availability of illicit and prescription opioids among people who inject drugs in a Canadian setting, 2010-2014.The American Journal of Drug and Alcohol Abuse. Published online Oct 19, 2017. PMID: 29048952

Increasing availability of illicit and prescription opioids among people who inject drugs in a Canadian setting, 2010–2014.

DISCLOSURE

Financial disclosures: a Canadian Institutes of Health Research (CIHR) New Investigator Award supports one author. Another one is supported by a Michael Smith Foundation for Health Research (MSFHR)/St. Paul's Hospital Foundation-Providence Health Care Career Scholar Award and a CIHR New Investigator Award. And, another author is supported by a CIHR New Investigator Award, a MSFHR Scholar Award, and the National Institutes of Drug Abuse. His institution has received an unstructured gift from NG Biomed, Ltd., to support his research. All authors declare no conflict of interests.

Funding:
The work was supported by the US National Institutes of Health (U01DA038886, R01DA021525) and the Canadian Institutes of Health Research (MOP–102742). This research was undertaken, in part, thanks to funding from the Canada Research Chairs program through a Tier 1 Canada Research Chair in Inner City Medicine which supports one of the authors, as well as a Canadian Institutes of Health Research Foundation grant supporting another author (FDN-148476).

ABSTRACT

Background: The increase over the past decade in the non-medical use of prescription opioids and illicit opioids in North America has resulted in significant health-related harms.

Objective: We sought to examine temporal trends and correlates of the availability of illicit and prescription opioids among people who inject drugs (PWID) in Vancouver, Canada.

Methods: Data were derived from three prospective cohort studies of PWID in Vancouver between 2010 and 2014. In semiannual interviews, participants reported the availability of five sets of illicit and prescription opioids: (1) heroin; (2) Percocet (oxycodone/acetaminophen), Vicodin (hydrocodone/acetaminophen) or Demerol (meperidine); (3) Dilaudid (hydromorphone); (4) Morphine; (5) oxycontin/OxyNEO (controlled-release oxycodone). We defined perceived availability as immediate (e.g., available within 10 minutes) vs. no availability/available after 10 minutes. The trend and correlation of immediate availability were identified by multivariable generalized estimating equations logistic regression.

Results: Among 1584 participants, of which 564 (35.6%) were female, the immediate availability of all illicit and prescribed opioids (except for oxycontin/OxyNEO) increased over time, independent of potential confounders. The Adjusted Odds Ratios of immediate availability associated with every calendar year increase were between 1.09 (95% confidence interval 1.05-1.12) (morphine and Dilaudid) and 1.13 (95% confidence interval 1.09-1.17) (Percocet/Vicodin/Demerol) (all p-values <0.05).

Conclusion: The availability of most prescription opioids had continued to increase in recent years among our sample of PWID in Vancouver. Concurrent increases in the availability of heroin were also observed, raising concerns regarding combination of both illicit and prescription opioids use among PWID that could potentially increase the risk of overdose.

Word Count: 250

Keywords: Prescribed opioids, Illicit opioids, Availability, Injected drugs

INTRODUCTION

While opioids have been an invaluable tool for pain management in clinical settings, the rising trend in the non-medical use of prescription opioids has become a national epidemic with both economic and healthcare implications (1). In 2012, the National Survey of Drug Use and Health estimated that 2.1 million people in the United States had a substance-use disorder related to prescription opioids, compared to 467,000 with a substance use disorder related to heroin (2). More recently, a study demonstrated a 200% increase in rates of death related to opioid overdose since 2000 and the age-adjusted rate of death involving synthetic opioids (other than methadone) increased by 80% between 2013 and 2014 alone (3). Similar trends in illicit and prescription opioid use have been observed in Canada. Non-medical prescription opioids use in Canada increased by 70% between 2009 and 2014 (4). Opioid related death, with more than 90% accounted for by prescription opioids use, increased by three-fold between 2006 and 2011 in Ontario, Canada (5). Despite several strategies such as prescription monitoring program adopted by the provincial ministry to improve opioid prescribing, the rate of high-dose opioid dispensing increased by 23% between 2006 and 2011 (6). Increases in non-medical prescription opioids availability and use have also been observed among people who use illicit drugs. Specifically, a 24% increase in non-medical prescription opioids use was observed among people who use illicit drugs in Canada between 2002 and 2005 (7).

