Risk Factors for Nonfatal Overdose at Seattle-Area Syringe Exchanges

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ABSTRACT *Opioid-involved overdose deaths are on the rise, both nationwide and in the state of Washington. In a survey of 443 participants at syringe exchanges in Seattle, Washington, 16% had overdosed in the last year. Several factors were significantly associated in bivariate analysis: lack of permanent housing; incarceration of five or more days in the past year; gender of sex partners; sharing of syringes and other injection paraphernalia; use of speedballs (cocaine and heroin together), goofballs (methamphetamine and heroin together), buprenorphine; injection use of crack cocaine and sedatives; and use of opioids with sedatives. Adjusting for other variables in multivariate logistic regression analyses, only recent incarceration and sharing of injection materials were still significantly associated with overdose. Correctional facilities, syringe exchange programs, and other agencies serving opioid injectors should include overdose prevention components in release planning and services.*

KEYWORDS *Overdose, Injection drug use, Heroin, Prescription opioids, Opiates, Needle exchange, Syringe exchange*

INTRODUCTION

Deaths caused by opioid overdose are preventable, but are increasing in the United States and at an even faster rate in the state of Washington.[1–3] In 2005, the state of Washington had the 13th highest rate of unintentional and "undetermined intent" drug overdose deaths in the country.[4] As the most populous county in Washington, King County is home to Seattle and more overdoses than any other county in the state.[5] Overdoses involving opioids (heroin and/or pharmaceutical) increased from 125 to 195 between 1997 and 2008 in King County, an increase in the rate per 100,000 from 7.4 to 10.4.[5] The rate of ED visits for non-medical uses of pharmaceutical opioids was higher in the Seattle area than any other metropolitan area included in the US Drug Abuse Warning Network in 2007 and Seattle ranked fourth nationally for heroin.[6]

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Existing literature on nonfatal overdose among injection drug users (IDU), from a variety of drugs, identifies risk factors related to drug use that include heroin injection, cocaine injection, use of heroin mixed with methamphetamine ("goofballs") or heroin mixed with cocaine ("speedballs"), non-injection use of methamphetamine, and use of benzodiazepines.[7–9] Polydrug use, binge drug use, alcohol use, and withdrawal symptoms have also been found to be associated with nonfatal overdose.[8,10–12] Longer heroin-using career and greater heroin dependence have also been linked to nonfatal overdose.[12]

Other risk factors include lifetime or recent incarceration experience, homelessness, syringe sharing, and homosexual or bisexual behavior.[8,9,11,13] Prior history of overdose has also been identified as a risk factor.[10,14,15] There are conflicting findings regarding the impact of age, with both younger and older age predicting nonfatal overdose in multivariate analyses.[8,10,11] At least one study identified female gender as a risk factor, though gender has not generally been significant in most multivariate analysis.[7]

Interventions to prevent overdose vary widely by country, state, and city. In Europe, Australia, and Canada, there are safe injection facilities or drug consumption rooms where drug use occurs under supervision. In the United States, no such facilities exist and naloxone distribution is increasingly common, though no formal programs currently exist in King County or the state of Washington. Naloxone is an opioid antagonist used as an antidote to reverse opioid overdose, and is commonly administered by emergency medical personnel. Serious adverse effects of naloxone are rare, and are likely related to the overdose rather than the medication, when administered in either clinical or street settings.[16–23] In March 2010, the Governor of the State of Washington signed overdose intervention legislation that permits the prescription and possession of naloxone, and administration to others suffering from opioid overdoses.[24] This legislation became effective in June 2010 and also includes another relatively uncommon overdose prevention measure in the US—limited immunity from prosecution for drug possession charges for individuals who overdose or seek medical assistance in drug overdoses.

METHODS

Study Design and Setting
Over two consecutive weeks at the end of April and beginning of May 2009, clients at five syringe exchange sites in King County were asked to complete a brief survey, after exchanging syringes. Sites included two indoor and two outdoor exchanges in Seattle, as well as a mobile exchange in suburban King County. All participating sites were run by the local health department, Public Health—Seattle and King County. Participants gave verbal consent before the survey began. No names or other identifying information were recorded. The survey was conducted to satisfy reporting requirements by syringe exchange funding sources and for program planning purposes. Data analysis was conducted by University of Washington researchers. The University's institutional review board determined that these data were exempt from review due to the use of anonymous, secondary data.

