (Carlson et al., 2005; Falck et al., 2005) and formative stage of the study. This included questions on NPB and other drug use history ("How old were you the very first time you used [drug]?"); sources of NPB ("In the past 6 months, when you used non-prescribed buprenorphine, how did you get it most often?"); mode of administration of heroin/fentanyl and other drugs ("In the past 6 months, how did you most often administer [drug]?"); use of other drugs (alcohol, marijuana, cocaine, methamphetamine, benzodiazepines, gabapentin) in the past 6 months ("During the past 6 months, how often did you use [drug]?"); lifetime history of buprenorphine-based treatment participation ("How many times have you been a patient in a substance abuse treatment program, including doctor's office, where you were prescribed/received buprenorphine?"); experiences with homelessness ("Have you been homeless in the past 6 months?"); and chronic pain ("Have you ever been diagnosed with chronic pain?"). Participants were asked about heroin/fentanyl use as one drug category because of the prevalence of heroin/fentanyl combinations being sold on the streets and the difficulty differentiating between the two drugs (Daniulaityte et al., 2019a; Daniulaityte et al., 2017).

The computerized version of the Diagnostic Interview Schedule-5 (DIS-5) was used to ascertain current diagnoses of major depressive disorder, generalized anxiety disorder, and PTSD (Robins et al., 2002). The Timeline-Follow-Back-Method (Robinson et al., 2014; Sobell and Sobell, 1992) was used to assess past 6-month use of NPB (including mode of administration and reasons for use), heroin/ fentanyl, prescribed and non-prescribed pharmaceutical opioids (separately) such as hydrocodone, oxycodone and other, overdose experiences, hospitalization, incarceration, and use of formal treatment services for substance use disorders (including if they received buprenorphine, methadone or Vivitrol while in treatment).

### 2.4. Statistical Analyses

A combination of latent class analysis (LCA) (which uses categorical indicators) and latent profile analysis (which uses continuous indicators) was used to find salient groups based on the latent construct, "pattern of opioid use among individuals with current opioid use disorder." Additionally, auxiliary variable means and proportions were compared across classes using the 3-step approach of Asparouhov and Muthén (Asparouhov and Muthén, 2012).

Descriptive statistics (mean, SD; n and %) for all variables were calculated. Latent class indicators were: 1) years since first NPB use; 2) days of NPB use in the past 6 months (6m); 3) years since first use of any other illicit opioids; 4) days of heroin/fentanyl use in the past 6m; 5) ever using NPB to get high in the past 6m; 6) ever using non-prescribed pain pills (non-prescribed hydrocodone, oxycodone, methadone and/or other pharmaceutical opioids, excluding non-prescribed buprenorphine) in the past 6m; 7) ever using prescribed pain pills

(hydrocodone, oxycodone and other pharmaceutical opioids, including methadone if prescribed for pain, not for treatment of opioid use disorder) in the past 6m; and 8) use of formal substance use disorder treatment in the past 6m (including any type of substance use disorder treatment, such as buprenorphine, methadone, or Vivitrol-based and/or non-medication assisted/abstinence-based programs; because of relatively low numbers (see Table 1), it was not feasible to include separate variables for specific types of treatment services in the LCA analyses).

The choice of the optimal number of classes was based on a combination of Akaike's Information Criterion (AIC), Bayesian Information Criterion (BIC), homogeneity, latent class separation, interpretability, and class size, with priority given to interpretability and class size.

Building on prior literature on NPB use (Lofwall and Havens, 2012; Walker et al., 2018), the following auxiliary variables were selected to assess association with LCA classes: 1) socio-demographics (age, sex, race/ethnicity (non-Hispanic white vs. other), education (some college vs. other), relationship status (married/living with partner vs. other), employment status (full/part-time vs. disability vs. unemployed non-disability); 2) comorbid conditions (lifetime chronic pain and past year DSM-5 depression, anxiety, and PTSD); 3) modes of administration of illicit opioids in the past 6 months: a) non-oral use of NPB (ever), b) non-oral use of other non-prescribed pharmaceutical opioids (most common route in the past 6 months), c) injection use of heroin/fentanyl (most common route in the past 6 months); 4) Number of times ever attended buprenorphine-based treatment; 5) Sources of NPB in the past 6 months (bought from dealer vs. other); 6) Frequent use of other drugs (alcohol, marijuana, cocaine, benzodiazepines, gabapentin, methamphetamine) in the past 6 months (≥3 days per week vs. less frequently); and 7) Adverse experiences in the past 6 months: unintentional drug-related overdose, hospitalization, incarceration, and homelessness.

