



## Full length article

## Patterns of polysubstance use and overdose among people who inject drugs in Baltimore, Maryland: A latent class analysis

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## ABSTRACT

**Background:** Opioid-related overdose rates continue to climb. However, little research has examined the reach of overdose education and naloxone trainings among people who inject drugs (PWID). Understanding gaps in coverage is essential to improving the public health response to the ongoing crisis.

**Methods:** We surveyed 298 PWID in Baltimore City, MD. We conducted a latent class analysis of drug use indicators and tested for differences by class in past month overdose, having received overdose training, and currently having naloxone.

**Results:** Three classes emerged: cocaine/heroin injection (40.2%), heroin only injection (32.2%), and multi-drug/multi-route use (27.6%). The prevalence of past month overdose differed marginally by class ( $p = 0.06$ ), with the multi-drug/multi-route use class having the highest prevalence (22.5%) and the heroin only class having the lowest (4.6%). The prevalence of previous overdose training differed significantly by class ( $p = 0.02$ ), with the heroin/cocaine class (76.5%) having more training than the other two classes. Training was least common amongst the multi-drug/multi-route class (60.3%), though not statistically different from the heroin only class (63.0%). Classes did not differ significantly in current naloxone possession, although the multi-drug/multi-route class exhibited the lowest prevalence of naloxone possession (37.2%).

**Conclusions:** People who inject multiple substances are at high risk for overdose and are also the least likely to receive overdose trainings. The current service landscape does not adequately reach individuals with high levels of structural vulnerability and high levels of drug use and homelessness. Actively including this subgroup into harm reduction efforts are essential for preventing overdose fatalities.

## 1. Introduction

Overdose rates have risen dramatically in the United States. More than 72,000 individuals died of an overdose in the US in 2017, representing a 3.1-fold increase in overdose fatalities since 2002 (National Institute on Drug Abuse, 2018). Approximately 49,000 of the 2017 overdose deaths involved opioids, a four-fold increase since 2002 (National Institute on Drug Abuse, 2018). Opioid related overdose fatalities have skyrocketed in recent years, largely due to the introduction of fentanyl to the drug supply (O'Donnell et al., 2017). More than 20,000 of the 49,000 opioid deaths in 2017 were fentanyl involved (National Institute on Drug Abuse, 2018).

Beyond fatal overdoses, there were an additional 142,557 non-fatal opioid-involved overdoses identified in emergency departments

between July 2016 and September 2017 (Vivolo-Kantor et al., 2018). This statistic underestimates the actual burden of non-fatal overdoses in the US, as many people who use drugs do not call emergency services during an overdose or refuse transport to a hospital after being revived by emergency services (Levine et al., 2016). Non-fatal overdose is a key risk factor for fatal overdose (Caudarella et al., 2016). Given the extent of this burden, overdose is a public health emergency that needs to be ameliorated through scaled up prevention and harm reduction efforts. A nuanced understanding of overdose contributors and gaps in service delivery is essential for tailoring and targeting interventions and maximizing their impact.

A number of drugs have been implicated with risks of both fatal and non-fatal opioid overdoses. Correlates of overdose include concomitant use of cocaine, benzodiazepines, and/or alcohol with opioid use (Coffin

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et al., 2003; Darke et al., 2005). In fact, the risk of overdose when opioids and central nervous system depressants (e.g., alcohol, benzodiazepines) are combined contributes substantially to the global burden of drug related morbidity (Degenhardt and Hall, 2012). This literature begins to suggest that understanding opioid use within an individual's substance use profile can improve our ability to identify individuals at high risk for overdose. Latent class analysis (LCA) is a powerful tool to identify polysubstance use profiles. LCA allows researchers to identify subgroups of individuals with similar substance use profiles. To date, multiple LCAs in US based samples have focused on college students and the general adult population (Agrawal et al., 2007; Brooks et al., 2017; Evans-Polce et al., 2016; Haardörfer et al., 2016). However, few studies have explicitly studied profiles of polysubstance use among people who inject drugs (PWID) or other high-risk groups in the context of the ongoing opioid epidemic in the US.