Study Protocol
All syringe exchange clients were asked to complete the survey every time they exchanged syringes during the 2-week period. All clients were asked if they had already completed the survey. Repeat clients answered only questions on basic demographic information (age, gender, and race) and whether they were exchanging

for others. Occasionally, no interviewer was available to approach a client because all staff were conducting surveys or serving clients. When possible, front-line syringe exchange staff recorded how many clients had not been approached and their demographic characteristics. Clients were offered a small piece of candy for completing the survey. Trained staff read survey questions to clients and recorded their responses on paper. Data were later entered in an electronic database, and data quality was assessed after data entry and again prior to analysis.

Measures

The survey included questions on basic demographic characteristics (age, gender, race, housing status), incarceration in the past year, gender of sex partners in the past year (opposite/same/both), and sharing of syringes or other injection paraphernalia in the last 3 months.

For drug use questions, participants were asked whether they used a particular drug since the beginning of the year and if so, whether they injected it. Since the surveys were conducted in April and May of 2009, these questions referred to a 4-month period from January 2009 until the day the survey was completed. Interviewers asked specifically about these drugs, in the following order: heroin; crack cocaine; powder cocaine; speedballs (heroin and cocaine together); methamphetamine; goofballs (heroin and methamphetamine together); methadone; buprenorphine; downers like Valium, Xanax, Klonopin, Soma; pain pills like OyxContin or Vicodin; and any other drugs the participant listed.

Participants who reported any opioid use (heroin, speedballs, goofballs, methadone, buprenorphine, or prescription-type opioids) were also asked how often they used alcohol or sedatives "within a couple hours" before or after using opioids.

Participants were then asked whether they had experienced an overdose in the past year, involving heroin or prescription-type opioids. Interviewers read this definition of overdose: "when a person's skin, lips or fingers turn blue; they stop breathing or breathe really slow; or they nod off and can't be woken up."

Data Analysis

Analysis was restricted to 447 clients who reported opioid use since the beginning of the year (between January 2009 and the date the survey was administered in April or May of 2009) and had complete data on personal history of overdose. We restricted analysis of incarceration to stays of five or more days, after which an opioid user may have reduced tolerance and greater susceptibility to overdose. Opioid use included heroin, speedballs (heroin and cocaine mixture), goofballs (heroin and methamphetamine mixture), methadone, buprenorphine, or prescription-type opioids. Participants who endorsed pain pill use or other opioids in non-pill form (e.g., fentanyl patches) were combined in a prescription-type opioid category. This category did not include methadone or buprenorphine, which were analyzed separately due to their use in both pain and addiction treatment.

We compared patient characteristics by overdose history with the chi-square statistic for categorical variables and the two sample t test for age. All participants who did not report white race were categorized into a non-white race category, due to small numbers in some groups. Drug use data were analyzed according to whether a substance was injected, used through non-injection routes (e.g., smoked, snorted, swallowed), or not used at all. Almost no clients reported non-injection use of heroin, speedballs, and goofballs, while very few clients reported injection use of

buprenorphine. Consequently, analysis of these four drug types compared only users to non-users.

Variables with $p<0.2$ were then included in an unconditional multivariate logistic regression model. Even though gender did not meet the $p<0.2$ threshold, it was included because previous studies found a significant relationship between gender and overdose.[7] Due to small numbers ($n=3$), transgender participants were excluded from the logistic regression models. In order to examine the impact of different types of variables, we used three multivariate models. Each successive model added additional variables, with the models as follows: (1) age and gender; (2) age, gender, and other factors associated with overdose in previous studies; and (3) all characteristics that were significant in bivariate logistic regression analysis, as well as gender. In the multivariate models, we collapsed the categorical age variable in Table 1 from four categories to two: participants under 26 and those who were 26 and over. We report odds ratios (ORs) and 95% confidence intervals (CI). Analysis was conducted with SPSS version 12.0 (SPSS Inc, Chicago, IL).

