Research Paper

Stigma and drug use settings as correlates of self-reported, non-fatal overdose among people who use drugs in Baltimore, Maryland

Carl A. Latkin[a,*], Rachel E. Gicquelais[b], Catie Clyde[a], Lauren Dayton[a], Melissa Davey-Rothwell[a], Danielle German[a], Seun Falade-Nwulia[c], Haneefa Saleem[d], Michael Fingerhood[e], Karin Tobin[a]

[a] Johns Hopkins Bloomberg School of Public Health, Department of Health, Behavior and Society, United States
[b] Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, United States
[c] Johns Hopkins School of Medicine, Division of Infectious Diseases, United States
[d] Johns Hopkins Bloomberg School of Public Health, Department of International Health, United States
[e] Johns Hopkins Bayview Medical Center, Department of Medicine, Chemical Dependence, United States

ABSTRACT

Background: Fatalities from opioid overdose quadrupled during the last 15 years as illicit opioid use increased. This study assesses how stigma and drug use settings are associated with non-fatal overdose to identify targets for overdose risk reduction interventions and inform overdose education and naloxone distribution programs.
Methods: We surveyed 444 people who used drugs in Baltimore, Maryland, USA, from 2009 to 2013 as part of a randomized clinical trial of a harm reduction intervention. Participants reported demographic characteristics, drug use, overdose history, use of a local syringe services program, involvement in the local drug economy, and whether they experienced discrimination from others (i.e., enacted stigma) or stigmatized themselves (i.e., internalized stigma) related to their drug use. We used multinomial logistic regression models to identify correlates of experiencing a non-fatal overdose within the past year or > 1 year ago relative to participants who never experienced an overdose.
Results: Stigma was positively associated with experiencing a non-fatal overdose in the past year (adjusted Odds Ratio [aOR]: 1.7, 95% Confidence Interval [CI]: 1.1–2.7) and > 1 year ago (aOR [95% CI]: 1.5 [1.1–2.0]) after adjustment for demographic and substance use characteristics. The association of stigma with overdose was stronger for enacted versus internalized stigma. The number of public settings (shooting gallery, crack house, abandoned building, public bathroom, outside) where participants used drugs was also positively associated with experiencing an overdose.
Conclusions: Stigma related to drug use and using drugs in more settings may increase overdose risk. The effectiveness of overdose prevention and naloxone training may be improved by reducing discrimination against people who use drugs in community and medical settings and diversifying the settings in which overdose prevention trainings are delivered. These efforts may be enhanced by use of peer outreach approaches in which people who use drugs diffuse prevention messages through their social networks and within settings of drug consumption outside the medical setting.

Introduction

The quadrupling of opioid overdose mortality in the US, and in Baltimore, during the past two decades highlights a pressing need to prevent both fatal and non-fatal overdose (National Institute on Drug Abuse, 2018). The urgent need to prevent overdoses has become only more evident alongside the recent surge in fentanyl-related deaths (Seth, Scholl, Rudd, & Bacon, 2018). Fentanyl overdose deaths in Baltimore City, where the data for the present study were collected,

increased 36.8% from 2016 to 2017 from 419 to 573 deaths (MDHMH, 2017, 2018). Overdose mortality may be reduced by diffusing overdose prevention and response skills and training people who use drugs (PWUD) and other community members likely to witness an overdose to administer naloxone, a lifesaving overdose reversal antidote.

Preventing overdose fatalities requires identifying individuals who are at risk for opioid overdose and reducing their risk through harm reduction and other types of interventions (Hawk, Vaca, & D'Onofrio, 2015; Lagisetty, Bohnert, & Fendrick, 2018). Throughout the US,

including in Baltimore, local programs have implemented overdose response training and distributed naloxone through existing syringe exchange programs (Green, Heimer, & Grau, 2008; Tobin, Sherman, Beilenson, Welsh, & Latkin, 2009) with apparent success in increasing participants' knowledge and skills to respond to an overdose event (Seal et al., 2005; Tobin et al., 2009). However, many individuals at risk of overdose do not frequent syringe exchange services, highlighting the need to diversify the locations providing harm reduction services (Beletsky et al., 2014; Gindi, Rucker, Serio-Chapman, & Sherman, 2009; Treloar & Cao, 2005). The current study sought to explore correlates of self-reported, non-fatal overdoses, including stigma and drug use settings, among PWUD in Baltimore City to inform future overdose prevention efforts.

The self-stigma and discrimination experienced by PWUD because of their drug use (i.e., stigma related to drug use) has not been adequately considered as a risk factor for opioid overdose despite increasing evidence linking stigma with health outcomes, injection-related risk behaviors, and utilization of harm reduction services (Cama, Brener, Wilson, & von Hippel, 2016; Couto E Cruz, Salom, Dietze et al., 2018; Kulesza, Larimer, & Rao, 2013; Latkin et al., 2010; Rivera, DeCuir, Crawford, Amesty, & Lewis, 2014; von Hippel, Brener, & Horwitz, 2018; Wilson, Brener, Mao, & Treloar, 2014). Internalized stigma (i.e. self-stigma), the negative feelings PWUD have about themselves because of their drug use, has been previously linked to depression and decreased psychological well-being (Cama et al., 2016; Kulesza et al., 2013; von Hippel et al., 2018), which are known to increase overdose risk (Tobin & Latkin, 2003). Rivera et al. (2014) also found that among people who inject drugs, higher internalized stigma was associated with decreased recent use of syringe exchange programs. Additionally, enacted stigma (i.e. experiences of discrimination or being stereotyped because of drug use) has similarly been associated with depression and poor mental and physical well-being (Couto E Cruz, Salom, Dietze et al., 2018; Kulesza et al., 2013), as well as with injection behaviors that increase overdose risk, such as being injected by someone else (Wilson et al., 2014). To our knowledge, only one study has examined the association of discrimination with overdose and found that experiencing discrimination because of drug use on a weekly or more frequent basis was associated with 60% higher odds of overdosing (Couto E Cruz, Salom, Dietze et al., 2018).