The comparison of auxiliary variables between classes was done using the 3-step approach of Asparouhov and Muthén. In this approach, each individual is assigned to their most likely LCA class, but the uncertainty in this assignment is taken into account when comparing auxiliary variables between classes. The Hommel method (Hommel, 1988) was used to adjust for multiple testing across all the auxiliary variables to preserve a familywise $\alpha = 0.05$ level of significance. The Hommel method was carried out using SAS PROC MULTTEST in SAS 9.4 (SAS Institute Inc., 2012). The LCA and analysis of auxiliary variables were carried out in Mplus 8.2 (Muthén and Muthén, 2017).

## 3. Results

### 3.1. Participant Characteristics

A total of 357 individuals were recruited for the study. One person was excluded from LCA analyses because of missing data, resulting in a final sample size of 356. About half (49.7%) of the study participants were female, and the majority (88.8%) were non-Hispanic whites. Just over 44% reported some college education, and the mean age was 39.2 years. Only 23.0% reported being married or living with a partner (Table 1).

Although eligibility criteria specified moderate or severe opioid use disorder in the past 12 months, almost all recruited participants (99%) met criteria for severe opioid use disorder. The mean number of days of heroin/fentanyl use in the past 6 months (184 days) was 103.7 (SD 67.25). Over 60% reported injection as their most common route of administration of heroin/fentanyl in the past 6 months. The majority reported long histories of illicit opioid use (mean number of years since first use 18.45).

The mean number of years since first NPB use was 4.0 (SD 3.3). Participants reported lifetime non-medical use of various buprenorphine products, most commonly, Suboxone film (93.0%), Suboxone tablets or generics (86.6%), and Subutex (73.7%). A little over 10% reported ever using Zubsolv non-medically. The mean number of days of NPB use in the past 6 months was 26.9 (SD 37.6). Almost 90% reported using NPB for self-treatment of withdrawal, and only about 16% used it to get high on at least one occasion in the past 6 months. Most participants (68.2%) obtained NPB from family and friends, and 26% reported dealers as their most common source (Table 1).

About a third (32.9%) of the sample reported never being enrolled in any type of buprenorphine-based treatment in their lifetime, and 36.8% reported being enrolled on at least 2 or more occasions (Table 1). About half (50.6%) reported at least one day of enrollment in formal treatment program for substance use disorders in the past 6 months, most commonly (37.5%) in buprenorphine-based treatment, 3.9% in methadone-based treatment, 6.4% in Vivitrol-based treatment, and 13.8% in abstinence-based program. The mean number of formal treatment days in the past 6 months for the sample as a whole was 40.0 (SD 58.2). The mean number of days of attending buprenorphine-based treatment in the past 6 months was 26.0 (SD 49.9) (Table 1).

Over 50% reported ever being diagnosed with chronic pain, nearly half (45.5%) screened positive for generalized anxiety disorder, about a third (34.3%) for major depressive disorder, and about a fourth (27.5%) for PTSD. More than half (54.8%) reported being homeless, and 27.8% reported experiencing at least one unintentional drug-related overdose in the past 6 months (Table 1).

### 3.2. Optimal Number of Latent classes

Models with more than three classes had multiple classes with < 10% membership, including one class with < 4%. Nevertheless, we considered using a 4-class model based on a local minimum value of BIC (see Table 2). However, this led to estimation instability when comparing auxiliary variables due to the small size of the smallest class. The 3- and 4-class models had very similar interpretations, with the class we labeled “intense NPB use” in our 3-class model (see below) splitting into two small classes in the 4-class model. Thus, based on interpretability and class size, we concluded that a 3-class model best captured the salient groupings of participants.