RESULTS

Of 1,267 syringe exchange clients who were approached, 1,030 (81.3%) completed the survey. Overall, 477 of the completed surveys (46.3%) were from unduplicated clients. Of 447 clients who endorsed any opioid use, four were excluded from the study sample because of incomplete data on recent overdose, resulting in a final analytic data set of 443 respondents. Multivariate analysis was restricted to 428 participants who had complete data on all of the variables included in the full model.

Most participants were male (70%), white (73%), and the median age was 38 years old. Most participants reported that heroin was their primary drug (86%). Only 13 of 443 participants (3%) reported no heroin use. Seven of those participants (2% of overall sample) reported use of prescription-type opioids, 9 reported use of methadone (2%), and 3 reported both prescription-type opioids and methadone, but not heroin.

Among 72 participants (16%) who reported having overdosed in the past year, there were 133 total overdose events (mean: 1.8 per participant reporting a recent overdose). In bivariate analysis, lack of permanent housing, incarceration of five or more days in past year, gender of sex partners, and sharing syringes or other injection paraphernalia (cottons, cookers, rinse water) were significantly associated with reporting an overdose in the past year (Table 1). The mean age of participants who had overdosed was 35 years, compared to 38 years for participants who had not overdosed ($p=0.020$). Sixty-eight percent of our sample ($n=299$) reported injecting on a daily basis, and daily injection was not associated with overdose.

Crack cocaine injection, prescription-type opioid injection, and use of speed-balls, goofballs, or buprenorphine were also significantly associated with recent overdose, as was opioid use with sedatives like Valium, Xanax, Klonopin, or Soma (Table 2).

In multivariate logistic regression, age under 26 was significantly associated with recent overdose in Model 1 (adjusted OR, AOR=1.94, 95% CI=1.07, 3.55), as seen in Table 3. Incarceration of five or more days in the past year was significant in Model 2 (AOR=1.90, 95% CI=1.08, 3.36).

In the full model (Model 3), only past year incarceration of five or more days (AOR=1.88, 95% CI=1.04, 3.40) and sharing syringes and/or other injection

TABLE 1   Comparison of participants based on recent overdose experience—demographic and social factors

Characteristic	No overdose (%) $n=371$	Overdose (%) $n=72$	Total $N=443$	p value
Gender[a]				0.386[a]
Male	262 (71)	48 (67)	310 (70)	
Female	107 (29)	23 (32)	130 (29)	
Transgender	2 (1)	1 (1)	3 (1)	
Race				0.242[a]
White	271 (73)	51 (71)	322 (73)	
African-American	34 (9)	3 (4)	37 (8)	
Native American/Alaska Native	16 (4)	8 (11)	24 (5)	
Native Hawaiian/Pacific Islander	4 (1)	0 (0)	4 (1)	
Asian/South Asian	4 (1)	0 (0)	4 (1)	
Latino/Hispanic	21 (6)	5 (7)	26 (6)	
Multi-racial	21 (6)	5 (7)	26 (6)	
Age				0.052
Under 26	58 (16)	21 (29)	79 (18)	
26–35	109 (29)	17 (24)	126 (28)	
36–45	100 (27)	18 (25)	118 (27)	
Over 45	104 (28)	16 (22)	120 (27)	
Age				0.020[b]
Mean (SD)	38 (12)	35 (12)	38 (12)	
No permanent housing	201 (54)	50 (69)	251 (57)	0.017
Incarceration of 5+days in last year	102 (28)	30 (42)	132 (30)	0.016
Gender of sex partners				0.013[a]
No sex	75 (20)	6 (8)	81 (18)	
Opposite sex only	253 (68)	51 (71)	304 (68)	
Same sex only	21 (6)	3 (4)	24 (5)	
Both sexes	18 (5)	9 (13)	27 (6)	
Missing[c]	4 (1)	3 (4)	7 (2)	
Daily injection	248 (67)	51 (71)	299 (67)	0.528
Missing[c]	1 (0)	0 (0)	1 (0)	
Shared syringes or other injection paraphernalia	149 (40)	52 (72)	201 (45)	<0.0001
Missing[c]	4 (1)	0 (0)	4 (1)	

[a]Fisher's exact test used, cell size expected <5
[b]Two-sample *t* test used
[c]Missing values were not included in *p* value calculations
SD standard deviation; percentages may add up to more or less than 100, due to rounding

paraphernalia (AOR=2.65, 95% CI=1.43, 4.94) were significantly associated with recent overdose. While 98 participants (22% of 439 with data on this item) reported sharing syringes, 189 (43% of 435 with data) reported sharing other injection materials. In the full model, injectors of prescription-type opioids were almost twice as likely to overdose than those who did not use prescription-type opioids, though this association was also not significant (AOR=1.84, 95% CI=0.70, 4.80). Young age was no longer significant in the full model (AOR=1.25, 95% CI=0.64, 2.45). There was no significant interaction effect between young age and sharing-related risk (*p*=0.402).