In addition to individual-level factors, the micro-level risk environment, specifically the settings in which people use drugs, may influence the outcome of an overdose. Using drugs in public spaces, such as abandoned buildings or outside, has been associated with both calling for medical help and fatal overdose compared to use in private spaces (e.g., a participant's home) (Bohnert, Tracy, & Galea, 2009; Tracy et al., 2005). In addition, setting may influence bloodborne virus risk through its influence on injection norms and practices (Rhodes et al., 2006). However, it is unknown whether using drugs in public versus private settings influences whether an overdose occurs. Setting-specific drug use norms may influence overdose risk. PWUD in settings other than their private residences may have less control over what transpires, may rush to use, and/or may fear police or others interrupting their drug use. Additionally, the number of settings where drugs are used may be indicative of drug use frequency and addiction severity.

Examining contextual and structural risk factors for experiencing an overdose, such as stigma and drug use settings, could inform overdose prevention programming. The primary aim of this analysis was to examine how stigma was associated with overdose history. We anticipated that higher levels of internalized and enacted stigma would be positively associated with experiencing a drug overdose. The secondary aim was to assess how drug use settings relate to overdose history. We hypothesized that using drugs in more settings, and especially in public settings, would be positively associated with experiencing a drug overdose. Finally, we examined how other factors, including drug use, syringe exchange use, selling drugs, and demographic factors related to

overdose history.

Methods

Workshop study

Study participants were recruited in Baltimore, Maryland from July 2009 to July 2013 as part of the Workshop study, a randomized clinical trial addressing psychological distress and HIV risk behaviors among inner-city PWUD residing in impoverished neighborhoods (Tobin et al., 2017). Recruitment was conducted through street-based outreach, word-of-mouth, flyers, advertisements in local newspapers, and referrals from community agencies. Inclusion criteria for enrollment were: (1) age 18–55; (2) willing to attend group sessions, which was the mode of the clinical trial intervention; and (3) HIV risk behavior, satisfying at least one of the following categories: (3a) injected drugs more than 3 times in the past week, or (3b) snorted or sniffed heroin or cocaine or smoked crack in the past 6 months AND had one of the following sexual risk behaviors in the past 6 months: two or more sex partners, sex with a partner who injected drugs, sex with a partner who smoked crack, or sex with a partner who was HIV-positive. All study protocols were reviewed by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board, and all participants provided written informed consent prior to study enrollment. Data reported here were obtained from the study's baseline survey, which was conducted from 2009 to 2012. All drug use questions were administered via audio computer assisted self-interviewing (ACASI). The remaining data were collected during face-to-face interviews. The present analysis includes 444 study participants with complete data on survey items related to drug overdose, stigma, opioid use, drug use settings, and other measures described below.

Survey measures

Overdose history

To assess history of experiencing drug overdose, participants were introduced to the definition of an overdose as "a life-threatening condition that occurs after someone has taken drugs by injection or by any other route." They were then asked: (1) "How many times in your life have you overdosed?" and (2) "When was your most recent overdose?" The latter item served as the main outcome variable for analysis. Reports of experiencing an overdose were categorized as "in the past year," "over a year ago," or "never." Lifetime overdose frequency was explored in a sensitivity analysis.

Opioid use and addiction treatment history

Participants estimated the last time they used several substances through various modes of administration. This analysis summarized the following items: sniffing or snorting heroin, injecting heroin, injecting speedball (a combination of heroin and cocaine), and using prescription opioids "to get high" (i.e., to become intoxicated). Participants reported whether their use was "in the past year," "more than a year ago," or "never." Heroin and/or speedball injection were summarized as a single measure for the same time period. To identify participants who received addiction treatment, we summarized whether participants stayed overnight in a residential drug treatment program, attended an outpatient program, took buprenorphine, or took methadone "in the past year," "more than a year ago," or "never." We summarized receipt of any addiction treatment using the participant's most recent timeframe for any of the four treatments. Variable values for "never" were coded as 0, for "more than a year ago" were coded as 1, and "in the past year" were coded as 2.

Drug use settings

Participants were asked whether they had used substances in a variety of settings over the past six months. Settings included a place

they lived, a friend's residence, a "shooting gallery" (i.e. a location where PWUD gather to inject drugs), a "crack house," (i.e. a location where PWUD gather to use drugs), an abandoned building, a public bathroom, and "outside" (i.e. street, park, alley, etc.). For the present analyses, these items were assessed both individually and in a combined score ranging from 0 to 7 settings (median: 3). We also created two subscores reflecting the number of public spaces used (i.e., shooting gallery, crack house, abandoned building, public bathroom, and/or outside; range: 0–5, median: 1) and private spaces used (i.e. a place they lived or a friend's residence; range: 0–2, median: 2).

Stigma related to drug use

An overall stigma measure was assessed using a 17-item scale of 10 questions about enacted stigma and 7 questions about internalized stigma (Supplemental Table 1). Enacted stigma questions captured discriminatory experiences and times when PWUD were treated differently because of their drug use when interacting with others (e.g., "Other people are uncomfortable around me because I use drugs"). Internalized stigma (i.e., self-stigma) referred to feelings that the participant had towards themselves because of their drug use (e.g., "I feel set apart, isolated from the rest of the world because of my drug use"). Responses were recorded on a five-point scale from "(1) strongly disagree" to "(5) strongly agree." We formed three measures by summing all 17-items, the 10 enacted stigma items, and the 7 internalized stigma items. The overall scale's Cronbach's alpha was 0.91. The Cronbach alpha for internalised and enacted stigma were 0.85 and 0.89, respectively. For the analysis, responses were converted to z-scores to facilitate ease of interpretation.