A previous study in Vancouver, Canada showed an increase in availability of prescription opioids from 2006-2010 among street-involved people who use drugs while availability of other more traditional drugs of abuse such as heroin and crack remained stable during the same period (8). However, beyond 2010, little is known regarding recent trends in illicit and prescription opioid availability among this population despite accumulating evidence suggesting rising trends in both illicit and prescription opioid use in the general population (3, 9, 10). In fact, in response to increase in drug related overdose in British Columbia, the province's senior public health official declared a public health emergency in April 2016 (11).

Recent US studies have indicated a shifting pattern of prescription opioids and heroin use. Cicero, Ellis (12) found an annual increase of 10.3% in concurrent heroin use with prescription opioids use between 2008 and 2014 despite a steady annual decrease of 6.3% in prescription opioids use, suggesting that prescription opioids users were transitioning to heroin use. However, the factors contributing to the transition were not clearly established in the study except that 73% of respondents in a separate online survey conducted reported practical factors, including cost and accessibility, as the primary reasons for transitioning from prescription opioids to heroin. In this context, it is of significance to investigate the trends in the retail price and availability of both illicit and prescription opioids. Specifically, we selected to look into opioid availability among people who inject drugs (PWID) as overdose remains a key risk among PWID with 30-45% of PWID experiencing at least one non-fatal overdose in their lifetime (13-15); overdose, in turn, can lead to further morbidity including acute hypoxia and other end-

organ damage (16) and mortality due to fatal injury (17). Therefore, the objective of our study was to examine temporal trends and correlates of availability of illicit and prescription opioids among PWID with a history of opioid use in Vancouver between 2010 and 2014.

METHODS

Study Procedure

Data of this study were obtained from the At-Risk Youth Study (ARYS), the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS), and the Vancouver Injection Drug Users Study (VIDUS). Details of these ongoing open prospective cohort studies have been described elsewhere (18). Briefly, VIDUS follows HIV-negative PWID and ACCESS follows HIV-positive people who use illicit drugs (other than or in addition to cannabis) (19, 20). ARYS enrolls street-involved youth aged 14-26 years who use illicit drugs (other than or in addition to cannabis) (21). All participants had to reside in the Greater Vancouver region and provide informed consent at study enrollment.

All studies utilized harmonized recruitment and data collection tools, allowing for combined analyses. All eligible participants were invited to complete an interviewer-administered questionnaire to obtain information regarding their sociodemographic characteristics, HIV risk behaviour, substance use patterns, and engagement with health and social services. Participants were followed up every 6 months and were remunerated with $40 CAD for each visit. These studies have been

approved by the University of British Columbia/Providence Health Care Research Ethics Board.

Participants and Outcome Measure

VIDUS, ACCESS and ARYS participants aged ≥18 years who had completed at least one study visit between June 1, 2010 and November 30, 2014, had ever injected drugs, had ever used heroin or prescription opioids by injection or non-injection, and had provided at least one valid answer to the questions about availability of five opioids at each visit were included in this study. The five categories for opioids included: (1) heroin; (2) Percocet (oxycodone/acetaminophen), Vicodin (hydrocodone/acetaminophen) or Demerol (meperidine); (3) Dilaudid (hydromorphone); (4) Morphine; (5) Oxycontin/OxyNEO (controlled-release oxycodone). The assessment of oxycontin availability was switched to OxyNEO after May 31, 2012 as oxycontin was removed from the British Columbia formulary in March 2012. As in a previous study (8), substance availability was assessed based on the question "How difficult would it be for you to get the following drugs right now in the area where you typically obtain your drugs?" The responses were categorized at five levels: (1) within 10 minutes; (2) within 90 minutes; (3) within a day; (4) in more than a day; (5) could not access this drug. For the present analyses, the availability was dichotomized into two groups: immediate availability (within 10 minutes) and delayed (i.e., > 10 minutes) availability or not available. We focused on immediate availability as our sample had a history of injecting drug use and already had access to opioids.

