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Denial of Prescription Analgesia Among People Who Inject Drugs in a Canadian Setting

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Abstract

Introduction and Aims—Despite the high prevalence of pain among people who inject drugs (PWID), clinicians may be reluctant to prescribe opioid-based analgesia to those with a history of drug use or addiction. We sought to examine the prevalence and correlates of PWID reporting being denied prescription analgesia (PA). We also explored reported reasons for and actions taken after being denied PA.

Design and Methods—Using data from two prospective cohort studies of PWID in Vancouver, Canada, multivariate logistic regression was used to identify the prevalence and correlates of reporting being denied PA. Descriptive statistics were used to characterize reasons for denials and subsequent actions.

Results—Approximately two thirds (66.5%) of our sample of 462 active PWID reported having ever been denied PA. We found that reporting being denied PA was significantly and positively associated with having ever been enrolled in methadone maintenance treatment (MMT) (adjusted odds ratio [AOR]=1.76, 95%CI: 1.11–2.80) and daily cocaine injection (AOR=2.38, 95%CI: 1.00–5.66). The most commonly reported reason for being denied PA was being accused of drugseeking (44.0%). Commonly reported actions taken after being denied PA included buying the requested medication off the street (40.1%) or obtaining heroin to treat pain (32.9%)

Conflict of interest:

JSGM has received educational grants from, served as an ad hoc advisor to or spoken at various events sponsored by Abbott Laboratories, Agouron Pharmaceuticals Inc., Boehringer Ingelheim Pharmaceuticals Inc., Borean Pharma AS, Bristol-Myers Squibb, DuPont Pharma, Gilead Sciences, GlaxoSmithKline, Hoffmann-La Roche, Immune Response Corporation, Incyte, Janssen-Ortho Inc., Kucera Pharmaceutical Company, Merck Frosst Laboratories, Pfizer Canada Inc., Sanofi Pasteur, Shire Biochem Inc., Tibotec Pharmaceuticals Ltd., and Trimeris Inc. The remaining authors do not have conflicts to declare.

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Discussion and Conclusions—These findings highlight the clinical challenges of addressing perceived pain control needs and the need for strategies to prevent high-risk methods of self-managing pain, such as obtaining diverted medications or illicit substances for pain. Such strategies may include integrated pain management guidelines within MMT and other substance use treatment programs.

Keywords

pain; prescription opioids; diversion; drug seeking; methadone

1. INTRODUCTION

Worldwide, chronic pain is a mounting public health concern, particularly among people who inject drugs (PWID). While there is currently a lack of data to estimate the prevalence of pain among PWID in particular, one recent systematic review estimated that 16% to 74% of individuals with chronic non-cancer pain have a lifetime history of substance use disorder [1]. Potential causes of acute or chronic pain among this often socioeconomically disadvantaged population include injection-related trauma, injuries, infections and complications of chronic infectious diseases such as HIV and hepatitis C [2–4]. Indeed, PWID experience a high prevalence of chronic health conditions compared to the general population. For instance, the prevalence of HIV among PWID (13%) is estimated to be 22 times higher than the general population [5], and HIV-positive PWID have been shown to demonstrate a significantly higher prevalence of pain compared to people living with HIV who do not inject drugs [6, 7].

Appropriate pain management involving person-specific approaches to restore function and well-being has been recognized as a fundamental human right [8] and is paramount for promoting optimal health and treatment outcomes including improved quality of life, decreased lengths and frequencies of hospital admissions, increased confidence and engagement in the medical system and increased likelihood of accessing health care and addiction treatment [3, 9]. Currently, there exists a wide range of pain management and treatment options including pharmacological (e.g., opioids, non-steroidal antiinflammatories, antidepressants, anticonvulsants, muscle relaxants, topical agents), interventional (e.g., nerve blocks or injection therapy, surgery, implantable devices, spinal cord stimulation), psychological (e.g., operant conditioning, cognitive-behavioural therapy including acceptance- and mindfulness-based therapy), physical rehabilitation, and complementary and alternative (e.g., spinal manipulation, massage, acupuncture, transcutaneous electric nerve stimulation) approaches [10]. Unfortunately, despite this array of multimodal therapeutic options for pain management, individuals with a history of substance use are significantly more likely to receive inadequate pain treatment due to practitioners' concerns regarding diversion and addiction-related opioid-seeking behaviours [11, 12]. Consequently, PWID may experience perceived stigma and mistreatment, and subsequently resort to self-managing pain in ways that pose high risk for morbidity and mortality (e.g., injecting heroin, obtaining diverted analgesics) [13].