In response to the growing opioid overdose epidemic, overdose education and naloxone distribution trainings have been scaled up in many settings for over 20 years (McDonald et al., 2017). The new fentanyl era has introduced additional challenges for take home naloxone implementation. As higher doses and repeated administrations of naloxone are needed to reverse late presenting fentanyl-involved overdoses, it is more urgent than ever to get take home naloxone into the hands of those who use any drugs that may be contaminated with fentanyl (Fairbairn et al., 2017). Many efforts have focused on training health care providers and first responders (e.g., emergency medical services providers and law enforcement officers) to administer naloxone (Davis et al., 2014a,b; Rando et al., 2015). While these trainings of first responders can make a life-saving difference in some situations, people experiencing or witnessing an overdose do not always call 911 due to lingering fears of police based on previous experiences (Baca and Grant, 2007; Latimore and Bergstein, 2017; Pollini et al., 2006). Policing policies in response to the rise in overdoses have exacerbated these fears and contradict the spirit of laws protecting those who call for help during an overdose emergency.

For example, as of 2016, the Baltimore City Police Department's policy of treating overdose locations as potential crime scenes, where witnesses are questioned, negates the potential benefits of local Good Samaritan laws due to this mandatory police response (Baltimore Police Department, 2016). Similar policies have been enacted in many other jurisdictions as well, jeopardizing the benefits of widespread Good Samaritan laws. Thus, in many locales, trained medical professionals may not ever be notified of and reach individuals experiencing overdoses in order to administer naloxone.

Interventions like overdose trainings can only save lives if they reach the individuals actually present during an overdose emergency. The World Health Organization has specifically recommended expanding access to naloxone and related trainings among lay people likely to witness or experience an overdose, particularly people who use opioids and their peers (World Health Organization, 2014). Some US cities have made substantial efforts to engage PWID directly into overdose reversal trainings (Baltimore City Health Department, 2018; Tobin et al., 2009; Wheeler et al., 2015). These trainings have been tremendously successful in saving lives, as the Centers for Disease Control and Prevention estimated that more than 26,000 overdoses were successfully reversed with naloxone administered by peers between 1996 and 2014 (Wheeler et al., 2015). However, data regarding overdose training and naloxone coverage among PWID population are not widely available. Understanding how well overdose trainings are penetrating communities of PWID is important for identifying gaps in services and underserved subpopulations.

### 1.1. Current study

In the present study, we examine how distinct combinations of substance use and routes of administration are associated with non-fatal overdose and with receiving overdose training. Our goal is to

understand if individuals who are most at risk for overdose based on their polysubstance use are also the ones receiving overdose response trainings most frequently and are carrying naloxone so that they can respond in an emergency. Identifying these differences can help identify gaps in current public health responses to the overdose epidemic so that we can more effectively protect the lives of PWID.

## 2. Methods

### 2.1. Study design and recruitment

The data for the current analysis are from a parent study examining a change in syringe distribution practices of the Baltimore City Health Department mobile, van-based Syringe Service Program (SSP) (Hunter et al., 2018; Park et al., 2018; Sherman et al., 2018). Data were collected between April–November 2016. Participants were sampled from all Baltimore SSP sites in proportion to the number of clients that visit each site. Study staff screened potential participants for eligibility after they finished at the SSP. Participants completed an anonymous Computer Assisted Personal Interview (CAPI) survey. SSP clients who participated referred their non-client peers to participate as well. Participants had to be 18 years old or older and able to provide consent orally in English. We compensated participants with a \$25 gift card. All participants had injected drugs in their lifetime. Our analytic sample size was 298. This study was reviewed and approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board.

### 2.2. Measures

#### 2.2.1. Past month drug use

We included 11 binary variables indicating whether or not a participant used specific drugs via different routes of administration. These variables addressed the following drug/route combinations: marijuana, crack (smoked), heroin (smoked/snorted), heroin (injected), cocaine (smoked/snorted), cocaine (injected), speedball (injected), pain relievers (swallowed), pain relievers (injected), tranquilizers (swallowed), and buprenorphine (swallowed).

#### 2.2.2. Overdose and naloxone outcomes

Participants reported their own overdose history (“When was your last overdose?”). We created a binary variable indicating whether or not a participant had experienced an overdose in the past month. We asked participants if they had ever received any overdose training in their lifetime (yes/no). Participants also indicated whether they currently had any form of naloxone currently on their person or in their home (yes/no).

