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Prescription opioids prior to injection drug use: comparisons and public health implications

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Abstract

Background—The intertwining prescription opioid and heroin epidemic is a major public health problem in the United States, with increasing morbidity and mortality among persons who use these substances. We examined differences between persons who reported being hooked on prescription opioids prior to injecting for the first time and those who did not by demographics, injection and non-injection characteristics, and overdose.

Methods—Between June and December 2015, persons who inject drugs were recruited using respondent-driven sampling as part of the National HIV Behavioral Surveillance system in Denver, Colorado.

Results—Of 599 participants (median age, 40: IQR, 19–69; 71% male; 58% white, non-Hispanic), 192 (32%) reported being hooked on prescription opioids before they injected for the very first time. Compared to participants who were not hooked before they injected, participants who reported being hooked were significantly more likely to be younger, more recent injectors, report a slightly older age at first injection, and report heroin as the first drug injected as well as the drug most frequently injected. Those who reported being hooked were also more likely to be more frequent users of benzodiazepines, non-injection prescription opioids, and non-injection heroin as well as report injecting on a daily or more than daily basis. Being hooked on prescription opioids prior to injection drug use was associated with a 1.55 (95% CI: 1.14, 2.10) fold increase in the risk of at least one overdose in the past 12 months.

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Author Contributions:

AA undertook the literature review, data analysis, and writing of this brief communication. AA also oversaw all data collection activities. SK and PR provided critical review of earlier drafts. All authors contributed to the writing of this brief communication and have approved of the final communication.

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Conclusions—Being hooked on prescription opioids prior to injection might result in a higher risk profile for persons who inject drugs.

1. INTRODUCTION

In the United States, heroin use has increased significantly during the past decade.[1] The increase in heroin use is mirrored by an increase in heroin-related overdose deaths, with a dramatic increase in 2014. The Centers for Disease Control and Prevention concludes that the 2014 overdose data "demonstrate that the United States' opioid overdose epidemic includes two distinct but interrelated trends: a 15-year increase in overdose deaths involving prescription pain relievers and a recent surge in illicit opioid overdose deaths, driven largely by heroin."[2] A recent review outlines the complex and reciprocal nature of the intertwining prescription opioid and heroin epidemics.[3] The review concludes that "fundamentally, prescription opioids and heroin are each elements of a larger epidemic of opioid-related disorders and death."

While overdose deaths related to the interrelated prescription opioid and heroin epidemics are well documented in the National Vital Statistics System,[2] less is known about nonfatal overdose events related to these intertwining epidemics. Existing studies of nonfatal overdose have focused primarily on heroin injectors with a handful of studies reporting on nonmedical use of prescription opioids. In a recent systematic review of the literature related to unintentional drug overdose worldwide published in 2015, only 5 of the 44 studies reporting on the experience of nonfatal overdoses examined prescription opioids in addition to heroin use.[4–9] An additional study published after the systematic review showed that the odds of nonfatal overdose for those who injected both heroin and prescription opioids was 2.46 (95% Confidence Interval: 1.81–3.30) compared to those who injected heroin alone.[10]

Given the complex nature of the intertwining prescription opioid and heroin epidemics, we sought to describe differences between those who initiated injection drug use after becoming hooked on prescription opioids and those who were not. We also examine the association between the two injection trajectories and the experience of nonfatal overdose in a sample of persons who inject drugs (PWID).

2. METHODS

2.1. National HIV Behavioral Surveillance System

The NHBS system was established in 2003 by the Centers for Disease Control and Prevention (CDC) to monitor risk behaviors among three populations at highest risk for HIV infection in the United States: gay, bisexual, and other men who have sex with men, persons who inject drugs (PWID), and heterosexuals at increased risk for HIV. NHBS involves rotating 12-month cycles of surveillance activities in these three populations. Surveillance activities include ethnographic formative research, an in-depth behavioral survey, and HIV testing during each cycle. The analyses presented in the current short communication are from the 2015 NHBS cycle among PWID in Denver, Colorado.

2.2. Study Design and Protocol

Between June and December 2015, participants were recruited using respondent-driven sampling (RDS), a peer-referral sampling methodology.[11] Each eligible participant was allowed to refer up to five persons from their network. Participants were instructed to recruit someone they knew who injects drugs and who they had seen in the past 30 days. Persons were eligible to participate if they were at least 18 years or older, had injected drugs during the preceding 12 months, resided in the Denver metropolitan statistical area, had not previously participated in the 2015 NHBS cycle, and were able to provide informed consent. Additional eligibility criteria included having physical evidence of recent injection (fresh track marks) or having current knowledge of drug preparation and injection technique and syringe description.

Verbal informed consent was obtained from eligible participants. Participants completed a standardized interviewer-administered behavioral risk survey using handheld computers.