To further investigate pain management experiences among PWID, we sought to explore the prevalence, correlates, reasons for, and outcomes of reporting being denied prescription analgesia (PA) among PWID in Vancouver, Canada.

2. METHODS

Data for these analyses were derived from two prospective observational cohorts in Vancouver, Canada: the AIDS Care Cohort to Evaluate Exposure to Survival Services (ACCESS) of HIV-seropositive injection drug users and the Vancouver Injection Drug Users Study (VIDUS) of HIV-seronegative injection drug users. These cohorts have previously been described in detail [14]. In short, over 2,500 subjects have been recruited into these cohorts through snowball sampling and street outreach methods. At baseline and semi-annually, participants answer a standardized interviewer-administered questionnaire and provide blood samples for serologic analysis (among HIV negative individuals) or disease monitoring (among HIV-positive individuals), and are referred as necessary to medical care and drug and alcohol treatment. All participants provide written informed consent and receive a \$20 stipend at the end of each study visit. These studies have received annual ethics approval from the University of British Columbia and Providence Health Care Office of Research Services.

The present analyses were restricted to interviews that were conducted from December 1, 2011 to May 31, 2013. To exclude the analysis of PA denial among PWID who did not report pain, we restricted our analysis to active injection drug users who reported moderate to extreme pain as determined by a "yes" response to the question "I have moderate pain or discomfort" or "I have extreme pain or discomfort" in the standardized Eurogol EQ-5D health utility instrument, which has been shown to be a valid, responsive and reliable survey instrument among individuals with pain and substance users [15–17]. Participants were first asked if they had ever requested a prescription for analgesia (yes vs. no). If the participant responded yes, they were then asked whether they had ever been denied a prescription for analgesia (yes vs. no). Those who reported being denied PA were also asked what actions they took after being denied PA. For this open-ended question, the interviewer recorded the participant's response by either check-marking a box if the response was consistent with one of the pre-defined, hypothesized responses (e.g., "Nothing," "Went a to different doctor/ clinic"), or by transcribing the participant's response if the response did not fit into a structured response category. The transcribed data were analysed individually by the authors and manually categorized.

We compared those who did and did not report being denied PA to identify the factors associated with PA denial. The socio-demographic characteristics considered in the analyses were: age, gender, homelessness, residence in Vancouver's Downtown Eastside (DTES), education status, HIV status, sex work, incarceration, physical disability, and self-managed pain. The variables related to drug use included: daily crack use, daily crystal methamphetamine injection, daily heroin injection, daily cocaine injection, daily marijuana use, heavy alcohol use, nonmedical prescription opioid use, non-fatal overdose, enrolment in methadone maintenance treatment (MMT), and binge injection drug use. As per the National Institute on Alcohol Abuse and Alcoholism (NIAAA), heavy alcohol use was defined as

more than four drinks per day or more than fourteen drinks per week for males, or more than three drinks per day or more than seven drinks per week for females [18]. Nonmedical prescription opioid use was defined as the injection or non-injection use of prescription opiates not as prescribed or not prescribed to the individual [19]. As per the definition of bingeing in previous studies, binge injection drug use was defined as any period of time within the previous six months from the time of interview during which any drugs were injected more frequently than usual [20, 21].

We analysed the association of these variables with PA denial using bivariate and multivariate logistic regression analyses. An *a priori*-defined statistical protocol was applied based on examination of the Akaike Information Criterion (AIC) and p-values to construct a multivariate explanatory logistic regression model. We first constructed a full model including all variables that were significant at p<0.10 in the bivariate analyses. After noting the AIC of the model, we performed the iterative process of removing the variable with the largest p-value and built a reduced model until no variables remained for inclusion. The multivariate model with the lowest AIC score was selected. All statistical analyses were performed using SAS software version 9.3 (SAS, Cary, NC). All p-values were two sided. A significant association was defined as p<0.05.

As a secondary analysis using descriptive statistics, we analysed participant responses regarding reasons given to them for being denied PA and the actions they took after they were denied. Participants responded ad lib to these questions with more than one response if desired.