Explanatory Variables

We selected explanatory variables that we hypothesized might affect the availability of illicit and prescribed opioids based on previous studies (8, 13, 22). In addition to sex (male vs. female), age (per 10 years increase), and ethnicity/ancestry (Caucasian vs. others), we considered the following social and structural exposures: homelessness; incarceration (held overnight in jail, prison or a penitentiary at least once within the past six months); drug dealing; and sex work within the past six months. We also included residence in Downtown Eastside (DTES), one of the largest open drug scenes in North America, within the past six months as proximity to this area may predict higher accessibility to opioids (21). Substance-using behaviors and outcomes in the past six months included at least daily injection of prescription opioids (OxyNEO, oxycontin, Percocet, Tylenol 3, morphine, Dilaudid, Demerol, methadone, fentanyl, Vicodin, or Talwin), heroin, cocaine, and methamphetamine, respectively, at least daily crack smoking, heavy alcohol use (as defined by the National Institute on Alcohol Abuse and Alcoholism: an average of >three drinks per occasion, or >seven drinks per week among females, and an average of >four drinks per occasion, or >14 drinks per week among males), and non-fatal overdose. Variables related to healthcare access during the past six months included: enrollment in methadone maintenance therapy (MMT), experiencing barriers to accessing healthcare such as not having a regular physician and discrimination for being on MMT (any vs. none), and having tried but unable to access addiction treatment services. A history of having ever been refused a pain medication was also included as a time-updated variable. Lastly, we included calendar year of interview (per year increase) and cohort designation (ACCESS vs.

ARYS vs. VIDUS). All variables referring to behaviors and events during the past six months were treated as time-varying variables.

Statistical Analysis

To start, we examined the baseline sample characteristics stratified by availability of heroin and compared using the Pearson's Chi-squared test for categorical variables and Wilcoxon Rank Sum test for continuous variables. To analyze factors that we hypothesized to be associated with accessibility to opioids obtained from serial data for each participants, we used univariable and multivariable generalized estimating equations (GEE) that adjusted for multiple observations per person using an exchangeable working correlation structure. We started with univariable GEE analyses to examine factors associated with the availability of each of the five groups of opioids. We included all explanatory variables associated with availability of opioids at the level of $p < 0.10$ in univariable analyses in an initial full multivariable model and used an *a priori*-defined backward model selection procedure based on examination of quasilikelihood under the independence model criterion statistic (QIC). Specifically, we examined the QIC of the model, removed the variable with the largest *p*-value, built a reduced model, and continued this iterative process until we obtained a multivariable model with the lowest QIC value.

As a sub-analysis, we examined changes in the price of opioids during the study period. We presented the median and interquartile range of the price of each opioid for each calendar year. All statistical analyses were performed using SAS version 9.4 (SAS

Institute, USA). All tests of significance were two sided, and a $p < 0.05$ was selected for defining statistical significance.

RESULTS

During the study period, 2228 participants completed at least one study visit. We excluded 644 (29%) participants who never injected drugs, never used heroin, or prescription opioids, or did not have at least one valid answer to the availability of the five groups of opioids at each visit. In total, 1584 participants were included in this study. Among them, 564 (35.6%) were female, 981 (61.9%) reported Caucasian ancestry, and the median age at baseline was 41.9 years (interquartile range (IQR) = 30.3-49.3). The median number of visit per participant during the study period was 5 (IQR = 2-8). As shown in Table 1, 98 (6.2%) and 333 (21.0%) participants reported at least daily prescription opioid injection and heroin injection use within the past six months at baseline, respectively.

Figure 1 depicts changes in proportion of participants who reported immediate availability of each of the five groups of opioids investigated in this study. Between 2010 and 2014, there were increases in the proportion reporting immediate availability of all the opioids except for oxycontin/OxyNEO. Of note, the proportion of participants reported immediate availability to heroin increased from 77.3% in 2010 to 87.4% in 2014.

The results of the univariable and multivariable GEE analyses of factors associated with availability of the five groups of opioids are presented in Table 2 and 3. Calendar year of interview was independently and positively associated with

immediate availability of all five groups of opioids (adjusted odds ratio [AOR] ranging from 1.09 for morphine and Dilaudid to 1.13 for Percocet/Vicodin/Demerol; all $p < 0.05$) except for oxycontin/OxyNEO. DTES residence, recent involvement with drug dealing, and recent daily prescription opioid injection were independently and positively associated with immediate availability of all five groups of opioids (all $p < 0.05$).