Syringe exchange use, syringe and equipment sharing, & drug economy involvement

Participants were asked how often they exchanged syringes through the Baltimore City Needle Exchange Program (BCNEP) in the past six months. Participants who injected heroin and/or speedball in the past six months reported the number of different people they shared syringes with, defined as "using a needle after someone else." For analysis, receptive syringe sharing was categorized as binary variable comparing participants who shared with > 0 people versus did not share with anyone. Participants who injected heroin and/or speedball in the past six months also reported how often they shared equipment, defined as using a cooker previously used by another person, cotton used by another person, or rinse water after someone else had used it. Participants were considered to have shared equipment if they endorsed sharing at least one of these items. Syringe and equipment sharing were explored in bivariate analysis but were not included in the regression models as these questions were only asked of people who injected drugs within the last 6 months. Involvement in the drug economy was assessed by asking participants whether they sold drugs in the past six months.

Demographics

The survey assessed several demographic and socio-economic factors including age, race, gender, education, employment status, and homelessness. Participant age was dichotomized based on a median split (median = 45).

Statistical analysis

We compared the distributions of covariates between those who experienced an overdose within the last year, > 1 year ago, and who never experienced an overdose. We tested for statistical differences in bivariate associations using chi-squared tests. We then used multivariable multinomial logistic regression to summarize the associations of covariates with experiencing an overdose within the last year or > 1 year ago relative to participants who never experienced an overdose. We included all variables with a chi-squared p-value ≤0.20 in the multivariable model (stigma, number of drug use settings, heroin and/

or speedball injection, prescription opioid misuse, heroin snorting, syringe exchange use, addiction treatment, and selling drugs) as well as several demographic variables (age, gender, race, education, and homelessness) regardless of their statistical significance in bivariate associations. For regression models, we treated opioid use and addiction treatment variables as continuous ordinal measures ranging from 0 to 2 as described above. We assessed the relationship of stigma with overdose by using the 17-item z-score and total number of drug use settings as covariates in the main analysis and examined the enacted and internalized stigma scores and public and private drug use settings in three separate models as subanalyses. As a sensitivity analysis, we examined the association of stigma and number of drug use settings with the number of lifetime overdoses using zero-inflated negative binomial regression to account for the distributional form of overdose frequency (i.e. overdispersion [mean: 0.8 overdoses, variance: 2.0] and the large number of participants who had never experienced an overdose [62.6%]).

Results

Sample characteristics

This was an impoverished urban sample of 444 PWUD; 94.6% were unemployed, and 36.9% were homeless in the last 6 months. Most participants were African American (85.4%), while 12.6% identified as white and 2.0% were categorized as "other." Over half (58.1%) of the sample was male, and the median age was 45 years. Less than half (48.0%) completed high school. Nearly all participants (93.5%) used opioids, with 83.8% ever snorting heroin, 56.5% ever injecting heroin or speedball, and 35.8% ever misusing prescription opioids. Among those who injected heroin and/or speedball in the past 6 months, 53.1% shared syringes and 81.8% shared other injection equipment. A minority (13.1%) reported selling drugs in the past month. All 125 participants (28.2%) who exchanged syringes did so infrequently (less than once per month in the past 6 months). Nearly all (84.7%) had received some type of addiction treatment in their lifetime; buprenorphine maintenance treatment was most common. A total of 34 participants (7.7%) reported experiencing an overdose in the past year, 132 (30.2%) overdosed > 1 year ago, and 278 (62.6%) reported no history of overdose. Of the 7 injection settings, the median number reported was 3 (mean: 3.2). Most used in private settings (79.3% used where they lived and 76.4% used at a friend's residence). The most commonly used public setting was outside (49.5% of participants). Approximately one-third (36.1%) used in an abandoned building and one-quarter used in a public bathroom (26.8%), shooting gallery (25.1%), or crack house (24.8%).

Bivariate analysis

Participants who overdosed (within the past year and > 1 year ago) had higher average stigma scores than those who never overdosed (p < 0.001, Table 1). This trend of higher stigma among those who overdosed persisted when the total stigma score was divided into its component enacted and internalized stigma scores (analysis of variance results for enacted: p < 0.001, internalized: p = 0.02). Participants who overdosed more commonly used drugs in public spaces (a shooting gallery, crack house, abandoned building, public bathroom, or outside) compared to participants who never overdosed. Use of a syringe exchange program, selling drugs, receiving addiction treatment (residential, methadone, or buprenorphine), injecting heroin or speedball, snorting heroin, and misuse of prescription opioids were positively associated with experiencing an overdose. A higher proportion of participants who never overdosed were African American relative to those who overdosed (p = 0.001).

Table 1

Bivariate associations of overdose experiences with participant social and demographic characteristics, drug use history, drug use settings, and stigma among people who use drugs in Baltimore, MD – 2009–2012 (n = 444).