3. RESULTS

Of the 462 participants who reported active injection drug use in the six months prior to being interviewed, 135 (29.2%) were women and 207 (44.8%) were HIV-positive. The median age was 48 years (IQR: 43 to 53 years). A lifetime history of homelessness (n=315, 91.6%), unstable housing (n=315, 61.8%), or residence in Vancouver' Downtown Eastside (n=412, 89.2%) were common in this sample. Furthermore, a lifetime history of physical disability was commonly reported (n=427, 92.4%). Other demographic proportions of this sample are shown in Table 1. In total, almost two-thirds of this sample (n=307, 66.5%) reported having ever been denied PA.

As shown in Table 1, the bivariate analyses indicated that being denied PA was associated with daily heroin injection, daily cocaine injection, and having ever been enrolled in MMT. In multivariate analysis, as shown in Table 2, being denied PA remained independently associated with daily cocaine injection (Adjusted Odds Ratio [AOR] = 2.38, 95% Confidence Intervals [CI] = 1.00 - 5.66) and having ever been enrolled in MMT (AOR = 1.76, 95% CI = 1.11 - 2.80).

As shown in Table 3, all of the 307 individuals who reported being denied PA provided self-reported reasons for being denied PA, including: being accused of drug-seeking (n=135, 44.0%), attending a clinic with a policy of not prescribing narcotics (n=80, 26.1%), being told that methadone is sufficient (n=58, 18.9%), not being given a reason for PA denial (n=51, 16.6%), and physician concern regarding the individual's history of drug use and/or

potential for dependence/addiction (n=44, 14.3%). The primary self-reported actions taken after being denied PA included: buying the requested medication off the street (n=123, 40.1%), buying a different pain medication off the street (n=107, 34.9%), no action taken (n=102, 33.2%), obtaining heroin (n=101, 32.9%), and going to a different doctor or clinic (n=67, 21.8%).

4. DISCUSSION

In the present study, almost two-thirds of our community-recruited sample of PWID reported having ever been denied PA. We found that being denied PA was significantly and positively associated with having ever been enrolled in methadone maintenance treatment and daily cocaine injection. The most commonly reported reasons for being denied PA were being accused of drug-seeking, attending clinics with a policy of not prescribing narcotics, and being told that methadone is sufficient. After being denied PA, PWID frequently bought pain medication off the street, obtained heroin, took no further action, or went to a different doctor or clinic.

These findings suggest that being denied PA is relatively common among PWID. This may serve as one explanation for why previous research has found that pain is often undertreated among people with a history of substance use [11, 12], particularly as this often socioeconomically disadvantaged population often contends with chronic health conditions that contribute to pain (e.g., HIV, hepatitis C) [22, 23]. We found only one other study that investigated PA denial among individuals with a history of substance use, in which 34 out of 150 (22.7%) participants reported having ever been denied prescription opioids, of which 13 (38.2%) were PWID [24]. Further research is needed to characterize the comparative prevalence of PA denial among PWID versus non-substance users and the general population, as there is currently a paucity of research in these areas. Furthermore, while the present study did not find a statistically significant gender difference related to PA denial, future analyses would be warranted in this area given the limited research on gender differences within illicit drug using populations [25]. Across various population subgroups, increased monitoring of PA requests and denials will become an important area of research in light of recent efforts to curb prescription opioid misuse by targeting prescribing practices [26], which may result in more denials of PA and potentially adverse effects for individuals suffering from pain who are denied opioids without being given an effective analgesic alternative.

Our findings further suggest that PWID who have ever been enrolled in MMT may be more likely to be denied a request for PA, and that clinicians may deny additional analgesia to individuals already on methadone treatment. This finding may serve to explain other literature indicating that, despite the high prevalence of pain among individuals on MMT [27], pain may often be undertreated for MMT patients [28, 29]. In fact, MMT patients with a prolonged history of chronic pain have been shown to require significantly higher doses of methadone than MMT patients with no pain or short pain durations [30], potentially due to the lower pain thresholds and heightened opioid tolerance that is characteristic of individuals with long-term opioid dependence [31]. A root cause of undertreated pain among MMT patients may be the tendency for clinicians to dichotomize MMT as either a pain treatment

or an addiction treatment, rather than recognizing the comorbid nature of pain and addiction in individuals with a history of substance use [32]. Therefore, there is a pressing need to integrate evidence-based guidelines and programming for pain management within MMT and other substance use treatment programs.