### 3.3. Latent Class Definitions and Prevalence

Class prevalences and conditional means and prevalences of latent class indicators are shown in Table 3. Class 1, entitled “Heavy Heroin/Fentanyl Use and Sporadic NPB Use” (“Heavy Heroin/Fentanyl” for short) accounted for 61% of the sample and was distinguished from

other classes by the highest average frequency of heroin/fentanyl use (152.6 of 184 days). It also had the highest prevalence of non-prescribed pharmaceutical opioid use (58%) and the lowest frequency of NPB use (15.5 of 184 days).

Class 2, entitled “More Use of Formal Treatment, Low NPB Use” (“Formal Treatment” for short) accounted for 29% of the sample and had the greatest prevalence of substance use disorder treatment use (73%) and prescribed pharmaceutical opioid use in the past 6 months (29%). It also differed from other classes in having a shorter history of other illicit opioid use (16.3 years) and reported a low frequency of heroin/fentanyl use (25.7 of 184 days). The Formal Treatment class was also most likely to report NPB use to get high (23%).

Class 3, entitled “Intense NPB Use, Less Formal Treatment” (“Intense NPB Use” for short) accounted for 10% of the sample, and reported the greatest average frequency of NPB use (121.7 of 184 days). Compared to other classes, it had the lowest prevalence of use of non-prescribed and prescribed pharmaceutical opioids (35% and 5%, respectively). The “Intense NPB Use” class also had the lowest prevalence of using formal substance use disorder treatment (25%). Frequency of heroin/fentanyl use (43.5 of 184 days) was much lower than Class 1, but greater than Class 2.

### 3.4. Class Association with Auxiliary Variables

Among socio-demographic characteristics, only educational level was meaningfully different between classes, but not significantly so after adjusting for multiple testing (Table 4). More than (54.3%) of the “Formal Treatment” group reported some college education, compared to about 26.9% of the “Intense NPB Use” group.

There were no statistically significant differences in chronic pain and psychiatric comorbidity between classes. However, after adjusting for multiple testing, the classes differed significantly in injection use of heroin/fentanyl (vs. snorting) and prevalence of frequent cocaine use with the greatest prevalences reported by the “Heavy Heroin/Fentanyl” class and lowest by the “Intense NPB Use” group. Although not significant after adjusting for multiple testing, the Intense NPB Group had the lowest prevalence of non-oral administration of non-prescribed pharmaceutical opioids.

The three classes differed meaningfully in adverse experiences reported in the past 6 months. The Intense NPB Use group had the lowest prevalence of reported unintentional overdose (11.5%), hospitalization (14.6%), incarceration (26.6%), and homelessness (27.3%), while the “Heavy Heroin/Fentanyl” class had the highest prevalence of overdose (34.2%) and homelessness (58.9%) in the past 6 months. After adjusting for multiple testing, class differences in overdose and homelessness were statistically significant.

## 4. Discussion and Conclusions

This is the first study to identify distinct patterns of NPB and other opioid use among individuals with opioid use disorders and their association with selected socio-demographic, other drug use, and health-related characteristics. Our data confirm that NPB use among individuals with opioid use disorder is driven by self-treatment related reasons because

nearly 90% reported using NPB in the past 6 months to self-treat opioid withdrawals, and only about 16% indicated use for euphoric purposes. These findings are consistent with prior studies that emphasized self-treatment related reasons of NPB use among individuals with opioid use disorders in the U.S. (Carroll et al., 2018; Cicero et al., 2018). Distinct LCA classes, however, highlight varying intensity of NPB and other opioid use that reflects distinct long-term goals and relative successes of self-treatment strategies. The most prevalent class (61%) (Class 1, “Heavy Heroin/Fentanyl” use) is characterized by near-daily use of heroin/fentanyl and sporadic use of NPB. This pattern of use is consistent with other studies that described intermittent use of NPB as a backup measure to relieve withdrawal symptoms for brief substitution in situations when the preferred primary opioid becomes unavailable or too inconvenient to use (Allen and Harocopos, 2016).