	Timing of Most Recent Overdose			
	Past Year N (%)	> 1 Year Ago N (%)	Never N (%)	Chi-Squared p-value
Total	34 (100)	132 (100)	278 (100)	–
Number of Overdoses in Lifetime, Median (IQR)	3 (2-3.75)	2 (1-2)	0 (0-0)	< 0.001[d]
Male Gender	17 (50.0)	79 (59.8)	162 (58.3)	0.58
Aged < 45 Years	18 (52.9)	56 (42.4)	128 (46.0)	0.52
African American	25 (73.5)	104 (78.8)	250 (89.9)	0.001[c]
Education ≤11th Grade	14 (41.2)	69 (52.3)	148 (53.2)	0.41
Unemployed[a]	33 (97.1)	126 (95.5)	261 (93.9)	0.75[c]
Homelessness[a]	17 (50.0)	45 (34.1)	102 (36.7)	0.23
Incarcerated[a]	8 (23.5)	40 (30.3)	71 (25.5)	0.54
Any Addiction Treatment				
Never	2 (5.9)	12 (9.1)	54 (19.4)	0.039
> 1 Year Ago	7 (20.6)	23 (17.4)	46 (16.5)	
≤1 Year Ago	25 (73.5)	97 (73.5)	178 (64.0)	
Residential Addiction Treatment				
Never	12 (35.3)	50 (37.9)	145 (52.2)	0.034
> 1 Year Ago	13 (38.2)	57 (43.2)	86 (30.9)	
≤1 Year Ago	9 (26.5)	25 (18.9)	47 (16.9)	
Outpatient Addiction Treatment				
Never	22 (64.7)	94 (71.2)	200 (71.9)	0.90[c]
> 1 Year Ago	8 (23.5)	25 (18.9)	51 (18.3)	
≤1 Year Ago	4 (11.8)	13 (9.8)	27 (9.7)	
Methadone Treatment				
Never	21 (61.7)	65 (49.2)	203 (73.0)	< 0.001[c]
> 1 Year Ago	3 (8.8)	33 (25.0)	9.0 (25)	
≤1 Year Ago	10 (29.4)	34 (25.8)	50 (18.0)	
Buprenorphine Treatment				
Never	12 (35.2)	32 (24.2)	139 (50.0)	< 0.001
> 1 Year Ago	6 (17.6)	28 (21.2)	35 (12.6)	
≤1 Year Ago	16 (47.1)	72 (54.5)	104 (37.4)	
Prescription Opioid Misuse				
Never	15 (44.1)	77 (58.3)	193 (69.4)	0.0094[c]
> 1 Year Ago	2 (5.9)	8 (6.1)	18 (6.5)	
≤1 Year Ago	17 (50.0)	47 (35.6)	67 (24.1)	
Snorted Heroin				
Never	4 (11.8)	21 (15.9)	47 (16.9)	< 0.001
> 1 Year Ago	9 (26.5)	44 (33.3)	36 (12.9)	
≤1 Year Ago	21 (61.8)	67 (50.8)	195 (70.1)	
Injected Heroin and/or Speedball				
Never Injected Heroin and/or Speedball	4 (11.7)	15 (11.4)	174 (62.6)	< 0.001[c]
Injected Heroin and/or Speedball > 1 Year Ago	2 (5.9)	14 (10.6)	21 (7.6)	
Injected Heroin and/or Speedball ≤1 Year Ago	28 (82.4)	103 (78.0)	83 (29.9)	
Shared Syringes[e]	18 (64.3)	58 (56.9)	35 (44.3)	0.11
Shared Other Injection Equipment[e]	24 (85.7)	87 (85.3)	60 (75.9)	0.23
Exchanged Syringes through the BCNEP[a]	16 (47.1)	57 (43.2)	52 (18.7)	< 0.001
Sold drugs[b]	8 (23.5)	22 (16.7)	28 (10.1)	0.032[c]
Drug Use Settings[a]				
Shooting Gallery[a]	16 (47.1)	54 (40.9)	40 (14.4)	< 0.001
Crack House[a]	15 (44.1)	40 (30.3)	55 (19.8)	0.0017
Abandoned Building[a]	19 (55.9)	66 (50.0)	75 (27.0)	< 0.001
Public Bathroom[a]	15 (44.1)	43 (32.6)	61 (21.9)	0.0045
Outside[a]	18 (52.9)	77 (58.3)	126 (45.3)	0.045
Place where Participant Lives[a]	30 (88.2)	110 (83.3)	212 (76.3)	0.10
Friend's Place[a]	28 (82.4)	100 (75.8)	211 (75.9)	0.69
Total Number of Drug Use Settings, Median (IQR)	4 (3-5.75)	3.5 (2-5)	3 (2-4)	< 0.001[d]
Total Number of Public Drug Use Settings, Median (IQR)[f]	2 (1-4)	2 (0-4)	1 (0-2)	< 0.001[d]
Total Number of Private Drug Use Settings, Median (IQR)[f]	2 (1.25-2)	2 (1-2)	2 (1-2)	0.093[d]
Total Stigma Z-Score, Mean, (Standard Deviation)	0.48 (1.1)	0.24 (0.91)	−0.18 (0.99)	< 0.001[g]
Enacted Stigma Z-Score, Mean (Standard Deviation)	0.56 (1.1)	0.26 (0.92)	−0.19 (0.98)	< 0.001[g]
Internalized Stigma Z-Score, Mean (Standard Deviation)	0.25 (1.0)	0.16 (0.99)	−0.10 (0.99)	0.016[g]

Abbreviations: BCNEP: Baltimore City Needle Exchange Program; IQR: Interquartile Range.

[a] In the past 6 months.

[b] In the past 30 days.

[c] Fisher exact test used instead of chi-squared to accommodate small expected cell sizes.

[d] Kruskal-Wallis test for differences in rank by group.

[e] Among participants who injected heroin and/or speedball in the past six months (n = 28 who overdosed in the past year, n = 102 who overdosed > 1 year ago, and n = 79 who never overdosed).

[f] Public settings include: shooting gallery, crack house, abandoned building, public bathroom, or outside. Private settings include participant's home or a friend's place.

[g] Analysis of variance test for differences in means.

Table 2

Adjusted associations of overdose experiences with stigma, drug use settings, and drug use history among people who use drugs in Baltimore, MD – 2009–2012 (n = 444).