The present study also found that daily cocaine injection was significantly associated with being denied PA. Approximately 4% of the participants who reported being denied PA in this study reported subsequently using cocaine or crack cocaine for pain. This finding may reflect the high rates of comorbidities among frequent cocaine injectors [33, 34] or the potential modulatory effect of stimulants on pain experiences [35–37]. Further longitudinal and qualitative analyses may help unpack the potential relationship between high intensity cocaine use and reported denial of PA.

In this study, the most commonly reported reason for being denied PA was being accused of "drug-seeking" (44.0%). In a similar study, 22.7% of individuals with a history of substance use were denied PA and were also often identified as drug-seeking [24]. This phenomenon of health professionals interpreting requests for analgesia as "drug-seeking" among individuals with a history of substance use represents a broader, systemic issue of frequent and disproportionate stigma and marginalization toward substance users within health care systems [38]. Negative stereotypes about substance users may manifest as care delivery that is ineffective or even inhumane. Specifically, when addressing pain and requests for analgesia, prescribers may feel the need to distinguish between "real" versus "feigned" pain, and are in a position of power to withhold treatment based on their interpretations [39, 40]. In turn, substance users often feel stigmatized or mistreated, and may consequently choose to avoid health care and self-manage their pain instead [2, 41].

The second most commonly reported reason for being denied PA in this study was attending a clinic with a policy of not prescribing narcotics. Moreover, after being denied PA, PWID in this study reported attending a different physician or clinic (21.8%) or attending the emergency room (1.6%). While further investigation is needed to identify potential correlations between specific types of medical facilities (e.g., emergency department, family physician, walk-in clinic) and PA denial among PWID, these findings draw attention to the many barriers that PWID face when seeking analgesia at various points of care. These findings also highlight the migration of PWID between health facilities, which may be negatively interpreted as "doctor shopping" or "double doctoring", when the root problem may be other reasons such as a shortage of regular family physicians willing to take on PWID as patients, or a need to facilitate greater awareness among PWID regarding how and where to best access chronic pain management (e.g., through a regular physician or pain specialist rather than the emergency department) and the various treatment options available for pain management (e.g., non-narcotic).

Our findings further suggest that PWID who are denied PA may self-manage their pain through high-risk methods including the acquisition of diverted analgesics from street-based drug markets or the use of illicit drugs, particularly heroin. This is consistent with a study of PA denial among young adults, which found that approximately half of the participants self-medicated with diverted opioids or heroin after being denied PA [24]. Consequently, self-

managed pain as a result of PA denial poses risks for adverse effects including overdose, toxicity, or mortality [42, 43], which should be taken into consideration by clinicians when weighing the benefits and harms of prescribing analgesia to PWID [43].

Specifically, providers must balance concerns regarding PA diversion, misuse, or overprescribing with the goal of optimal pain management and restoration of function when possible [11, 44, 45]. Innovative strategies that can facilitate safe administration of PA include tamper-resistant formulations that may discourage PA misuse [46], daily witnessed ingestion through pharmacies or other point-of-care programs, dispensing medications in small quantities with defined therapeutic end-points [43], and involvement of both pain and addiction specialists in the clinical care of PWID [43].

This study has several limitations. First, the cross-sectional design limited our ability to determine temporal relationships between variables that predicted or preceded denial of PA, although descriptive statistics provide some insight into the reasons that preceded PA denial and subsequent behaviours. The associations noted in this study should be further examined through longitudinal analyses. Second, our study relied on self-reported data that is susceptible to socially desirable reporting and recall bias. Third, because the study sample was not randomly selected, these results may not be generalizable to other PWID populations. Finally, our analysis did not define a particular class of PA (e.g., opioids), health care setting (e.g., acute care versus primary care), or frequency of PA requests or denials in the interview questions, which are relevant considerations that should be examined in future studies.