The “Formal Treatment” class included almost 30% of all participants and is characterized by sporadic NPB use, greater use of formal substance use treatment and the lowest frequency of heroin/fentanyl use. Prior research has noted that poor access to treatment is often associated with greater engagement in NPB use (Cicero et al., 2018; Lofwall and Havens, 2012). Continued use of NPB among individuals who also report greater use of treatment services suggests that individuals are crafting complex quitting and recovery strategies that combine both formal and informal elements. Indeed, the circulation of NPB among opioid-dependent individuals may represent strategies of mutual-aid among a vulnerable population, as NPB is used to supplement, or bridge gaps in, formal treatment (Lofwall and Havens, 2012). Interestingly, this class was also the most likely to report use of buprenorphine for the purposes of getting high. As was noted by Cicero et al., increased access to prescribed medications may also increase non-medical use of those medications for non-therapeutic purposes (Cicero et al., 2007).

Sporadic patterns of NPB use among these two LCA classes contrast sharply with near-daily use in the third class, “Intense NPB Users.” This class is the smallest among the three classes (10% prevalence) but represents unique and powerful examples of NPB use as a tool for self-change that is unassisted by formal treatment services (Biernacki, 1986; Klingemann and Sobell, 2007).

There were significant differences among the classes in injection use of heroin/fentanyl. About 75% of the “Heavy Heroin/Fentanyl” use class reported injection as a primary mode of administration of heroin/fentanyl, compared to about 40% in the “Intense NPB Use” class (adjusted $p<0.001$). A similar magnitude of relative proportions was observed with non-oral administration of non-prescribed pharmaceutical opioid use. It is possible that reduced use by injection or non-oral routes (for pharmaceutical opioids) could indicate an engagement in harm minimization strategies that are in line with recovery and self-treatment-related goals associated with patterns of intense NPB use. Prior research has established the significance of route of administration in increasing the rate of drug absorption and associated risk of experiencing unintentional drug overdose and other adverse consequences (Allain et al., 2015; Carlson et al., 2016).

More than a quarter of the sample reported frequent use of cocaine. Concomitant use of cocaine and heroin/fentanyl is commonly referred to as “speedballing” (Siegal et al., 1994).

The two drugs are viewed as balancing each other's effects, and heroin/fentanyl dealers in the area often sell cocaine to cater to the preferences of illicit opioid users (Ohio Substance Abuse Monitoring Network, 2017). There were notable differences among the LCA classes in prevalence of cocaine use (adjusted p=0.044). Prior research has also noted an association between decreased use of illicit opioids and decreases in cocaine use among individuals attending methadone-based treatment (Maremmani et al., 2007). Lower prevalence of cocaine use in the "Intense NPB Use" and "Formal Treatment" classes is consistent with opioid use patterns indicative of general recovery-oriented goals.

About 16% of the sample also reported frequent use of methamphetamine in the past 6 months. Overdose death data from Montgomery County (where the city of Dayton is located) show a notable increase in methamphetamine-positive cases over the past few years (Daniulaityte et al., 2019b). Emerging research suggests distinct motivational strategies associated with methamphetamine use among illicit opioid users. While some may use methamphetamine to "balance out" the effects of illicit opioids, others also describe self-treatment-related strategies of using methamphetamine to help reduce heroin/fentanyl use (Ellis et al., 2018). These distinct motivations of use might partially explain the lack of statistically significant differences in methamphetamine use among LCA classes.

The Dayton (Montgomery County), Ohio, area has been recognized as an epicenter of the opioid epidemic with overdose mortality rates among the highest in the U.S. (Ohio Department of Health, 2018). In 2017, 566 people died from unintentional overdoses in the Dayton area (Montgomery County) (Public Health Dayton & Montgomery County, 2018), and the raw death rate reached 100 per 100,000. Notable differences in non-fatal overdose experiences among the three LCA classes are of paramount public health significance. Those in the "Intense NPB Use" class had a lower prevalence of reported overdose (11.5%) than those in the "Formal Treatment" (19.2%) class and "Heavy Heroin/Fentanyl Use" class (31.4%) (adjusted p=0.023). Prior research has shown that participation in buprenorphine-based treatment reduces risks of unintentional overdose (Dupouy et al., 2017). This study is among the first to identify differences in overdose-related risks between distinct NPB and other opioid use classes.