TABLE 2 Comparison of participants based on recent overdose experience—drug use

Characteristic	No overdose (%) $n=371$	Overdose (%) $n=72$	Total $N=443$	p value
Heroin	359 (97)	71 (99)	430 (97)	0.703[a]
Speedballs	151 (41)	41 (57)	192 (43)	0.011
Goofballs	34 (9)	15 (21)	49 (11)	0.004
Buprenorphine	96 (26)	28 (39)	124 (28)	0.024
Crack cocaine				0.011
No use	177 (48)	30 (42)	207 (47)	
Non-injection use	123 (33)	17 (24)	140 (32)	
Injection use	71 (19)	25 (35)	96 (22)	
Powder cocaine				0.400
No use	212 (57)	37 (51)	249 (56)	
Non-injection use	29 (8)	4 (6)	33 (7)	
Injection use	130 (35)	31 (43)	161 (36)	
Methamphetamine				0.264[a]
No use	291 (78)	51 (71)	342 (77)	
Non-injection use	17 (5)	3 (4)	20 (5)	
Injection use	63 (17)	18 (25)	81 (18)	
Methadone				0.397[a]
No use	186 (50)	30 (42)	216 (49)	
Non-injection use	170 (46)	39 (54)	209 (47)	
Injection use	15 (4)	3 (4)	18 (4)	
Downers/sedatives				0.031[a]
No use	204 (55)	34 (47)	238 (54)	
Non-injection use	161 (43)	33 (46)	194 (44)	
Injection use	6 (2)	5 (7)	11 (3)	
Prescription-type opioids				0.060
No use	231 (62)	35 (49)	266 (60)	
Non-injection use	115 (31)	28 (39)	143 (32)	
Injection use	25 (7)	9 (13)	34 (8)	
Opioids with alcohol	121 (33)	30 (42)	151 (34)	0.156
Opioids with sedatives	100 (27)	28 (39)	128 (29)	0.045

[a]Fisher's exact test used, cell size expected <5
Percentages may add up to more or less than 100, due to rounding

DISCUSSION

We demonstrated an independent association between nonfatal overdose and recent incarceration of 5 or more days, consistent with several other studies.[8,9,11,25] Because of this finding, we analyzed post-hoc whether an incarceration of any length of time in the past year was associated with nonfatal overdose. In bivariate analysis, any incarceration was significant ($p=0.033$), but was not significant in the multivariate models (Model 2 AOR=1.63, CI=0.93, 2.86; Model 3 AOR=1.49, CI=0.83, 2.67). While any period of abstinence from drug use may elevate the risk of overdose, there was a stronger association when duration of incarceration was 5 days or longer.

The independent association we found between recent nonfatal overdose and sharing of syringes or other paraphernalia is less commonly reported.[13] Of those who had overdosed in the past year, 72% reported sharing injection materials,

TABLE 3 Risk factors for nonfatal overdose in past year—multivariate analysis ($n = 428$)