The behavioral risk survey includes questions about sexual behaviors, injection behaviors, substance use, and HIV testing. In addition to the behavioral risk survey, which is the core NHBS survey and administered nationally across all sites, participants completed a shorter local questionnaire. Local questionnaires are developed during the formative research phase of NHBS, which includes interviews with key informants and focus groups to identify salient issue of concern or interest for the target population. The following question was included in the local questionnaire to capture information on nonmedical use of prescription opioids prior to injection: “Think back to the very first time that you injected any kind of drug. Were you hooked on painkillers, such as Oxycontin®, Vicodin®, morphine, or Percocet®, before you injected drugs for the very first time?” Similar to a group in Seattle, we used the term “hooked on” to avoid the word “dependence” which can be interpreted in different ways by non-clinicians. [12]

Participants were also offered a rapid HIV test in addition to a rapid test for Hepatitis C Virus (HCV). Participants were given $35 for completing the survey, $35 for HIV and HCV testing, and $20 for each eligible person they recruited. All NHBS activities were voluntary and no names were collected. The study protocol was reviewed and approved by the Colorado Multiple Institutional Review Board.

2.3. Statistical Analysis

Chi-square (X^2) statistics were calculated to assess differences based on being hooked on prescription opioids prior to injection drug use. Generalized linear models with log link and binomial error distribution were used to estimate prevalence ratios (PR) and associated 95% confidence intervals (CI) for the association between prior nonmedical use of prescription opioids and overdose. All analyses were conducted using StataSE Version 12 (StataCorp, College Station, TX).

3. RESULTS

3.1. Characteristics of the Study Population

A total of 712 persons were screened for the 2015 cycle of NHBS in Denver, of whom 603 (84.7%) were eligible to participate and 599 (84.1%) completed the local questionnaire. The final sample included 19 (3.2%) seed participants, all of whom were 29 years or younger. Younger seeds were purposefully recruited in an attempt to generate a sample which more accurately represents the PWID population. Approximately three quarters (70.4%) of participants were male and more than half (58.2%) identified as non-Hispanic white (Table 1). Nearly one-quarter (22.0%) were 29 years old or younger. A large proportion of participants reported experiencing homelessness with 66.4% reporting being currently homeless and 15.1% reporting being homeless, but not in the past 12 months.

3.2. Nonmedical Use of Prescription Opioids Prior to Injection

Overall, 192 (32.1%) of participants reported being hooked on painkillers, such as Oxycontin, Vicodin, morphine, or Percocet, before they injected drugs for the very first time (Table 1). Compared to participants who did not report being hooked on prescription opioids before they injected, those who were hooked on prescription opioids were significantly more likely to be younger (under age 29), to be new injectors (i.e. less than 1 years since their first injection), to have injected heroin as their first drug, and to report heroin as the drug most frequently injected. Though those who reported being hooked on prescription opioids were more likely to be under the age of 29, they were also more likely to report a slightly older age of first injection with the mean age at first injection being 24.6 (95% CI: 23.5, 25.7) compared to a mean age of 22.4 (95% CI: 21.5, 23.2) for those who were not hooked on prescription opioids prior to their first injection.

3.3. Overdose Experience

Participants were asked about the number of times they had overdosed in the past 12 months. A definition of overdose was not included in the question. Overall, 71 (12.0%) reported overdosing once in the past 12 months, 26 (4.3%) reported overdosing twice, and 31 (5.2%) reported overdosing 3 or more times in the past 12 months (Table 2). Reporting being hooked on prescription opioids prior to injection drug use was associated with a 1.55 (95% CI: 1.14, 2.10) fold increase in the risk of at least one overdose in the past 12 months. To control for factors that could potentially confound this association, we included variables that were associated with being hooked on prescription opioids prior to injection that might also be associated with the risk of overdose in a multivariate model. The association between being hooked and overdose was attenuated when we adjusted for age, years since first injection, non-injection use of heroin or prescription opioids, use of benzodiazepines, and participation in a treatment program in the past 12 months (prevalence ratio 1.36, 95% CI: 0.97–1.91). On the other hand, participants who reported being hooked on prescription opioids prior to injection drug use were also more likely to report obtaining a take-home naloxone kit in the past 12 months (44.3% vs 26.5%, $p<0.001$).

3.4. Non-injection Drug Use and Frequency of Injection

Participants who reported being hooked on prescription opioids prior to injection drug use were more likely to report more frequent (i.e. more than once a day) use of benzodiazepines, non-injection prescription opioids, and non-injection heroin, 13.6%, 13.1%, and 15.7% compared to those who were not hooked, 4.7%, 5.4%, and 7.7%, respectively (Table 2). Participants who reported being hooked on prescription opioids before injecting were also slightly more likely to report injecting one or more times a day compared to those who did not report being hooked (84.3% vs. 75%, p=0.024).