#### 2.2.3. Demographic covariates

Sex (male, female), race (White, Black, Other), age (18–44, 45 and older), education (less than high school, 12th grade or GED, some college or more), and living situation (own home/apartment, other's home/apartment, homeless) were all reported by participants. We included these variables as covariates to adjust the distal outcome model (described below).

### 2.3. Analysis

First, we used a latent class analysis (LCA) approach to identify profiles of polysubstance use in our sample using the 11 drug use variables as indicators. LCA is used to identify subgroups of individuals that are homogenous in terms of the LCA indicators, in this case, use of different drugs/routes of administration (Goodman, 1974; Lazarsfeld and Henry, 1968). To do this, we estimated a series of class models with increasing numbers of class (up to 5 classes). We then used the following fit statistics to select the preferred model: log likelihood, Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC), model

entropy, and Lo- Mendell-Rubin Likelihood Ratio Tests (LRT). For the log likelihood and entropy, larger values are favored. For the AIC and BIC, smaller values are preferred. The LRT tests a given model against a model with one fewer classes to determine if the larger model fits significantly better than the smaller model. A significant p-value for the LRT indicates that the smaller model does not fit as well as the larger model, and therefore the larger model is preferred. In addition to considering the fit statistics to choose a model, we also considered the substantive interpretations of the classes in each model to select the final number of classes. To test the associations between latent classes and the outcomes of interest (overdose, overdose training, and current naloxone possession) and to adjust for covariates, we used the Vermunt 3-step approach (Vermunt, 2010). This approach accounts for potential misclassification in the latent classes due to their unobserved nature, in contrast to treating the latent class as an observed variable by formally grouping participants into their most likely class and then testing for differences in outcomes. We adjusted the associations between latent classes and outcomes for sex, race, age, education, and living situation. To compare the prevalence of the overdose and naloxone outcomes between the classes, we used Wald Tests to identify overall differences in outcome between groups. We then followed up the significant Wald Tests with additional “model constraints” to identify any pairwise differences. Fig. 1 shows a depiction of this distal outcome analysis modeled. Analyses were conducted using Mplus8 (Muthén and Muthén, 1998- 2017Muthén and Muthén, 2017Muthén and Muthén, 1998-2017).

### 3. Results

The prevalence of the demographic characteristics, past month drug use indicators, and outcomes are displayed in Table 1. The sample was mostly male (68.8%) and Black (57.7%). Most of the sample (54.7%) was age 45 or older. Only 18.5% had a greater than high school education. Participants’ living situations were relatively evenly distributed between staying in their own home/apartment (37.9%), staying in someone else’s home/apartment (28.5%), and being homeless (33.6%). The prevalence of drug use indicators varied between 9.1% (pain reliever injection) and 89.9% (heroin injection). Fourteen percent of the sample had an overdose in the past month. Most (67.7%) had previously received overdose training, and half (50.9%) currently had naloxone in their possession.

**Table 1**  
Prevalences of Class Indicators, Outcomes, and Sample Characteristics (N = 298).

	Prevalence (%)
<b>Demographic Characteristics</b>	
Sex	
Male	68.8
Female	31.2
Race	
White	37.3
Black	57.7
Other	5.0
Age	
18-44	45.4
45 and older	54.7
Education	
Less than HS	37.9
12th grade or GED	43.6
Some college or more	18.5
Living Situation	
Own house/apartment	37.9
Other’s house/apartment	28.5
Homeless	33.6
<b>Past Month Drug Use</b>	
Marijuana	42.6
Crack (smoked)	47.3
Heroin (smoked/snorted)	30.5
Heroin (injected)	89.9
Cocaine (smoked/snorted)	13.4
Cocaine (injected)	47.0
Speedball (injected)	54.4
Pain Relievers (swallowed)	24.2
Pain Relievers (injected)	9.1
Tranquilizers (swallow)	25.5
Buprenorphine (swallow)	12.8
<b>Overdose and Training Outcomes</b>	
Past Month Overdose	14.1
Previous Overdose Training	67.7
Current Naloxone Possession	50.9