More than half of the total sample reported experiencing homelessness in the past 6 months. Prior studies have also shown that homelessness is a common symptom of spiraling down trajectories of drug-related consequences and depletion of social and economic resources (Eyrich-Garg et al., 2008). The "Intense NPB Use" class was significantly less likely to have experienced homelessness in the past 6 months, compared to other LCA classes (adjusted p=0.044).

The study was conducted in one area of the Midwest U.S., and the findings may not be generalizable to other areas. Although we attempted to make the sample as representative as possible for a study with hidden populations by using targeted and respondent-driven sampling, it may contain biases due to non-random recruitment. The majority of the recruited individuals were non-Hispanic whites, and about half were female. The racial/ethnic composition of the recruited sample is consistent with other local and national data sources (Martins et al., 2015; Ohio Department of Health, 2018) indicating lower prevalence

of ethnic minorities among individuals engaged in illicit opioid use. In terms of age, our sample was similar to other data sources related to opioid-related overdose mortality in the Dayton area (Daniulaityte et al., 2019b). Our sample had high prevalence of other mental health disorders, such as depression (34.3%) and anxiety (45.5%), and use of other substances was common, which is consistent with prior studies conducted among individuals with opioid use disorders in the U.S. (Wu et al., 2016).

The sample included a greater proportion of females compared to national data on individuals with opioid use disorders and local data on opioid-related overdose mortality, which generally show a greater proportion of males compared to females (Daniulaityte et al., 2019b). Greater participation of female respondents may be related to the fact that eligibility requirements targeted individuals who had used non-prescribed buprenorphine in the past 6 months, which may be construed as a form of self-treatment and self-care strategy by some. Prior research has noted that the social construction of gender identities in the U.S. may contribute to females generally being more likely than males to adopt health behaviors associated with risk mitigation and self-care (Courtenay, 2000).

In addition, RDS-based recruitment methods might contribute to potential biases in LCA analyses because of the social-network based linkages among the study participants. However, over 30% of the study participants were “seeds” that were recruited through multiple targeted recruitment venues. We believe that the mix of recruitment methods employed in the study helped increase access to a diversity of unrelated networks of individuals with opioid use disorders in the Dayton area. Finally, the findings are based on self-reports; however, there is substantial support for the validity of self-reported data (Darke, 1998). In addition, there was a high concordance between self-reported buprenorphine use and urine toxicology.

Lower prevalence of overdose and homelessness reported by the “Intense NPB Use” class link to prior qualitative insights about use of diverted MAT medications as “indigenous harm reduction strategies” (Harris and Rhodes, 2013) to help minimize adverse consequences of heroin and other illicit opioid use. Because of the cross-sectional nature of the data collected, a causal relationship between the NPB use and lower risk of adverse experiences could not be established. Future analysis of the longitudinal data will provide more robust insights into the nature of these associations. In addition, future analyses of our qualitative interview data will provide a more complete and contextualized account of reasons and motivations associated with NPB use.

Increased understanding of patterns of NPB and other opioid use is important to help address medical provider and policy maker concerns about buprenorphine diversion and contribute to development of less punitive and more harm-reduction oriented attitudes towards its use, thereby expanding access to life-saving medication in the context of the ravaging opioid crisis. Although the availability of substance use disorder treatment services has increased substantially in the Dayton area, our study findings indicate continuing reliance on street buprenorphine and untapped treatment gaps in this highly vulnerable population. There is a need for innovative service delivery strategies and more widespread adoption of low-threshold treatment approaches--such as emergency department-initiated

buprenorphine-based treatment (D'Onofrio et al., 2017), utilization of unobserved or home-based induction of buprenorphine treatment (Bhatraju et al., 2017) or provision of mobile treatment services to justice-involved individuals (Krawczyk et al., 2019), that would help engage more individuals in high quality and compassionate care they desperately need.

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## Highlights

- Nearly 90% used non-prescribed buprenorphine for self-treatment.
- Latent Class Analysis identified 3 classes of non-prescribed buprenorphine/other opioid use.
- Class 1 (Heavy Heroin/Fentanyl Use) included 61% of the sample.
- Class 2 (More Use of Formal Treatment) included 29%.
- Class 3 (Intense Non-Prescribed Buprenorphine Use) included 10%.
- Class 3 had lower prevalence of injection, cocaine use, overdose and homelessness.