At least daily heroin injection (AOR = 1.50, 95% confidence interval [CI]: 1.25-1.79), daily cocaine injection (AOR = 1.69, 95% CI: 1.24-2.32) and daily crack smoking (AOR = 1.23, 95% CI: 1.03-1.47) were independently and positively associated with immediate availability of heroin, but not other opioids. Heavy alcohol use, on the other hand, was negatively associated with immediate availability of heroin (AOR = 0.80, 95% CI: 0.68-0.93). Enrollment in MMT was independently and positively associated with immediate availability of heroin (AOR = 1.34, 95% CI: 1.16-1.55). History of being refused pain medication was independently and positively associated with immediate availability of all opioids ($p \leq 0.05$) except for heroin. Male sex was independently associated with immediate availability of Dilaudid only (AOR = 1.17, 95% CI: 1.02-1.34), and older age was independently and positively associated with immediate availability of Percocets/Vicodin/Demerol and OxyNEO/oxycontin (all $p < 0.05$).

In the sub-analysis, between 2010 and 2014, there was no change in the median price for all the opioids except for OxyNEO/oxycontin (Table 4), for which the median price had increased from $10 to $20 CAD per 40mg pill since 2010, and

Percocets/Vicodin/Demerol, for which the median price had increased from $3 to $5 CAD per pill. Otherwise, the price remained stable at a median of $10 CAD per pill.

DISCUSSION

Among these cohorts of PWID with history of opioid use in Vancouver, a significant increase in the immediate availability of illicit and prescription opioids (except for OxyNEO/oxycontin) was observed between 2010 and 2014. This increase persisted despite no significant change in their median prices of drugs, and even after accounting for potential confounders such as residence in drug scenes, engagement in drug dealing and high intensity opioid use. Male sex, older age, daily heroin or cocaine injection, daily crack smoking, enrollment in MMT, and history of being refused pain medications were independently and positively associated with immediate availability of some but not all formulations of illicit and prescription opioids.

Our findings suggest that previously reported increasing trends of prescription opioids availability documented between 2006 and 2010 among street drug-using populations in this setting were continuing to rise through to 2014 (8). This continued increase in the availability of prescription opioids is particularly worrisome as multiple strategies to reduce prescription opioids access have been implemented, including increasing awareness and education to healthcare professionals, enforcing prescription surveillance, and implementing policies to counter opioid use and overdose over the last five years (23). However, a significant decrease in immediate availability of oxycontin/OxyNEO was observed between 2010 and 2014 in our study. The decrease

was likely a result of the policy change regarding oxycontin and OxyNEO prescription. In 2012, oxycontin was removed and OxyNEO was restricted from the formulary in seven provinces in Canada, including British Columbia, and the provincial program covering the cost of these opioids was discontinued. OxyContin and OxyNEO were only prescribed to patients with chronic pain in situations where the physician requested Special Authority Approval for exceptional coverage supported with adequate rationale (24). The discontinuation of oxycontin and restriction of OxyNEO could contribute to the increasing demand in other illicit and prescription opioids, as previously hypothesized by Fischer & Keates (2012). The proposed rationale was that oxycontin and OxyNEO users resorted to using other prescription opioids such as hydromorphone and morphine as they had similar potency and potential for overuse (25, 26). At the same time of the discontinuation, an abuse-deterrent formulation of oxycontin, which was more difficult to crush or dissolve, was introduced to the market with intention to discourage use through injection or inhalation. The formulation was found to reduce the selection of oxycontin as the primary drug among a cohort of patients with opioid dependence who used prescription opioids as their primary drug from 35.6% to 12.8% after 21 months since the abuse-deterrent formulation was introduced (27). Sixty-six percent of the cohort reported switching to a different opioid, with heroin being the most common opioid people switched to as heroin was said to be easier to use, cheaper, and more readily available. This finding resonates with the increase in immediate heroin availability noted in our study. While our study cannot determine causation between the delisting of oxycontin and the increase in availability

of other illicit and prescription opioids, it is certainly an area that necessitates further research.