In summary, almost two thirds of PWID in our study had been previously denied PA. We found that PWID who were denied PA were more likely to have ever been enrolled in MMT and frequently inject cocaine. The most commonly reported reason for being denied PA was being accused of "drug-seeking." Being denied PA often resulted in acquisition of diverted medications and heroin use. To prevent the high-risk behaviours following denial of PA, clinical strategies that can facilitate optimal pain and addiction management should be implemented and rigorously evaluated.

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Table 1

(n = 462)

Vomoblo	Denie	Denied PA†	Unadineted odds notice (050% CT)	orlor a
v at table	Yes 307 (66.5%)	No 155 (33.6%)	Onaujusteu odus rado (75 /0C1)	p-value
Age				
> 48 years	158 (51.5)	68 (43.9)	1.36(0.92-2.00)	0.1236
48 years	149 (48.5)	87 (56.1)		
$\mathbf{Gender}^{\dagger}$				
Male	218 (71.0)	108 (69.7)	1.08 (0.71 - 1.65)	0.7273
Female	88 (28.7)	47 (30.3)		
Homelessness//				
Yes	285 (92.8)	138 (89.0)	1.60 (0.82 - 3.10)	0.1681
No	22 (7.2)	17 (11.0)		
Unstable housing// \dagger	4//4			
Yes	212 (69.1)	103 (66.5)	1.10(0.72-1.68)	0.6626
No	88 (28.7)	47 (30.3)		
DTES residence//				
Yes	278 (90.5)	134 (86.5)	1.50 (0.83 - 2.73)	0.1823
No	29 (9.5)	21 (13.5)		
Education status// \dagger	//+			
High school	153 (49.8)	69 (44.5)	1.27 (0.86 - 1.88)	0.2330
< High school	145 (47.2)	83 (53.6)		
HIV serostatus				
Positive	130 (42.4)	77 (49.7)	0.74 (0.51 - 1.10)	0.1350
Negative	177 (57.6)	78 (50.3)		
Sex work//				
Yes	151 (49.2)	81 (52.3)	0.88 (0.60 - 1.30)	0.5330
No	156 (50.8)	74 (47.7)		
$Incarceration^{\prime\prime}$				
Yes	149 (48.5)	61 (39.4)	1.45 (0.98 - 2.15)	0.0619

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Vomohlo			(10) (10) (1) (1) (1) (1) (1) (1	•
v at table	Yes 307 (66.5%)	No 155 (33.6%)	Unadjusted odds ratio (95%cLl)	<i>p</i> -value
No	158 (51.5)	94 (60.6)		
Physical disability $^{\prime\prime}$	ity//			
Yes	287 (93.5)	140 (90.3)	1.54 (0.76 - 3.09)	0.2279
No	20 (6.5)	15 (9.7)		
Self-managed pain $^{\prime\prime}$	ain//			
Yes	306 (99.7)	151 (97.4)	8.11 (0.90 - 73.15)	0.0623
No	1 (0.3)	4 (2.6)		
Any injection dr	Any injection drug use at baseline $^{/\!/7}$			
Yes	304 (99.0)	154 (99.4)	0.99 (0.09 - 10.97)	0.9915
No	2 (0.7)	1 (0.6)		
Daily crack use $^{* op}$	+*			
Yes	66 (21.5)	43 (27.7)	0.72 (0.46 - 1.12)	0.1466
No	239 (77.9)	112 (72.3)		
Daily crystal me	Daily crystal methamphetamine injection *	ction*		
Yes	26 (8.5)	13 (8.4)	1.01 (0.50 - 2.03)	0.9762
No	281 (91.5)	142 (91.6)		
Baily heroin injection	ection*			
Yes	73 (23.8)	22 (14.2)	1.89 (1.12 – 3.18)	0.0172
No	234 (76.2)	133 (85.8)		
Daily cocaine injection $^{* op}$	jection $^{* au}$			
Yes	31 (10.1)	7 (4.5)	2.39 (1.03 – 5.56)	0.0429
No	274 (89.3)	148 (95.5)		
Daily marijuana use $^{* au}$	*7 use			
Yes	75 (24.4)	37 (23.9)	1.04 (0.67 – 1.64)	0.8508
No	229 (74.6)	118 (76.1)		
Heavy alcohol use $^{* op}$	se*†			
Yes	52 (16.9)	26 (16.8)	1.02 (0.61 - 1.70)	0.9528
Z	254 (82.7)	129 (83.2)		