Covariate	Timing of Most Recent Overdose (Ref: Never Overdosed)			
	≤1 Year Ago		> 1 Year ago	
	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
Stigma[a]	2.0 (1.4–2.9)*	1.7 (1.1–2.7)*	1.5 (1.2–1.9)*	1.5 (1.1–2.0)*
Total Number of Drug Use Settings[b]	1.5 (1.2–1.8)*	1.3 (1.0–1.7)*	1.3 (1.2–1.5)*	1.3 (1.1–1.6)*
Injected Heroin and/or Speedball	3.9 (2.3–6.6)*	4.3 (2.2–8.3)*	3.6 (2.7–4.8)*	3.9 (2.7–5.7)*
Snorted Heroin	0.9 (0.6–1.5)	0.9 (0.5–1.6)	0.7 (0.6–1.0)*	0.8 (0.5–1.1)
Misused Prescription Opioids	1.8 (1.2–2.6)*	1.3 (0.9–2.1)	1.3 (1.1–1.7)*	1.1 (0.8–1.4)
Any Addiction Treatment	1.6 (0.9–2.7)	1.4 (0.7–2.5)	1.5 (1.1–2.0)*	1.3 (0.9–1.9)
Exchanged Syringes through the BCNEP[b]	3.7 (1.8–8.1)*	0.7 (0.3–1.9)	3.3 (2.1–5.2)*	0.6 (0.3–1.2)
Sold Drugs[c]	2.7 (1.1–6.6)*	1.8 (0.6–5.1)	1.8 (1.0–3.3)	1.3 (0.6–2.7)
Age < 45 Years	1.3 (0.6–2.7)	0.5 (0.2–1.2)	0.9 (0.6–1.3)	0.4 (0.2–0.8)*
Male Gender	0.7 (0.4–1.5)	0.5 (0.2–1.1)	1.1 (0.7–1.6)	0.7 (0.4–1.2)
African American	0.3 (0.1–0.7)*	1.1 (0.4–3.3)	0.4 (0.2–0.7)*	1.1 (0.5–2.4)
Education ≤11th Grade	0.6 (0.3–1.3)	0.5 (0.2–1.1)	1.0 (0.6–1.5)	0.8 (0.5–1.4)
Homelessness[b]	1.7 (0.8–3.5)	1.1 (0.4–2.7)	0.9 (0.6–1.4)	0.6 (0.4–1.1)
Incarcerated[b]	0.9 (0.4–2.1)	–	1.3 (0.8-2.0)	–
Unemployed[b]	2.2 (0.3–16.7)	–	1.4 (0.5-3.6)	–

Abbreviations: aOR: Adjusted Odds Ratio; BCNEP: Baltimore City Needle Exchange Program; OR: Bivariate Odds Ratio; Ref: referent category; 95% CI: 95% Confidence Interval.

[a] Z-Score.

[b] In the past 6 months.

[c] In the past 30 days.

* p < 0.05.

Multivariable analysis

In the multivariable multinomial model, drug-related stigma score was positively associated with overdose (Table 2). Each one-unit increase in stigma z-score was associated with 70% higher odds of experiencing an overdose in the past year (95% Confidence Interval [CI]: 1.1–2.7) and 50% higher odds of experiencing an overdose over a year ago (95% CI: 1.1–2.0) after adjustment for age, race, gender, education, homelessness, number of drug use settings, opioid use, receiving addiction treatment, syringe exchange use, and selling drugs. In subanalyses that separately examined the association of stigma subtypes, enacted stigma score was positively associated with overdosing in the past year (adjusted Odds Ratio [aOR]: 2.0, 95% CI: 1.3–3.2) and > 1 year ago (aOR: 1.6, 95% CI: 1.2–2.1, Supplemental Table 2). However, internalized stigma score was not associated with overdosing in the past year (aOR: 1.2, 95% CI: 0.8–1.8) and was marginally associated with overdosing > 1 year ago (aOR: 1.3, 95% CI: 1.0–1.7, p = 0.07).

The total number of drug use settings reported by a participant was also positively associated with experiencing an overdose both in the last year and over a year ago. For each additional drug use setting reported by a participant, the odds of overdosing was 30% higher regardless of the timing of the last overdose. In subanalyses that examined the type of space, each additional public setting was associated with a 40% higher odds of overdosing (regardless of the timing of the last overdose) whereas the number of private spaces was not associated with overdose (Supplemental Table 2). Injecting heroin or speedball was associated with approximately a 4-fold higher odds of experiencing an overdose. Snorting heroin, misusing prescription opioids, syringe exchange use, and selling drugs were not significantly associated with overdose in the adjusted multinomial regression model. A sensitivity analysis suggested that the associations of overdose with stigma and drug use settings were driven by occurrence rather than frequency of overdose (Supplemental Table 3).

Discussion

We found that experiencing discrimination from others (i.e., enacted stigma) related to using drugs and using drugs in public settings were associated with recent and lifetime overdose history. These findings highlight the need to identify the mechanisms by which enacted stigma increases overdose risk so that overdose prevention strategies in Baltimore City and beyond can address the excess risk of overdose among stigmatized individuals. In addition, our finding of an association of overdose with injection at multiple venues suggests that PWUD should be recruited from multiple types of public settings for overdose education and response training and naloxone distribution.

Our findings around enacted stigma agreed with a study by Couto E Cruz, Salom, Dietze et al. (2018), who found that experiencing persistent discrimination was associated with a 60% higher odds of experiencing an overdose among a sample of Australians who injected drugs. Surprisingly, internalized stigma was only marginally associated with overdose in our study, and the relationship was weaker in magnitude than that for enacted overdose. The differing associations of overdose with internalized and enacted stigma suggest that overlapping mechanisms by which both types of stigma increase overdose risk, such as through their positive associations with depression, do not fully explain the relationship of enacted stigma with overdose (Cama et al., 2016; Couto E Cruz, Salom, Dietze et al., 2018; Couto E Cruz, Salom, Maravilla et al., 2018; Kulesza et al., 2013; von Hippel et al., 2018). One plausible mechanism by which enacted stigma could increase overdose risk is by encouraging dangerous injection behaviors, such as rushing to use drugs, to avoid being observed by bystanders. While there is limited prior work to inform this hypothesis, studies on police presence, which has been cited as a reason for rushed injecting, may be relevant, as a motivation for avoiding arrest by police is to avoid being identified as a person using drugs by bystanders (Cooper, Moore, Gruskin, & Krieger, 2005; Ti et al., 2015). In addition, Wilson et al. found an association between perceived discrimination with being injected by someone else, another injection risk behavior that could lead to an overdose (Wilson et al., 2014). Hesitancy to attend overdose prevention trainings or carry naloxone, using alone, hiding drug use, and discrimination from addiction treatment or other healthcare providers could also contribute to the increased risk of overdose that is associated with enacted stigma. It is also possible that greater addiction severity may lead to more drug buying, selling, consumption, and other consequences of drug use (e.g., incarceration) that increase stigma and

overdose risk concurrently (Couto E Cruz, Salom, Maravilla et al., 2018; Kulesza et al., 2013).