The observed increase in heroin availability in concurrence with the increase in prescription opioids availability is concerning from the public health perspective. Previous studies have suggested that heroin use patterns among PWID correspond with market availability of heroin – heroin users may reduce heroin use when supply is scarce, but actively seek heroin when it is available (28, 29). Therefore, the increasing availability of both heroin and prescription opioids may correspond with potentially increasing prevalence of PWID using both heroin and prescription opioids or transitioning back to heroin. Such trend is not benign as previous research had shown that PWID who use both heroin and prescription opioids and heroin alone may be at significantly higher risk of non-fatal overdose compared to PWID who uses prescription opioids alone (30). In view of the increasing trend in both heroin and prescription opioid availability, further research is necessary to clearly identify how prescription opioid use impacts heroin use among PWID.

Participation in MMT was found to be independently associated with immediate availability of heroin. MMT is commonly used to treat opioid use disorder (31), and therefore, it is plausible that PWID on MMT had a history of high intensity heroin use and consequently retained social network or other characteristics associated with more immediate access to heroin. However, MMT patients also have a high prevalence (55-61%) of concurrent chronic pain (32). Voon, Callon (33) found enrollment in MMT was associated with denial of analgesia and inadequate pain management. Among a cohort

PWID enrolled in MMT in Vancouver between 2011 and 2014, 61.1% of them reported self-management of pain due to perception of inadequate analgesia secondary to under-treatment of pain or opioid-induced hyperalgesia (34). Voon, Callon (35) had shown that patients who self-manage pain often did so via high-risk methods including injection of heroin and diverted opioids, which could explain the association between MMT enrollment and immediate availability to heroin. In contrast, we also find that those who have ever been denied pain medications were more likely to report immediate availability of all opioids except for heroin. Portenoy, Dole (36) found that patients with pain disorder and concurrent substance use disorder were less likely to receive adequate pain management due to various reasons such as difficulty in distinguishing pain from drug seeking behavior and tolerance. This may suggest that PWID with pain disorder were resorting to use of prescription opioids from street markets to attain sufficient pain management.

Our study also found that those who engaged in heavy alcohol use were less likely to report immediate availability of heroin. Few studies have analyzed the association between opioids and alcohol use. Anglin, Almog (37) and Hser, Anglin (38) both found an inverse relationship between alcohol consumption and heroin use among a cohort of heroin users. This could be due to the substitution effect of the two substances both being central nervous system depressants and prevalence of media highlighting the danger of mixing the two substances (39, 40). In addition, previous research had shown a reduction in alcohol intake among opioid users enrolled in MMT (41). However, more recent studies had shown a high concurrence of alcohol and opioid

use, estimated at between 35-47%, in PWID enrolled in MMT (42-44). A systemic review by Srivastava, Kahan (45) revealed no clear pattern between alcohol use and MMT among people with opioid dependence as fifteen studies reviewed concluded inconsistent patterns of alcohol use. The relationship between alcohol and opioid use is inconclusive but is an area that requires further research as it has clinical implications regarding prognosis and adherence to opioid use disorder treatment.

Our study is not without limitations. First, VIDUS, ARYS and ACCESS were not randomly sampled from PWID in Vancouver and therefore it is unclear to what extent the results of this study can be generalized. Second, as an observational study, our study is subjected to unmeasured confounders that may have impacted the true temporal trends or correlates of availability of each of the opioids assessed in this study. Third, the data was obtained from self-report of the participants and may be subjected to reporting bias. Lastly, this study does not account for fluctuating drug purity which may affect the availability of the substances.

In conclusion, the present study demonstrated an increasing immediate availability of heroin in concurrence with prescription opioids (morphine, Dilaudid and Percocet/Vicodin/Demerol) among opioid users in Vancouver between 2010 and 2014, which persisted after extensive adjustment for potential confounders. The increasing availability of heroin along with prescription opioids is particularly worrisome given the recent shift in opioid use pattern. Further research is needed to determine how prescription opioid use affect heroin use and how availability of both illicit and prescription opioids affect the opioid use patterns among PWID.

Acknowledgments:

The authors appreciate the study participants of ACCESS, VIDUS, and ARYS for their contribution to the research, as well as current and past researchers and staff.

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Table 1: Baseline characteristics of 1584 Opioid Users in Vancouver, Canada, 2010–2014.