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77	Denied PA	I PA†	T 1: - 1:	
v ariable	Yes 307 (66.5%) No 155 (33.6%)	No 155 (33.6%)	Onadjusted odds rauo (95%C1) — p-vaine	<i>p</i> -value
Nonmedical pr	Nonmedical prescription opioid use			
Yes	92 (30.0)	39 (25.2)	1.27 (0.82 - 1.97)	0.2797
No	215 (70.0)	116 (74.8)		
Non-fatal overdose/	dose//			
Yes	217 (70.7)	98 (63.2)	1.40 (0.93 - 2.11)	0.1048
No	90 (29.3)	57 (36.8)		
Enrolled in $\mathbf{MMT}^{\prime\prime}$	MT//			
Yes	249 (81.1)	111 (71.6)	1.70 (1.08 – 2.67)	0.0209
No	58 (18.9)	44 (28.4)		
Binge injection drug use $^{* op}$	drug use $^{* extstyle{ au}}$			
Yes	109 (35.5)	59 (38.1)	0.90 (0.60 - 1.34)	0.6066
No	197 (64.2)	96 (61.9)		

CI: Confidence interval; DTES: Downtown Eastside; MMT: methadone maintenance treatment.

 $\overset{*}{\text{\begin{subarray}{c} *}}}$ Within the previous six months (from time of interview)

/B.10.

† Indicates missing responses as follows: Gender (1 missing response); unstable housing (12 missing responses); education status (12 missing responses); any injection drug use at baseline (1 missing responses); daily cocaine injection (2 missing responses); daily marijuana use (3 missing responses); heavy alcohol use (1 missing response); binge injection drug use (1 missing response).

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Table 2

Logistic regression analysis of factors associated with denial of prescription analysis among people who inject drugs in Vancouver, Canada. (n = 462)

Variable	Adjusted Odds Ratio	95% Confidence Interval	p - value
Self-managed pain//(Yes vs. no)	7.80	(0.86 - 70.44)	0.0674
Daily heroin injection * (Yes vs. no)	1.67	(0.98 - 2.86)	0.0606
Daily cocaine injection *† (Yes vs. no)	2.38	(1.00 - 5.66)	0.0498
Enrolled in MMT ^{//} (Yes vs. no)	1.76	(1.11 - 2.80)	0.0165

MMT: Methadone maintenance treatment.

 $^{^{\}prime\prime}$ Ever

^{*} Within the previous six months (from time of interview)

[†]Indicates 2 missing responses.

Table 3

Self-reported* reasons for and actions taken after being denied prescription analgesia among people who inject drugs in Vancouver, Canada (n = 307)

Self-reported responses	n (%), $n = 307^*$
Reasons for being denied prescription analgesia	
Accused of drug-seeking for personal use or illicit sales	135 (44.0)
Clinic policy of not prescribing narcotics	80 (26.1)
Told that methadone is sufficient	58 (18.9)
No reason given	51 (16.6)
Physician aware of individual's history of drug use and/or is concerned about dependence/addiction	44 (14.3)
Physician did not believe the person was in serious pain	38 (12.4)
Told that ibuprofen is sufficient	36 (11.7)
Told that other pain medications (other than methadone, ibuprofen or Tylenol #3) are sufficient	30 (9.8)
Other reasons	23 (7.5)
Told to and/or didn't see their regular physician, and/or accused of "double doctoring"	19 (6.2)
Told that Tylenol #3 is sufficient	14 (4.6)
Positive urine screen for cocaine	10 (3.3)
College of Physicians effect on	9 (2.9)
Told that pain medications may cause adverse effects (e.g., liver)	8 (2.6)
Additional lab work requested and/or positive drug test	6 (2.0)
Actions taken after being denied prescription analgesia	
Bought the requested medication off the street	123 (40.1)
Bought a different pain medication off the street	107 (34.9)
No action taken	102 (33.2)
Obtained heroin	101 (32.9)
Went to a different doctor/clinic	67 (21.8)
Other actions	23 (7.5)
Used medication from a friend/partner/acquaintance	16 (5.2)
Used cocaine/crack cocaine	12 (3.9)
Used over-the-counter medications (e.g., ibuprofen, acetaminophen)	9 (2.9)
Went to the emergency room	5 (1.6)

^{*}Participants were able to provide more than one answer.