Further research on the longitudinal and contextual relationships between enacted and internalized stigma and overdose may aid in developing overdose prevention interventions. Whereas interventions that engage PWUD directly may have a greater focus on internalized stigma, interventions that engage healthcare providers, family members, and that occur in community settings may focus on enacted stigma. Social marketing campaigns have successfully been used to reduce HIV stigma, and such approaches could also be utilized to address stigma towards PWUD (Blankenship, Bray, & Merson, 2000; Mahajan et al., 2008; Rimal & Creel, 2008). Online trainings may be effective to reduce negative and discriminatory attitudes among healthcare workers against PWUD (Brener, Cama, Hull, & Treloar, 2017).

The finding that a greater number of public drug use settings is associated with overdose suggests that expanding overdose prevention and naloxone training into public settings frequented by PWUD may help reach populations who do not access training through syringe exchange services. While just over a quarter of participants reported using the syringe exchange program in the past six months, half reported using outside, and many reported using in other locations. These results highlight the potential for diversification of settings for naloxone training and distribution as well as the potential to involve community members through a peer outreach approach to diffuse overdose prevention information in settings of drug consumption that may be difficult to reach by health professionals (e.g., shooting galleries and crack houses). Further, these results complement previous findings that supported expanding settings for overdose interventions based on the presence of overdose witnesses (Latkin, Edwards, Davey-Rothwell, Yang, & Tobin, 2018).

While harm reduction programs have trained people who use opioids to successfully administer naloxone, there remains a pressing need to train PWUD to educate their peers to diffuse overdose prevention and response training skills and encourage PWUD to carry naloxone (Sherman et al., 2009). Working with PWUD to identify contextual characteristics of drug use settings that influence overdose prevention and response may also be valuable to inform strategies for peer-driven intervention. For example, what are the range of norms and policies across different types of settings related to naloxone availability, expectations about peer monitoring, and overdose response procedures and what factors help to produce contexts that better facilitate safety? Whereas public bathrooms present challenges around identifying an overdose due to using alone (Fairbairn, Coffin, & Walley, 2017; Holloway, Hills, & May, 2018), shooting galleries have the opposite characteristic: an association with larger social networks and sharing injecting equipment (Tobin, Davey-Rothwell, & Latkin, 2010). The social relationships of PWUD in public settings, or lack thereof, may also guide expectations for responding to a witnessed overdose, calling for medical assistance, or monitoring overdose victims (Holloway et al., 2018). Future research should examine the mechanisms by which different drug use settings contribute to overdose so that the risks may be adequately addressed.

The association between syringe exchange utilization and experiencing an overdose was attenuated after adjusting for heroin and cocaine injection (i.e., speedball). This change is not surprising because the vast majority of individuals who attend syringe exchange programs inject drugs. Nonetheless, the fact that > 40% of participants who overdosed attended the syringe exchange provides strong support for continued outreach to people who inject drugs at syringe exchanges for overdose education and naloxone distribution. As overdose from heroin and synthetic opioids continues to present a major risk to people who inject drugs, the BCNEP's existing overdose prevention and naloxone program will be a critical resource in preventing overdose deaths.

This study has several limitations. The study's findings are limited in generalizability to individuals meeting the parent clinical trial's eligibility criteria (presence of HIV risk behaviors, aged 18–55, and willing

to attend study visits). Additionally, we relied on self-reported data for overdose history. Overdose was described to participants as "a life-threatening condition that occurs after someone has taken drugs by injection or by any other route." This leaves room for personal interpretation by the participant, and there is no way of determining whether overdose experiences were under- or over-reported. However, unlike medical records or hospital admissions, self-reported overdose data captures overdoses that are unreported (Darke, Mattick, & Degenhardt, 2003). Furthermore, it is unknown what percentage of reported overdoses were caused by drugs other than opioids and therefore would not respond to naloxone administration. However, 94% of study participants had a history of opioid use. Thus it is likely that most reported overdoses were caused by opioids or opioids in combination with other drugs. In addition, these data were cross-sectional and cannot establish the temporal sequence between stigma, drug use, and overdose. It is plausible that having an overdose, in and of itself, could increase stigma, and that this could in turn increase the risk of future overdose. Longitudinal studies to further characterize these relationships are warranted. We also did not have reports on where participants had injected more than 6 months ago. Participants in our study either never exchanged or exchanged syringes infrequently (less than once per month). We were therefore unable to examine the relationship of overdose and frequency of exchanging syringes or accessing other harm reduction services at the syringe exchange program. These data also do not capture the experiences of users who have succumbed to fatal overdose and therefore could not participate in the study. It is plausible that unique risk factors exist for fatal overdose and these should be addressed in future research.

It should also be noted that this study was conducted before the influx of synthetic opioids (i.e., fentanyl and fentanyl analogs) on the drug market and preceded recent local policies that increased the availability of naloxone. In October 2015, the Baltimore City Health Commissioner issued a standing order for naloxone (i.e., a blanket prescription covering anyone in the city who presents a certificate from a state-approved naloxone training program) (Baltimore City Health Department, 2015). Since then, more than 20,000 Baltimore residents have been trained through the Baltimore City Health Department, with > 800 reported overdose reversals (Baltimore City Health Department, 2017a). In June 2017, an additional standing order removed the training requirement, making naloxone accessible to all residents (Baltimore City Health Department, 2017b). The impact of standing orders on stigma and overdose prevalence and mortality has not yet been determined. It is unlikely that changes in rates of overdose or standing orders have dramatically changed the level of stigma experienced by PWUD.

Our results suggest the potential utility of supplementing existing overdose education and naloxone distribution policies in Baltimore with measures that reduce stigma. For example, peer educator programs that connect PWUD who are disengaged with harm reduction services to peers engaged with harm reduction services could help minimize the impact of stigma associated with drug use, which may facilitate carrying naloxone, attending overdose trainings, or accessing syringe services programs. Moreover, providing PWUD with prosocial options for engaging in harm reduction in the community, such as becoming peer educators, may help to reduce self-stigma. Further, additional training to destigmatize drug use is warranted for health professionals, social service providers, families of PWUD, and the general public.

Conflict of interest

None of the authors have financial conflicts of interests.