Characteristic	Total *n* (%)	Heroin immediate availability n=1199 (75.7%)	Heroin delayed availability or not available N=384 (24.2%)	*P* - value
Sex (male)	1020 (64.4)	770 (64.2)	249 (64.8)	0.824
Age (median [IQR])	41.9 (30.3-49.3)	41.9 (30.3-49.0)	41.6 (30.4-50.5)	0.525
Caucasian	981 (61.9)	748 (62.4)	232 (60.4)	0.489
Homelessness[a]	473 (29.9)	379 (31.6)	94 (24.5)	0.008
Live in DTES[a]	919 (58.0)	779 (65.0)	140 (36.5)	<0.001
Involved in Drug Dealing[a]	408 (25.8)	358 (29.9)	50 (13.0)	<0.001
Involved in Sex Work[a]	176 (11.1)	148 (12.3)	28 (7.3)	0.006
≥ Daily PO Injection Drug Use[a]	98 (6.2)	86 (7.2)	11 (2.9)	0.002
≥ Daily Heroin Injection Use[a]	333 (21.0)	285 (23.8)	48 (12.5)	<0.001
≥ Daily Cocaine Injection Use[a]	87 (5.5)	81 (6.8)	6 (1.6)	<0.001
≥ Daily Meth Injection Use[a]	103 (6.5)	83 (6.9)	20 (5.2)	0.241
≥ Daily Crack Smoking[a]	359 (22.7)	300 (25.0)	59 (15.4)	<0.001
Heavy Alcohol Use[a]	259 (16.4)	182 (15.2)	77 (20.1)	0.026
Overdose[a]	127 (8.0)	100 (8.3)	27 (7.0)	0.411
Participated in MMT[a]	812 (51.3)	644 (53.7)	168 (43.8)	<0.001
Unable to Access Addiction Treatment[a]	131 (8.3)	100 (8.3)	31 (8.1)	0.879
Barrier to Access Healthcare[a]	354 (22.3)	266 (22.2)	88 (22.9)	0.765
Ever Refused Pain Medications	484 (30.6)	367 (30.6)	116 (30.2)	0.754
Incarceration[a]	166 (10.5)	139 (11.6)	27 (7.0)	0.011

Cohort Designation:				
ACCESS	515 (32.5)	389 (32.4)	125 (32.6)	0.613
ARYS	294 (18.6)	214 (17.9)	80 (20.8)	0.161
VIDUS	775 (48.9)	596 (49.7)	179 (46.6)	ref

DTES, Downtown East Side; PO, Prescription Opioids; IQR, interquartile range; MMT, methadone maintenance therapy; PO, prescription opioid. ACCESS: AIDS Care Cohort to evaluate Exposure to Survival Services. VIDUS: Vancouver Injection Drug Users Study. ARYS (At-Risk Youth Study).

[a] denotes activities/events in the past 6 months.

Table 2: Univariable and multivariable GEE analyses of factors associated with more immediate availability (within 10 minutes) to heroin, Percocets/Vicodin/Demerol, and Dilaudid among opioid users in Vancouver, Canada (*n*=1584).