#### 3.1. Latent class analysis

Table 2 summarizes the fit statistics for each model estimated during the class enumeration procedure. Based on these fit statistics, we selected a three-class solution as this model was favored by both the BIC and LRT. The probabilities of the different indicators in each class are displayed in Fig. 2. The largest class contained 40.2% of the sample,

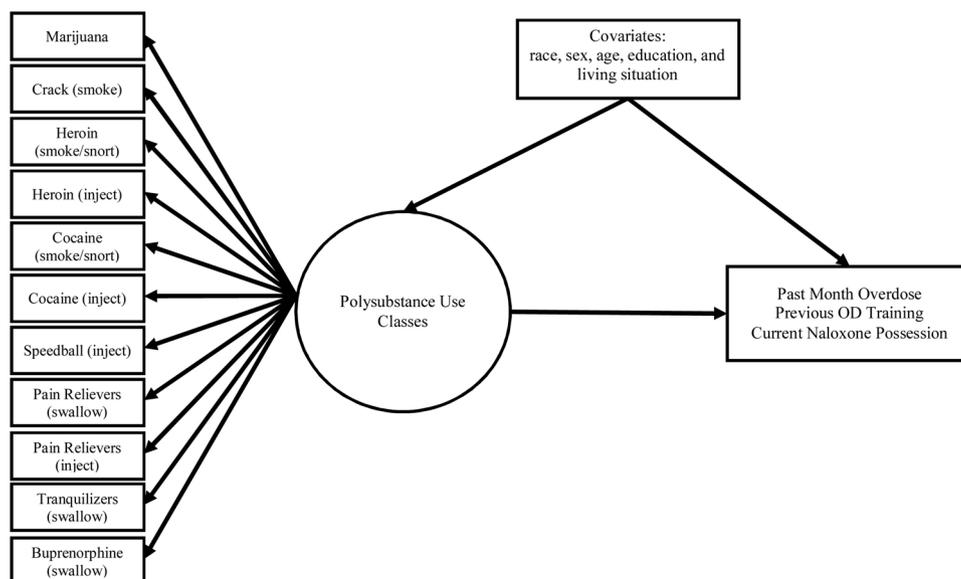


Fig. 1. Latent class analysis with distal outcomes model.

**Table 2**  
Latent Class Model Fit Statistics.

Classes	Smallest Class	Log Likelihood	AIC	BIC	Entropy	LRT p-value
2	47%	-1681.069	3408.137	3493.170	0.767	0.0188
3	27.6%	-1641.524	3353.048	3482.447	0.836	0.0136
4	13.3%	-1613.568	3321.136	3494.899	0.793	0.0946
5	4.1%	-1590.309	3298.617	3516.746	0.850	0.1613

based on posterior probabilities. This class was characterized by high probabilities of heroin, cocaine, and speedball injection and lower rated of other drug/route of administration indicators. We named this class as the “heroin/cocaine injection” class. The second class was the smallest (27.6% of the sample). This class was characterized by higher probabilities of non-injection drugs than other classes, plus a high probability heroin injection. We named this class the “multi-drug/multi-route” class. The final class made up 32.2% of the sample. This class had a high probability of heroin injection, but low probabilities of other drug use. We named this class the “heroin injection only” class.

3.2. Correlates of latent class membership

The prevalence of each correlate by latent class membership are presented in Table 3, where we did observe some variation in socio-demographic characteristics across classes. There were no significant differences in age between classes. The multi-drug/multi-route use class had marginally more females than the heroin/cocaine class ( $\chi = 0.66$ ,  $p = 0.10$ ). The multi-drug/multi-route use class also had a marginally lower proportion of Black individuals ( $\chi = -1.95$ ,  $p = 0.06$ ) and of having a 12<sup>th</sup> grade or equivalent education ( $\chi = -0.99$ ,  $p = 0.07$ ) than the heroin only class. We did not observe any other difference between classes by sex, race, or education. In terms of homelessness, the multi-drug/multi-route use class had the highest prevalence of homelessness (vs heroin only class:  $\chi = 2.09$ ,  $p < 0.01$ ; vs heroin/cocaine class:  $\chi = 0.82$ ,  $p = 0.06$ ). This class also had a marginally higher proportion of individuals staying in someone else’s home than the heroin/cocaine class ( $\chi = 0.84$ ,  $p = 0.08$ ). Furthermore, the heroin/cocaine class had more homeless individuals than the heroin only class ( $\chi = 1.27$ ,  $p = 0.003$ ).