Characteristic	Model 1			Model 2			Model 3		
	AOR	95% CI	p value	AOR	95% CI	p value	AOR	95% CI	p value
Female gender	1.14	0.66–1.99	0.64	1.31	0.73–2.35	0.37	1.08	0.59–1.99	0.80
Age under 26	1.94	1.07–3.55	0.03	1.74	0.92–3.29	0.09	1.25	0.64–2.45	0.51
Opioids with alcohol				1.28	0.73–2.25	0.39	1.23	0.69–2.22	0.49
Opioids with sedatives				1.21	0.67–2.18	0.53	1.08	0.59–1.98	0.81
Speedballs				1.16	0.66–2.06	0.61	1.02	0.56–1.86	0.95
Goofballs				2.08	1.00–4.33	0.05	1.63	0.75–3.53	0.22
Incarceration of 5+days				1.90	1.08–3.36	0.03	1.88	1.04–3.40	0.04
No permanent housing				1.63	0.91–2.93	0.10	1.51	0.82–2.79	0.19
Buprenorphine							1.54	0.84–2.80	0.16
Prescription-type opioids									
No use							–	–	–
Non-injection							1.34	0.74–2.43	0.33
Injection							1.84	0.70–4.80	0.21
Gender of sex partners									
No partner							–	–	–
Opposite sex only							2.17	0.85–5.53	0.10
Same sex only							2.60	0.52–12.85	0.24
Both sexes							3.18	0.91–11.18	0.07
Shared syringes or other injection paraphernalia							2.65	1.43–4.94	<0.01

AOR adjusted odds ratio; *CI* confidence interval

compared to 40% of those who had not. Syringe sharing has been associated with binge use or more frequent use in other studies, data that we did not collect but that could explain the association with overdose.[8,26–28] Other studies have shown associations of syringe sharing with unstable housing[29,30] and public drug use.[31] Syringe sharing may be a marker for those who have more risky behaviors overall, rather than being causally related to overdose.

The association between young age and overdose in multivariate Model 1 has been demonstrated in other studies.[10,11,14,32] Multiple studies have shown that young IDU are more likely to share syringes.[33–35] Over 63% of participants under 26 shared syringes or paraphernalia, compared to 42% of those 26 and over ($p < 0.0001$). However, in adjusted analysis, statistical tests indicated that the interaction between young age and sharing of syringes or other injection paraphernalia was not associated with drug overdose.

Many previous studies have limited participants to heroin users. We expanded our sample to include any opioid users, to reflect a recent upward trend of overdose among users of prescription-type opioids.[2,3,36,37] Though prescription-type opioid use was not independently associated with nonfatal overdose in our sample, it would be worthwhile to explore this association in future studies.

There were several limitations in our study. Because we used a convenience sample, there may be sampling bias and our results may not be representative of all syringe exchange clients or opioid injectors in King County. About 4% of participants in our final dataset had missing values for at least one variable and were excluded from our multivariate model. These exclusions may have introduced some bias in our final results.

We asked respondents about their crack and powder cocaine use before we asked them about their speedball use. As a result, we could not easily differentiate between those who used crack or powder cocaine independently versus in combination with heroin. This misclassification may have also occurred with methamphetamine and goofball use. As a result, we were limited in our ability to assess polydrug use.

Participants may have underreported risk behaviors, drug use, or overdose due to social desirability or recall bias, though previous studies have found self-report to be relatively accurate among drug users.[38–41] In addition, social desirability bias may have been limited because this survey was anonymous and conducted in syringe exchanges, which are by definition associated with drug use.

The survey did not include questions on several risk factors documented in other studies, including recent withdrawal symptoms, quantity of alcohol and drugs consumed, length of drug using career, and recent detoxification. We also did not ask participants for specific details regarding overdose events, such as substances used immediately prior to the event or whether overdose occurred upon release from jail, prison, or detoxification. As a result, we could not establish a temporal sequence or link specific substances to overdose events. We also did not ask about overdose history beyond the past year, so it was difficult to demonstrate whether previous overdose experience was associated with a higher risk for subsequent overdose events. Participants who had overdosed in the past year reported an average of 1.8 overdose events in that time period, suggesting that clients with a history of overdose may be at greater risk for subsequent overdose. Future analysis should include more information on overdose history beyond the past year.

CONCLUSIONS

This survey presents results from the first survey on nonfatal overdose risk among opioid injectors in Seattle, an area with relatively high overdose rates and ED visits related to both heroin and prescription opioids. Nonfatal overdose was highly associated with sharing syringes or other injection paraphernalia and a recent incarceration of 5 or more days. Though a less significant factor in our analysis, young age presents elevated risk and also warrants additional focus in overdose prevention. Syringe exchange programs and other agencies that serve opioid users should address these risks through education and other interventions aimed at reducing overdose. Correctional facilities should also emphasize overdose prevention in release-planning efforts.

ACKNOWLEDGMENTS

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