	Heroin		Percocets/Vicodin/Demerol		Dilaudid	
Characteristic	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**
Calendar Year of Interview (Per year later)	1.08 (1.04-1.12)	1.12 (1.07 –1.16)	1.12 (1.08 - 1.15)	1.13 (1.09 – 1.17)	1.07 (1.04 - 1.11)	1.09 (1.05 – 1.12)
Sex (Male vs. female)	1.03 (0.87 - 1.22)		1.14 (0.99 - 1.30)		1.14 (1.00 - 1.31)	1.17 (1.02 – 1.34)
Age (Per 10 year increase)	1.11 (1.03 - 1.19)		1.29 (1.22 - 1.37)	1.11 (1.03 – 1.19)	1.22 (1.15 - 1.29)	
Ancestry (Caucasian vs. others)	0.95 (0.81 - 1.12)		0.95 (0.83 - 1.08)		1.00 (0.88 - 1.14)	
Homelessness[a] (Yes vs. no)	1.22 (1.05 - 1.41)		0.93 (0.82 - 1.04)		0.97 (0.86 - 1.10)	
DTES residence[a] (Yes vs. no)	2.46 (2.14 - 2.84)	2.26 (1.96 – 2.60)	1.88 (1.68 - 2.10)	1.82 (1.62 – 2.04)	2.00 (1.79 - 2.23)	1.93 (1.72 – 2.17)
Drug Dealing[a] (Yes vs. no)	1.70 (1.47 - 1.96)	1.53 (1.30 – 1.79)	1.25 (1.11 - 1.40)	1.28 (1.12 – 1.45)	1.27 (1.13 - 1.43)	1.25 (1.10 – 1.41)
Sex Work[a] (Yes vs. no)	1.45 (1.15 - 1.83)		1.05 (0.87 - 1.25)		1.08 (0.91 - 1.29)	
PO injection[a] (≥daily vs. <daily)	1.46 (1.11 - 1.92)	1.48 (1.10 – 1.99)	1.41 (1.15 - 1.74)	1.41 (1.14 – 1.74)	1.75 (1.39 - 2.21)	1.80 (1.41 – 2.30)
Heroin injection[a] (≥daily vs. <daily)	1.69 (1.45 - 1.97)	1.50 (1.25 – 1.79)	1.12 (0.99 - 1.27)		1.17 (1.03 - 1.32)	1.09 (0.96 – 1.25)
Cocaine injection[a] (≥daily vs. <daily)	2.04 (1.56 - 2.67)	1.69 (1.24 – 2.32)	1.41 (1.16 - 1.72)	1.20 (0.97 – 1.48)	1.41 (1.17 - 1.71)	1.19 (0.97 – 1.46)
Meth injection[a] (≥daily vs. <daily)	1.27 (1.00 - 1.62)		1.05 (0.86 - 1.28)		1.09 (0.90 - 1.31)	

Crack smoking[a] (≥daily vs. <daily)	1.49 (1.28 - 1.74)	1.23 (1.03 – 1.47)	1.13 (0.99 - 1.28)		1.10 (0.98 - 1.25)	
Heavy alcohol use[a] (Yes vs. no)	0.80 (0.68 - 0.93)	0.80 (0.68 – 0.93)	0.99 (0.87 - 1.13)		0.97 (0.85 - 1.11)	
Overdose[a] (Yes vs. no)	0.95 (0.77 - 1.16)		0.88 (0.75 - 1.03)		1.01 (0.86 - 1.19)	
Participated in MMT[a] (Yes vs. no)	1.36 (1.19 - 1.55)	1.34 (1.16 – 1.55)	1.19 (1.06 - 1.33)		1.18 (1.05 - 1.32)	1.12 (0.99 – 1.26)
Unable to access addiction treatment[a] (Yes vs. no)	0.95 (0.76 - 1.18)		0.81 (0.66 - 1.00)		0.89 (0.72 - 1.09)	
Barrier to healthcare[a] (Any vs. none)	0.91 (0.79 - 1.04)		0.91 (0.81 - 1.03)		0.96 (0.86 - 1.08)	
Ever refused pain medications[b] (Yes vs. no)	1.22 (1.06 - 1.40)		1.37 (1.22 - 1.54)	1.13 (1.01 – 1.27)	1.36 (1.21 - 1.53)	1.19 (1.05 – 1.34)
Incarceration[a] (Yes vs. no)	1.17 (0.96 - 1.43)		0.89 (0.75 - 1.06)		0.99 (0.83 - 1.18)	
Cohort designation:						
(ACCESS vs. VIDUS)	0.92 (0.77 - 1.10)	0.96 (0.81 – 1.14)	1.01 (0.88 - 1.16)	1.04 (0.90 – 1.19)	0.99 (0.86 - 1.14)	1.03 (0.90 – 1.19)
(ARYS vs. VIDUS)	0.55 (0.44 - 0.69)	0.65 (0.51 – 0.82)	0.42 (0.34 - 0.51)	0.56 (0.43 – 0.72)	0.48 (0.40 - 0.59)	0.54 (0.44 – 0.67)

GEE: generalized estimating equations. OR: odds ratio. CI: confidence interval. DTES: Downtown Eastside. PO: prescribed opioids. MMT: methadone maintenance therapy. ACCESS: AIDS Care Cohort to evaluate Exposure to Survival Services. VIDUS: Vancouver Injection Drug Users Study. ARYS (At-Risk Youth Study).

[a] Denotes activities in the previous six months.

[b] Time-updated.