3.3. Overdoses, overdose training, and naloxone possession by latent class

The prevalence of having an overdose in the past month, ever having had an overdose training, and currently possessing naloxone by class are presented in Fig. 3. Overdose experiences differed marginally by class ( $\chi = 5.72$ ,  $p = 0.06$ ), with the multi-drug/multi-route class having the highest overdose rates (22.5%) and the heroin only class having the lowest (4.6%).

Prevalence of overdose trainings differed significantly by class

**Table 3**  
Distribution of Sociodemographic Characteristics by Latent Class Membership.

	Class 1 – Heroin/Cocaine Injection	Class 2 – Multi Drug/Multi Route	Class 3 – Heroin only Injection
Sex			
Male	75.5%	60.8%	67.3%
Female	24.5%	39.2%	32.7%
Race			
White	33.8%	49.0%	31.5%
Black	61.6%	42.3%	66.1%
Other	4.6%	8.7%	2.4%
Age			
18-44	41.9%	56.2%	40.3%
45 and older	58.1%	43.8%	59.7%
Education			
Less than HS	34.8%	38.2%	41.6%
12th grade or GED	48.4%	35.4%	44.7%
Some college or more	16.8%	26.4%	13.7%
Living Situation			
Own house/apartment	39.2%	22.5%	49.6%
Other’s house/apartment	22.8%	28.3%	35.8%
Homeless	38.0%	49.2%	14.6%

( $\chi = 7.58$ ,  $p = 0.02$ ). The multi-drug/multi-route class had the lowest trainings rates (60.3%), while the heroin/cocaine injection class had the highest (76.5%). The follow up tests identified that the heroin/cocaine class had higher overdose training rates than the other classes (vs multi-drug/multi-route class:  $p = 0.04$ ; vs heroin only class:  $p = 0.03$ ). The multi-drug/multi-route and heroin only classes did not differ in overdose training ( $p = 0.84$ ). There were no significant differences between classes in terms of current naloxone possession ( $\chi = 2.81$ ,  $p = 0.25$ ), but the multi-drug/multi-route class did have lower rates (37.2%) than the other classes (cocaine/heroin: 53.2%; heroin only: 59.7%).

4. Discussion

We identified three distinct classes of substance use among PWID in Baltimore, Maryland that had unique relationships with overdose related outcomes: those who primarily inject heroin only, those who inject both cocaine and heroin, those who inject heroin and use multiple non-injection drugs. The classes we identified are consistent with the findings of previous work that identified profiles of polysubstance use across people who use drugs, regardless of whether or not they inject any drugs (Kuramoto et al., 2011). Overall, 14% of our sample had experienced an overdose in the past month. This estimate is relatively high compared to existing estimates, which suggest approximately 14% of PWID in the US and 17% of PWID globally have had a non-fatal