Role of funding sources

design, analyses, interpretation, or writing.

Acknowledgements

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugpo.2019.03.012.

References

Baltimore City Health Department. (2015, September 30). Baltimore City Health Department. Retrieved November 1, 2018, from https://health.baltimorecity.gov/news/press-releases/2015-09-30-health-commissioner-wen-announces-plan-make-lifesaving-medication.

Baltimore City Health Department. (2017a, February 3). Baltimore City Health Department. Retrieved November 1, 2018, from https://health.baltimorecity.gov/news/bmore-healthy-blog/2017-02-03-baltimore-city-health-department-celebrates-20000-residents.

Baltimore City Health Department. (2017b, June 1). Baltimore City Health Department. Retrieved November 1, 2018, from https://health.baltimorecity.gov/news/press-releases/2017-06-01-baltimore-city-health-commissioner-signs-new-standing-order-opioid.

Beletsky, L., Heller, D., Jenness, S. M., Neaigus, A., Gelpi-Acosta, C., & Hagan, H. (2014). Syringe access, syringe sharing, and police encounters among people who inject drugs in New York City: A community-level perspective. *The International Journal on Drug Policy, 25*(1), 105–111. https://doi.org/10.1016/j.drugpo.2013.06.005.

Blankenship, K. M., Bray, S. J., & Merson, M. H. (2000). Structural interventions in public health. *AIDS (London, England), 14*(Suppl. 1), S11–21.

Bohnert, A. S. B., Tracy, M., & Galea, S. (2009). Circumstances and witness characteristics associated with overdose fatality. *Annals of Emergency Medicine, 54*(4), 618–624. https://doi.org/10.1016/j.annemergmed.2009.05.004.

Brener, L., Cama, E., Hull, P., & Treloar, C. (2017). Evaluation of an online injecting drug use stigma intervention targeted at health providers in New South Wales, Australia. *Health Psychology Open, 4*(1), https://doi.org/10.1177/2055102917707180.

Cama, E., Brener, L., Wilson, H., & von Hippel, C. (2016). Internalized stigma among people who inject drugs. *Substance Use & Misuse, 51*(12), 1664–1668. https://doi.org/10.1080/10826084.2016.1188951.

Cooper, H., Moore, L., Gruskin, S., & Krieger, N. (2005). The impact of a police drug crackdown on drug injectors' ability to practice harm reduction: A qualitative study. *Social Science & Medicine (1982), 61*(3), 673–684. https://doi.org/10.1016/j.socscimed.2004.12.030.

Couto E Cruz, C., Salom, C. L., Dietze, P., Lenton, S., Burns, L., & Alati, R. (2018). Frequent experience of discrimination among people who inject drugs: Links with health and wellbeing. *Drug and Alcohol Dependence, 190*, 188–194. https://doi.org/10.1016/j.drugalcdep.2018.06.009.

Couto E Cruz, C., Salom, C., Maravilla, J., & Alati, R. (2018). Mental and physical health correlates of discrimination against people who inject drugs: A systematic review. *Journal of Studies on Alcohol and Drugs, 79*(3), 350–360.

Darke, S., Mattick, R. P., & Degenhardt, L. (2003). The ratio of non-fatal to fatal heroin overdose. *Addiction (Abingdon, England), 98*(8), 1169–1171.

Fairbairn, N., Coffin, P. O., & Walley, A. Y. (2017). Naloxone for heroin, prescription opioid, and illicitly made fentanyl overdoses: Challenges and innovations responding to a dynamic epidemic. *International Journal of Drug Policy, 46*, 172–179. https://doi.org/10.1016/j.drugpo.2017.06.005.

Gindi, R. M., Rucker, M. G., Serio-Chapman, C. E., & Sherman, S. G. (2009). Utilization patterns and correlates of retention among clients of the needle exchange program in Baltimore, Maryland. *Drug and Alcohol Dependence, 103*(3), 93–98. https://doi.org/10.1016/j.drugalcdep.2008.12.018.

Green, T. C., Heimer, R., & Grau, L. E. (2008). Distinguishing signs of opioid overdose and indication for naloxone: An evaluation of six overdose training and naloxone distribution programs in the United States. *Addiction (Abingdon, England), 103*(6), 979–989. https://doi.org/10.1111/j.1360-0443.2008.02182.x.

Hawk, K. F., Vaca, F. E., & D'Onofrio, G. (2015). Reducing fatal opioid overdose: Prevention, treatment and harm reduction strategies. *The Yale Journal of Biology and Medicine, 88*(3), 235–245.

Holloway, K., Hills, R., & May, T. (2018). Fatal and non-fatal overdose among opiate users in South Wales: A qualitative study of peer responses. *The International Journal on Drug Policy, 56*, 56–63. https://doi.org/10.1016/j.drugpo.2018.03.007.

Kulesza, M., Larimer, M. E., & Rao, D. (2013). Substance use related stigma: What we know and the way forward. *Journal of Addictive Behaviors, Therapy & Rehabilitation, 2*(2), https://doi.org/10.4172/2324-9005.1000106.

Lagisetty, P., Bohnert, A., & Fendrick, A. (2018). *Meeting the opioid challenge: Getting*

naloxone to those who need it most. May 11, Retrieved May 22, 2018, from https://www.healthaffairs.org/do/10.1377/hblog20180510.164285/full/.

Latkin, C., Srikrishnan, A. K., Yang, C., Johnson, S., Solomon, S. S., Kumar, S., ... Solomon, S. (2010). The relationship between drug use stigma and HIV injection risk behaviors among injection drug users in Chennai, India. *Drug and Alcohol Dependence, 110*(3), 221–227. https://doi.org/10.1016/j.drugalcdep.2010.03.004.

Latkin, C. A., Edwards, C., Davey-Rothwell, M. A., Yang, C., & Tobin, K. E. (2018). The relationship between drug use settings, roles in the drug economy, and witnessing a drug overdose in Baltimore, Maryland. *Substance Abuse,* 1–6. https://doi.org/10.1080/08897077.2018.1439801.