4. DISCUSSION

In our sample of current PWID, those who reported being hooked on prescription opioids prior to injection drug use were significantly more likely to be younger, more recent injectors, report a slightly older age at first injection, and report heroin as the first drug injected as well as the drug most frequently injected. Those who reported being hooked were also more likely to be more frequent users of benzodiazepines, non-injection prescription opioids, and non-injection heroin as well as report injecting one or more times a day. Perhaps because of this higher risk profile, participants who reported being hooked on prescription opioids prior to injecting were also more likely to report at least one overdose during the past 12 months. However, when we adjusted for potential confounding factors this association was slightly attenuated.

Several papers have described patterns of heroin use among those who have reported nonmedical use or injection of prescription opioids[13–16] and a limited number have examined trajectories from nonmedical use of prescription opioids to heroin use.[12,17,18] One study examining data from the National Survey on Drug Use and Health used discrete-time hazard models to estimate the age-specific hazard of heroin initiation in young adults. Study authors reported a hazard ratio of 13.1 (95% CI: 10.7, 16.0) for the association between nonmedical use of prescription opioids and heroin initiation with the peak age of heroin initiation being 17–18 years.[19] However, the study does not specify the route of heroin administration. Another recent study described differences in initiation of heroin and prescription opioids by birth cohorts, but did not examine any characteristics beyond age.[20]

To our knowledge, this is the first paper to examine differences between those who reported being hooked on prescription opioids before they began injecting and those who were not in a large sample of PWID. Though the study from Peavy et al. also compares differences between those who reported being hooked on prescription opioids and those who were not, their question limited the response to those who were hooked prior to heroin injection.[12] While more than half of our participants who reported being hooked on prescription opioids before their first injection reported heroin as the first drug injected, a sizable portion reported cocaine and methamphetamine as the first injected drugs. This finding underscores the complexity of drug use patterns and suggests that the transition from prescription opioids to injection drug use is not limited to the injection of heroin or prescription opioids.

While the current study contributes to the existing literature by quantifying the differences between PWID who were hooked on prescription opioids before they began injecting and

those who were not, it is not without limitations. Because the survey was administered by an interviewer some participants might not have reported their behaviors accurately. Our results are limited to respondents in one urban city in the Western part of the United States and might not be generalizable to PWID in other parts of the country, or other countries.

Our findings that PWID who report being hooked on prescription opioids before they started injecting appear to have overall higher risk profiles point to the need for targeted interventions, such as provision of take-home naloxone kits and sterile injection supplies, to this group. In addition, research to identify factors that might accelerate or inhibit the transition from nonmedical use of prescription opioids to injection drug use is urgently needed.

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HIGHLIGHTS

- Dependence on prescription opioids prior to injection may result in higher risk profile.
- Prior dependence on prescription opioids is associated with increased overdose risk.
- Overdose prevention efforts should be targeted towards persons with high risk profiles.

Table 1

Demographic and injection characteristics by status of prescription opioid misuse prior to first injection in a sample of persons who inject drugs, National HIV Behavioral Surveillance (NHBS), Denver, Colorado, 2015

	Total	Hooked n (%)	Not hooked n (%)	p-value
Overall*	599	192 (32.1)	407 (67.9)	
Demographic Characteristics				
Gender				
Male	421 (70.9)	124 (65.3)	297 (73.5)	0.039
Female	173 (29.1)	66 (34.7)	107 (26.5)	
Race/Ethnicity				
White, non-Hispanic	346 (58.2)	123 (64.4)	223 (55.2)	0.025
Black, non-Hispanic	46 (7.7)	10 (5.2)	36 (8.9)	
Hispanic	151 (25.4)	49 (25.7)	102 (25.3)	
Other	52 (8.7)	9 (4.7)	43 (10.6)	
Age				
18–29	132 (22.0)	67 (34.9)	65 (16.0)	<0.001
30–39	161 (26.9)	70 (36.5)	91 (22.4)	
40–49	144 (24.0)	30 (15.6)	114 (28.0)	
≥50	162 (27.1)	25 (13.0)	137 (33.7)	
Homeless in past 12 months				
No	110 (18.5)	32 (16.7)	78 (19.3)	0.514
No, homeless longer than 12m	90 (15.1)	33 (17.3)	57 (14.1)	
Yes, currently homeless	396 (66.4)	126 (66.0)	270 (66.8)	
Injection Characteristics				
Age at first injection				
<= 14	70 (11.7)	10 (5.2)	60 (14.7)	<0.001
15–18	156 (26.0)	38 (19.8)	118 (29.0)	
19–22	113 (18.9)	36 (18.8)	77 (18.9)	
23–29	130 (21.7)	59 (30.7)	71 (17.4)	
>= 30	130 (21.7)	49 (25.5)	81 (19.9)	
Years since first injection				
<=1 year	43 (7.2)	22 (11.5)	21 (5.2)	<0.001
2 – 3 years	61 (10.2)	31 (16.2)	30 (7.4)	
4 – 6 years	66 (11.0)	33 (17.2)	33 (8.1)	
7 – 10 years	78 (13.0)	39 (20.3)	39 (9.6)	
> 10 years	351 (58.6)	67 (34.9)	284 (69.8)	
First drug injected				
Heroin	246 (41.1)	101 (52.6)	145 (35.6)	<0.001
Methamphetamine	173 (29.0)	24 (12.5)	149 (36.6)	
Cocaine	139 (23.2)	51 (26.6)	88 (21.6)	
Other	41 (6.8)	16 (8.3)	25 (6.1)	