**Table 1.**

Descriptive statistics of baseline sample (N=356) of individuals with current opioid use disorders and past 6 months use of non-prescribed buprenorphine, recruited in the Dayton, OH area.

| Characteristics | N or Mean | % or SD |
|---|---|---|
| **Socio-demographics** | | |
| Age (years) | 39.2 | 9.6 |
| Gender (Male) | 179 | 50.3% |
| Race/Ethnicity (White/Non-Hispanic) | 316 | 88.8% |
| Education (Some College or More) | 157 | 44.1% |
| Marital Status (Married/Living with Partner) | 82 | 23.0% |
| Employment status: | | |
| Full/Part time | 92 | 25.8% |
| Unemployed (disability) | 67 | 18.8% |
| Unemployed (other) | 197 | 55.3% |
| **Pain and psychiatric comorbidities** | | |
| Chronic pain diagnosis (ever, lifetime) | 199 | 55.9% |
| Major depressive disorder (past 12m) | 122 | 34.3% |
| Generalized anxiety disorder (past 12m) | 162 | 45.5% |
| PTSD (past 12m) | 98 | 27.5% |
| **History of non-prescribed buprenorphine (NPB) and other opioid use** | | |
| Types of non-prescribed buprenorphine products ever used: | | |
| Non-prescribed Suboxone tablets or generics | 308 | 86.5% |
| Non-prescribed Suboxone film | 331 | 93.0% |
| Non-prescribed Subutex | 262 | 73.6% |
| Non-prescribed Zubsolv | 38 | 10.7% |
| Non-prescribed Bunavail | 1 | 0.3% |
| Years since first use of non-prescribed pain pills or heroin/fentanyl * | 18.5 | 9.6 |
| Years since first non-prescribed buprenorphine use * | 4.0 | 3.3 |
| **Past 6 month use of non-prescribed buprenorphine and other opioids** ** | | |
| Heroin/fentanyl use (days in past 6 months) * | 103.7 | 67.25 |
| Non-prescribed buprenorphine use (days in past 6 months) * | 26.9 | 37.57 |
| Reasons of non-prescribed buprenorphine use: | | |
| To self-treat withdrawal symptoms (ever in past 6 months) | 317 | 89.0% |
| To get high (ever in past 6 months) * | 58 | 16.3% |
| Non-prescribed pain pill use (ever in past 6 months) * | 193 | 54.2% |
| Prescribed pain pill use (ever in past 6 months) * | 69 | 19.4% |
| **Past 6 month use of formal treatment services for substance use disorders** *** | | |
| Any type of treatment (ever in past 6 months) * | 180 | 50.6% |

| Characteristics | N or Mean | % or SD |
|---|---|---|
| Buprenorphine-based treatment (ever in past 6 months) | 134 | 37.6% |
| Methadone-based treatment (ever in past 6 months) | 14 | 3.9% |
| Vivitrol-based treatment (ever in past 6 months) | 23 | 6.5% |
| Abstinence-based treatment **** (ever in past 6 months) | 49 | 13.8% |
| Days in treatment for substance use disorders (any, days in past 6 months) | 40.0 | 58.2 |
| Days in buprenorphine-based treatment (days in past 6 months) | 26.0 | 49.9 |
| Days in methadone-based treatment (days in past 6 months) | 4.2 | 24.6 |
| Days in Vivitrol-based treatment (days in past 6 months) | 2.3 | 9.3 |
| Days in abstinence-based treatment **** (days in past 6 months) | 8.7 | 26.8 |
| **Lifetime history of participation in formal buprenorphine-based treatment** | | |
| Never | 117 | 32.9% |
| Once | 108 | 30.3% |
| Two or more times | 131 | 36.8% |
| **Mode of administration of non-prescribed buprenorphine and other opioids, past 6 months** | | |
| Non-prescribed buprenorphine taken non-orally (at least once) | 91 | 25.6% |
| Non-prescribed pain pills taken non-orally (most common route) | 106 | 29.8% |
| Heroin/fentanyl injected (most common route) | 225 | 63.2% |
| **The most common source of non-prescribed buprenorphine in the past 6 months** | | |
| Bought from a dealer | 93 | 26.1% |
| Obtained from family and/or friends | 243 | 68.2% |
| Other | 20 | 5.7% |
| **Frequent use of other drug use in the past 6 months (use on 3–7 days per week)** | | |
| Alcohol | 32 | 9.0% |
| Marijuana | 89 | 25.0% |
| Cocaine (powder or crack) | 90 | 25.3% |
| Non-prescribed benzodiazepines | 47 | 13.2% |
| Non-prescribed gabapentin | 49 | 13.8% |
| Methamphetamine | 57 | 16.0% |
| **Adverse consequences/experiences in the past 6 months** | | |
| Overdose (ever in past 6 months) | 98 | 27.5% |
| Hospitalization (ever in past 6 months) | 88 | 24.7% |
| Incarceration (ever in past 6 months) | 110 | 30.9% |
| Homelessness (ever in past 6 months) | 195 | 54.8% |