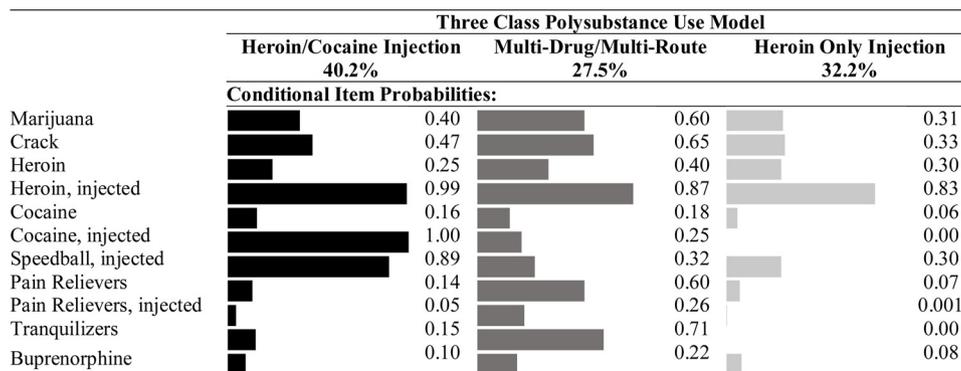
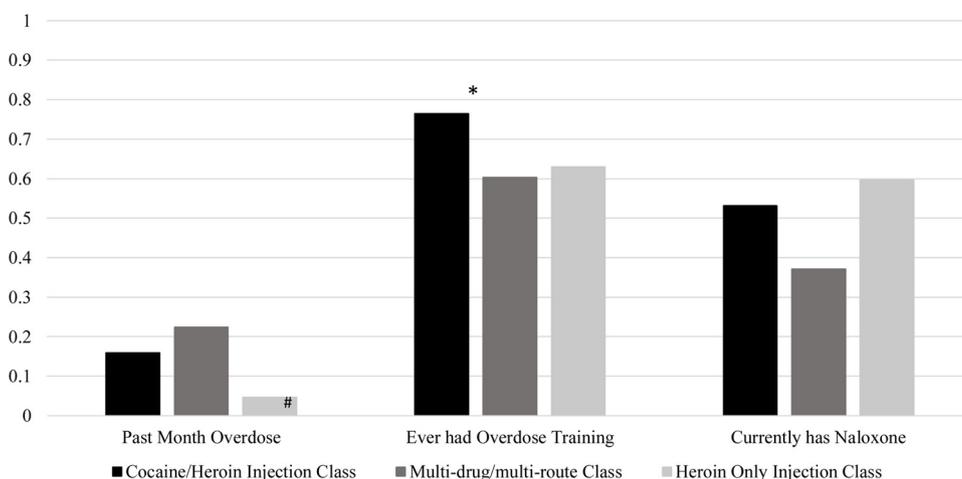


Fig. 2. Probabilities of drug use indicators in each class in the three class solution.



**Fig. 3.** Proportions of each polysubstance use class with each distal outcome.

*Note.* Overall Wald tests indicated that there were marginal differences between classes for overdose ( $p = 0.06$ ) and significant differences between classes for overdose training ( $p = 0.02$ ). Follow up tests indicated that the cocaine/heroin injection class had significantly higher rates of overdose training than the other classes.

# -  $p < 0.1$ , \* -  $p < 0.05$

overdose in the past year (Martins et al., 2015; Robinson et al., 2017). However, these estimates were made before the era of fentanyl, which has drastically increased the burden of overdose (Rudd et al., 2016). The classes differed marginally in terms of overdose prevalence (multi-drug/multi-route and heroin/cocaine classes higher than heroin only class) and significantly by overdose training history (heroin/cocaine class higher than multi-drug/multi-route and heroin only classes). Fifty-one percent of our sample overall currently had naloxone in their possession, which is on par with estimates from Seattle, Washington (44% past year possession) and Norwegian cities (62% current possession) (Glick et al., 2017; Madah-Amiri et al., 2018). However, our sample likely overestimates the total prevalence of PWID that have received overdose training and have naloxone, as the Baltimore SSP is a key provider of these programs in the city and our study specifically sampled SSP clients. The prevalence of current naloxone possession did not significantly differ by class, though the prevalence estimates ranged from 37% among the multi-drug/multi-route class to 70% among the heroin only class. Our results indicate the need for specific public health efforts to reach the most vulnerable subpopulations among PWID, a population typically regarded as homogenous.

Our results emphasize the importance of considering patterns of polysubstance use when addressing the ongoing overdose crisis from a public health perspective. There is a significant gap between overdose risk and overdose trainings among those with polysubstance use. The multi-drug/multi-route group had the highest prevalence of recent overdose but the lowest rates of training and current naloxone possession. This disparity is significant as those at the highest risk for overdose based on the types of drugs that they use have the least training and resources available to respond to an overdose. Despite extensive overdose training efforts in Baltimore City, individuals with polysubstance use are underserved (Baltimore City Health Department, 2018). This may be due to people with polysubstance use being harder to reach for interventions for a variety of possible reasons, including sociodemographic characteristics, long term involvement with street life, or structural vulnerability. For example, the multi-drug/multi-route use class had a high prevalence of homelessness compared to the other classes. Our study has begun to elucidate the gaps in overdose training coverage, but more research is needed to understand why people who use multiple drugs are less likely to receive these much-needed trainings. The ability of our survey to reach such individuals in itself provides evidence that the most vulnerable PWID can be reached by research and harm reduction programs. Barriers to overdose response trainings include both problems accessing trainings and competing survival interests, especially among the most marginalized PWID. Solutions to the gap in overdose training coverage we identified must address both system and individual level barriers in order to be most effective.