	Total	Hooked n (%)	Not hooked n (%)	p-value
Most frequently injected drug past 12 months				
Heroin	351 (58.9)	141 (73.8)	210 (52.9)	<0.001
Methamphetamine	174 (29.2)	26 (13.6)	148 (36.5)	
Cocaine	17 (2.9)	4 (2.1)	13 (3.2)	
Other	54 (9.1)	20 (10.5)	34 (8.4)	

NOTE:

*Subcategory total may not add to overall total due to missing data.

Table 2

Overdose, participation in drug treatment, and non-injection drug use characteristics in the past 12 months by status of prescription opioid misuse prior to first injection in a sample of persons who inject drugs, National HIV Behavioral Surveillance (NHBS), Denver, Colorado, 2015

	Total	Hooked n (%)	Not hooked n (%)	p-value
Overall*	599	192 (32.1)	407 (67.9)	
Overdose in past 12 months				
No	471 (78.6)	138 (71.9)	333 (81.8)	0.022
Once	71 (12.0)	30 (15.6)	41 (10.1)	
Two or more times	57 (9.5)	24 (12.5)	33 (8.1)	
Received take-home naloxone kit				
No	357 (59.6)	102 (53.1)	255 (62.7)	<0.001
Yes	193 (32.2)	85 (44.3)	108 (26.5)	
Don't know what Naloxone is	49 (8.2)	5 (2.6)	44 (10.8)	
Participated in drug treatment				
Yes	243 (40.8)	93 (48.7)	150 (37.0)	0.007
No	353 (59.1)	98 (51.3)	255 (63.0)	
Tried to get treatment but unable				
Yes	126 (21.1)	53 (27.8)	73 (18.0)	0.007
No	470 (78.9)	138 (72.2)	332 (82.0)	
Frequency of marijuana use				
Once a day or more	219 (36.7)	62 (32.4)	157 (38.8)	0.428
More than once a week	67 (11.2)	23 (12.0)	44 (10.9)	
Less than once a week	120 (20.1)	44 (23.0)	76 (18.8)	
Not in the past 12 months	190 (31.9)	62 (32.5)	128 (31.6)	
Frequency of benzo use				
Once a day or more	45 (7.6)	26 (13.6)	19 (4.7)	<0.001
More than once a week	59 (9.9)	24 (12.6)	35 (8.6)	
Less than once a week	161 (27.0)	68 (35.6)	93 (23.0)	
Not in the past 12 months	331 (55.5)	73 (38.2)	258 (63.7)	
Frequency of prescription opioid use				
Once a day or more	47 (8.0)	25 (13.1)	22 (5.4)	<0.001
More than once a week	63 (10.6)	28 (14.7)	35 (8.6)	
Less than once a week	164 (24.5)	63 (33.0)	101 (25.0)	
Not in the past 12 months	322 (54.0)	75 (39.3)	247 (61.0)	
Frequency of non-injection heroin use				
Once a day or more	61 (10.2)	30 (15.7)	31 (7.7)	<0.001
More than once a week	35 (5.9)	13 (6.8)	22 (5.4)	
Less than once a week	127 (21.3)	55 (28.8)	72 (17.8)	
Not in the past 12 months	373 (62.6)	93 (48.7)	280 (69.1)	
Frequency of injection				

	Total	Hooked n (%)	Not hooked n (%)	p-value
More than once a day	395 (66.3)	143 (74.9)	252 (62.2)	0.024
Once a day	70 (11.7)	18 (9.4)	52 (12.8)	
More than once a week	62 (10.4)	14 (7.3)	48 (11.9)	
Once a week or less	69 (11.6)	16 (8.4)	53 (13.1)	

NOTE:

* Subcategory total may not add to overall total due to missing data.