* Latent Class Indicator Variables

** "Days in past 6 months" variables have a maximum of 184 days.

*** Participants may have attended more than one type of treatment program in the past 6 months.

**** Abstinence-based included programs that did not provide buprenorphine, methadone or Vivitrol.

**Table 2.**

Latent class analysis comparison of models (bold indicates smallest, or locally smallest, values)

| # of classes | # of parameters | LL | AIC | BIC | SSI-BIC | Entropy |
|---|---|---|---|---|---|---|
| 1 | 12 | −6860.2 | 13744.3 | 13790.8 | 13752.8 | -- |
| 2 | 21 | −6728.7 | 13499.5 | 13580.8 | 13514.2 | 0.97 |
| 3 | 30 | −6622.8 | 13305.5 | 13421.8 | 13326.6 | 0.95 |
| 4 | 36 | −6580.9 | 13233.8 | **13373.3** | 13259.1 | 0.95 |
| 5 | 45 | −6556.8 | 13203.6 | 13378.0 | 13235.2 | 0.93 |
| 6 | 54 | −6491.3 | **13090.6** | **13299.9** | **13128.6** | 0.94 |

**Table 3.**

Patterns of Non-Prescribed Buprenorphine (NPB) and Other Opioid Use (N=356): Latent Class Indicator Means and Prevalences (3-class model; **Heavy H/F Use** = "Heavy Heroin/Fentanyl, Low Non-Prescribed (NPB) Use," **Formal Tx** = "More Use of Formal Treatment, Low NPB Use"; **Intense NPB Use** = "Intense NPB Use, Less Formal Treatment")

| **Latent Class Indicator Variables** | **Latent Classes** | | |
|---|---|---|---|
| | **Heavy H/F Use 61%** | **Formal Tx 29%** | **Intense NBP Use 10%** |
| *Lifetime characteristics:* | | | |
| Years since first NPB use, *mean* | 4.2 | 3.9 | 3.6 |
| Years since first use of other illicit opioids, *mean* | 19.2 | 16.3 | 20.5 |
| *Past 6 months characteristics:* | | | |
| Frequency of NPB use, mean days out of 184 (6 months) | 15.5 | 18.9 | 121.7 |
| Frequency of heroin/fentanyl, *mean days out of past 184 days (6 months)* | 152.6 | 25.7 | 43.5 |
| Taken NPB to get high (ever in past 6months), *proportion* | 13.7% | 23.2% | 11.1% |
| Taken NP pain pills (ever in past 6 months), *proportion* | 58.3 % | 52.2% | 35.1% |
| Taken prescribed pain pills (ever in past 6 months), *proportion* | 16.8% | 29.0% | 5.3% |
| Used substance use disorder treatment (ever in past 6 months), *proportion* | 43.3% | 73.0% | 25.4% |