Strategies that actively include hard to reach and vulnerable PWID in harm reduction interventions, like overdose trainings, are needed to close gaps in service coverage. One avenue towards closing this gap is making a particular effort to deliver overdose trainings and increase naloxone access to homeless PWID. In our sample the multi-drug/multi-route use class was more likely to be homeless and also had the least access to harm reduction services. Homeless populations are at higher risk for many outcomes, including overdose and difficulty accessing necessary services (Doran et al., 2018; Kerr et al., 2007; O'Driscoll et al., 2001). In order for overdose trainings to reach the most vulnerable PWID, outreach needs to happen where these individuals congregate, like shelters, homeless encampments, and homeless services.

Additionally, naloxone possession was lower in our sample than the prevalence of having received training, suggesting that individuals who use their naloxone are not always able to easily refill it. This gap was especially obvious in the high risk, multi-drug/multi-route use group. Making naloxone refills more accessible and affordable can help reduce this gap. Overall, additional efforts to reach the most vulnerable PWID with trainings and naloxone access are essential to effectively avert future overdose fatalities.

Furthermore, the public health response to the ongoing overdose crisis can take some important lessons from the response to HIV during the 1980s and 1990s. In particular, the response to overdoses in the United States would benefit from nimble data collection approaches that reach deep into marginalized communities, such as those employed in HIV epidemics among PWID. One such tool which could be adapted is a “rapid assessment” that employed qualitative methods aimed to quickly understand the nature of a drug scene and its associated HIV risks (Fitch et al., 2002, 2000). By utilizing the important lessons learned in past epidemics, we will be better able to optimize our response and save lives for the duration of the present opioid epidemic.

This study does have limitations. The primary limitation of this study is the relatively small sample size for a latent class analysis with distal outcomes. Due to the sample size, our study may have been underpowered to identify differences in the overdose and naloxone possession outcomes. It is also possible that we may have identified additional classes with a larger sample size. However, our results generally align with a previous study on polysubstance use profiles in Baltimore, which lends additional credibility to our results (Kuramoto et al., 2011). Given this, future studies should replicate and extend these findings in larger samples.

Furthermore, cohort studies are needed to establish if the classes we identified remain stable or change over time. Some initial evidence suggests that polysubstance use profiles may be relatively stable over time, but the research on this phenomenon is limited (Baggio et al., 2014). Our study also cannot provide insight into why the gap between overdose risk and overdose trainings exist. We do not have any

information as to why certain individuals did not receive trainings or did not have naloxone. Future research will need to address these topics to inform how trainings can be effectively expanded to reach the most at risk individuals. Despite these limitations, our study is an important step forward in identifying gaps in training coverage to prevent fatal overdoses.

Our study also has a number of strengths that make it an important addition to the literature. First, we were able to identify distinct profiles of substance use that have importantly different overdose outcomes. Second, we were able to identify an important mismatch between overdose risk and harm reduction service utilization, which can inform how service delivery can be supplemented in the future to reach the high risk and underserved subgroups. These strengths make the current study an important contribution to the literature and the public health response to the opioid crisis.

## 5. Conclusions

Among PWID, those who engage in polysubstance use have higher prevalence of non-fatal overdose than peers who only use heroin or combine cocaine and heroin. Those with polysubstance use are also less likely to receive overdose training and to be in possession of naloxone. This mismatch between risk and services represents a significant gap in the public health response to the overdose crisis. This service gap reflected the different levels of structural vulnerability among PWID, a population that is often regarded as homogenous. Going forward, public health practitioners need to find more effective ways to reach underserved, high risk and vulnerable populations for overdose trainings with specific consideration for their stability and particular needs.

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None.

## Contributors

SGS is the principle investigator of the study that collected the data used. JNP and STA contributed to data collection. KES performed the statistical analyses and led the writing of the manuscript. All authors have contributed to and approved the final manuscript.

## Disclosure

SGS is an expert witness in opioid litigation.

## Conflicts of interest

None conflict declared.

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