Mahajan, A. P., Sayles, J. N., Patel, V. A., Remien, R. H., Ortiz, D., Szekeres, G., & Coates, T. J. (2008). Stigma in the HIV/AIDS epidemic: A review of the literature and recommendations for the way forward. *AIDS (London, England), 22*(Suppl. 2), S67–S79. https://doi.org/10.1097/01.aids.0000327438.13291.62.

MDHMH (2017). *Drug- and alcohol-related intoxication deaths in Maryland, 2016*Retrieved from. Maryland Department of Health and Mental Hygiene1–54. https://bha.health.maryland.gov/Documents/Annual_Drug_Intox_Report_2016_revised.pdf.

MDHMH (2018). *Unintentional drug- and alcohol-related intoxication deaths in Maryland Annual Report, 2017*Retrieved from. Maryland Department of Health and Mental Hygiene1–58. https://bha.health.maryland.gov/OVERDOSE_PREVENTION/Documents/Drug_Intox_Report_2017.pdf.

National Institute on Drug Abuse (2018). *Overdose death rates.* August 9, Retrieved October 24, 2018, from https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates.

Rhodes, T., Kimber, J., Small, W., Fitzgerald, J., Kerr, T., Hickman, M., & Holloway, G. (2006). Public injecting and the need for "safer environment interventions" in the reduction of drug-related harm. *Addiction (Abingdon, England), 101*(10), 1384–1393. https://doi.org/10.1111/j.1360-0443.2006.01556.x.

Rimal, R. N., & Creel, A. H. (2008). Applying social marketing principles to understand the effects of the radio diaries program in reducing HIV/AIDS stigma in Malawi. *Health Marketing Quarterly, 25*(1–2), 119–146. https://doi.org/10.1080/07359680802126186.

Rivera, A. V., DeCuir, J., Crawford, N. D., Amesty, S., & Lewis, C. F. (2014). Internalized stigma and sterile syringe use among people who inject drugs in New York City, 2010–2012. *Drug and Alcohol Dependence, 144*, 259–264. https://doi.org/10.1016/j.drugalcdep.2014.09.778.

Seal, K. H., Thawley, R., Gee, L., Bamberger, J., Kral, A. H., Ciccarone, D., ... Edlin, B. R. (2005). Naloxone distribution and cardiopulmonary resuscitation training for injection drug users to prevent heroin overdose death: A pilot intervention study. *Journal of Urban Health: Bulletin of the New York Academy of Medicine, 82*(2), 303–311. https://doi.org/10.1093/jurban/jti053.

Seth, P., Scholl, L., Rudd, R. A., & Bacon, S. (2018). Overdose deaths involving opioids, cocaine, and psychostimulants — United States, 2015–2016. *MMWR Morbidity and Mortality Weekly Report, 67.* https://doi.org/10.15585/mmwr.mm6712a1.

Sherman, S. G., Gann, D. S., Tobin, K. E., Latkin, C. A., Welsh, C., & Bielenson, P. (2009). "The life they save may be mine": Diffusion of overdose prevention information from a city sponsored programme. *The International Journal on Drug Policy, 20*(2), 137–142. https://doi.org/10.1016/j.drugpo.2008.02.004.

Ti, L., Hayashi, K., Kaplan, K., Suwannawong, P., Wood, E., & Kerr, T. (2015). Contextual factors associated with rushed injecting among people who inject drugs in Thailand. *Prevention Science: The Official Journal of the Society for Prevention Research, 16*(2), 313–320. https://doi.org/10.1007/s11121-014-0477-z.

Tobin, K. E., & Latkin, C. A. (2003). The relationship between depressive symptoms and nonfatal overdose among a sample of drug users in Baltimore, Maryland. *Journal of Urban Health: Bulletin of the New York Academy of Medicine, 80*(2), 220–229. https://doi.org/10.1093/jurban/jtg025.

Tobin, K. E., Sherman, S. G., Beilenson, P., Welsh, C., & Latkin, C. A. (2009). Evaluation of the Staying Alive programme: Training injection drug users to properly administer naloxone and save lives. *The International Journal on Drug Policy, 20*(2), 131–136. https://doi.org/10.1016/j.drugpo.2008.03.002.

Tobin, K. E., Davey-Rothwell, M., & Latkin, C. A. (2010). Social-level correlates of shooting gallery attendance: A focus on networks and norms. *AIDS and Behavior, 14*(5), 1142–1148. https://doi.org/10.1007/s10461-010-9670-7.

Tobin, K., Davey-Rothwell, M. A., Nonyane, B. A. S., Knowlton, A., Wissow, L., & Latkin, C. A. (2017). RCT of an integrated CBT-HIV intervention on depressive symptoms and HIV risk. *PLoS One, 12*(12), e0187180. https://doi.org/10.1371/journal.pone.0187180.

Tracy, M., Piper, T. M., Ompad, D., Bucciarelli, A., Coffin, P. O., Vlahov, D., & Galea, S. (2005). Circumstances of witnessed drug overdose in New York City: Implications for intervention. *Drug and Alcohol Dependence, 79*(2), 181–190. https://doi.org/10.1016/j.drugalcdep.2005.01.010.

Treloar, C., & Cao, W. (2005). Barriers to use of Needle and Syringe Programmes in a high drug use area of Sydney, New South Wales. *International Journal of Drug Policy, 16*(5), 308–315. https://doi.org/10.1016/j.drugpo.2005.06.005.

von Hippel, C., Brener, L., & Horwitz, R. (2018). Implicit and explicit internalized stigma: Relationship with risky behaviors, psychosocial functioning and healthcare access among people who inject drugs. *Addictive Behaviors, 76*, 305–311. https://doi.org/10.1016/j.addbeh.2017.08.036.

Wilson, H., Brener, L., Mao, L., & Treloar, C. (2014). Perceived discrimination and injecting risk among people who inject drugs attending Needle and Syringe Programmes in Sydney, Australia. *Drug and Alcohol Dependence, 144*, 274–278. https://doi.org/10.1016/j.drugalcdep.2014.08.018.