**Table 4.**

Comparison of auxiliary variables across latent classes (3-class model; **Heavy H/F Use** = "Heavy Heroin/ Fentanyl, Low Non-Prescribed (NPB) Use," **Formal Tx** = "More Use of Formal Treatment, Low NPB Use"; **Intense NPB Use** = "Intense NPB Use, Less Formal Treatment")

| Characteristic | Heavy H/F Use (n=216) | Formal Tx (n=105) | Intense NBP Use (n=35) | p-value | Adjusted p-value† |
|---|---|---|---|---|---|
| **Socio-demographics** | | | | | |
| Age (years, Mean, SD) | 39.0 | 38.5 | 41.9 | 0.192 | 0.901 |
| Gender (Male) | 50.1% | 48.0% | 58.5% | 0.574 | 0.901 |
| Race/Ethnicity (White/Non-Hispanic) | 89.6% | 88.2% | 85.5% | 1.808 | 0.901 |
| Education (Some College or More) | 41.8% | 54.3% | 26.9% | **0.014** | 0.294 |
| Marital Status (Married/Living with Partner) | 23.8% | 22.4% | 20.5% | 0.901 | 0.901 |
| Employment status: | | | | | |
| Employed full or part time | 25.6% | 27.8% | 21.3% | 0.486 | 0.901 |
| Not employed due to disability | 15.9% | 22.1% | 26.6% | | |
| Unemployed for other reason | 58.5% | 50.1% | 52.1% | | |
| **Pain and psychiatric comorbidity** | | | | | |
| Chronic pain diagnosis (ever, lifetime) | 53.3% | 60.3% | 58.4% | 0.502 | 0.901 |
| Major depressive disorder (past 12m) | 32.0% | 41.3% | 26.5% | 0.179 | 0.901 |
| Generalized anxiety disorder (past 12m) | 42.3% | 52.4% | 43.9% | 0.247 | 0.901 |
| PTSD (past 12m) | 29.5% | 28.7% | 11.6% | 0.055 | 0.810 |
| **Mode of administration of non-prescribed buprenorphine (NPB) and other opioids in the past 6 months** | | | | | |
| NPB taken non-orally (at least on one occasion) | 29.0% | 19.5% | 23.5% | 0.176 | 0.901 |
| NP pain pills taken non-orally (most common route) | 33.7% | 26.5% | 15.5% | **0.037** | 0.635 |
| Heroin/fentanyl injected (most common route) | **76.7%** | **43.8%** | **39.5%** | **<.0001** | **<.0001** |
| **Lifetime history of participation in formal buprenorphine-based treatment** | | | | | |
| Never | 32.8% | 31.8% | 36.7% | 0.642 | 0.901 |
| Once | 33.0% | 25.7% | 28.6% | | |
| Two or more times | 34.3% | 42.5% | 34.8% | | |
| **The most common source of non-prescribed buprenorphine in the past 6 months** | | | | | |
| Bought NPB from a dealer (vs. family/ friends or other) | 28.9% | 21.5% | 23.2% | 0.360 | 0.901 |
| **Other drug se (3–7 days per week, past 6 months)** | | | | | |
| Alcohol | 8.4% | 11.5% | 5.0% | 0.471 | 0.901 |
| Marijuana | 24.1% | 25.6% | 28.5% | 0.871 | 0.901 |
| Cocaine (powder or crack) | **31.6%** | **16.2%** | **14.4%** | **0.002** | **0.044** |
| Non-prescribed benzodiazepines | 12.7% | 12.4% | 19.3% | 0.648 | 0.901 |
| Non-prescribed gabapentin | 13.2% | 10.5% | 27.3% | 0.140 | 0.901 |

| Characteristic | Heavy H/F Use (n=216) | Formal Tx (n=105) | Intense NBP Use (n=35) | p-value | Adjusted p-value† |
|---|---|---|---|---|---|
| Methamphetamine | 18.7% | 12.3% | 10.5% | 0.222 | 0.901 |
| **Adverse consequences/experiences in the past 6 months** | | | | | |
| Overdose (ever in past 6m) | **34.2%** | **19.2%** | **11.5%** | **0.001** | **0.023** |
| Hospitalization (ever in past 6m) | 23.0% | 31.4% | 14.6% | 0.092 | 0.901 |
| Incarceration (ever in past 6m) | 28.8% | 36.4% | 26.6% | 0.386 | 0.901 |
| Homelessness (ever in past 6m) | **58.9%** | **55.4%** | **27.3%** | **0.002** | **0.044** |

† p-values after adjusting for multiple testing across all auxiliary variables using Hommel method.