Table 3: Univariable and multivariable GEE analyses of factors associated with more immediate availability (within 10 minutes) to morphine and oxycontin/OxyNEO among opioid users in Vancouver, Canada (*n*=1584).

	Morphine		Oxycontin/OxyNEO	
Characteristic	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**
Calendar Year of Interview (Per year later)	1.07 (1.04 - 1.11)	1.09 (1.05 – 1.12)	0.95 (0.92 - 0.98)	0.96 (0.93 – 0.99)
Sex (Male vs. female)	1.10 (0.96 - 1.26)		1.09 (0.96 - 1.24)	
Age (Per 10 year increase)	1.23 (1.16 - 1.30)		1.17 (1.11 - 1.24)	1.08 (1.00 – 1.16)
Ancestry (Caucasian vs. others)	0.98 (0.86 - 1.12)		0.97 (0.86 - 1.10)	
Homelessness[a] (Yes vs. no)	0.99 (0.89 - 1.12)		1.02 (0.90 - 1.15)	
DTES residence[a] (Yes vs. no)	2.08 (1.87 - 2.32)	2.03 (1.81 – 2.27)	1.90 (1.71 - 2.11)	1.79 (1.61 – 2.00)
Drug Dealing[a] (Yes vs. no)	1.24 (1.10 - 1.40)	1.23 (1.09 – 1.39)	1.23 (1.09 - 1.39)	1.24 (1.09 – 1.40)
Sex Work[a] (Yes vs. no)	1.10 (0.92 - 1.31)		1.13 (0.95 - 1.34)	
PO injection[a] (≥daily vs. <daily)	1.70 (1.35 - 2.14)	1.78 (1.40 – 2.27)	1.46 (1.16 - 1.84)	1.39 (1.11 – 1.75)
Heroin injection[a] (≥daily vs. <daily)	1.16 (1.03 - 1.31)		1.10 (0.97 - 1.25)	
Cocaine injection[a] (≥daily vs. <daily)	1.40 (1.15 - 1.71)	1.20 (0.97 – 1.47)	1.42 (1.16 - 1.74)	1.22 (0.99 – 1.51)
Meth injection[a] (≥daily vs. <daily)	1.14 (0.94 - 1.38)		1.04 (0.85 - 1.26)	

Crack smoking[a] (≥daily vs. <daily)	1.14 (1.00 - 1.29)		1.19 (1.04 - 1.35)	
Heavy alcohol use[a] (Yes vs. no)	1.00 (0.87 - 1.14)		1.01 (0.88 - 1.17)	
Overdose[a] (Yes vs. no)	0.96 (0.81 - 1.13)		0.82 (0.68 - 0.99)	0.86 (0.70 – 1.05)
Participated in MMT[a] (Yes vs. no)	1.18 (1.05 - 1.32)	1.09 (0.97 – 1.22)	1.11 (0.99 - 1.24)	
Unable to access addiction treatment[a] (Yes vs. no)	0.88 (0.72 - 1.07)		0.93 (0.75 - 1.15)	
Barrier to healthcare[a] (Any vs. none)	0.96 (0.86 - 1.08)		0.87 (0.77 - 0.98)	0.90 (0.79 – 1.01)
Ever refused pain medications[b] (Yes vs. no)	1.39 (1.24 - 1.57)	1.22 (1.08 – 1.37)	1.18 (1.05 - 1.32)	1.12 (1.00 – 1.26)
Incarceration[a] (Yes vs. no)	1.03 (0.87 - 1.22)		0.93 (0.78 - 1.11)	
Cohort designation:				
(ACCESS vs. VIDUS)	1.04 (0.91 - 1.20)	1.08 (0.94 – 1.24)	1.05 (0.92 - 1.19)	1.07 (0.94 – 1.22)
(ARYS vs. VIDUS)	0.47 (0.39 - 0.58)	0.54 (0.44 – 0.67)	0.53 (0.43 - 0.65)	0.75 (0.58 – 0.98)

GEE: generalized estimating equations. OR: odds ratio. CI: confidence interval. DTES: Downtown Eastside. PO: prescribed opioids. MMT: methadone maintenance therapy. ACCESS: AIDS Care Cohort to evaluate Exposure to Survival Services. VIDUS: Vancouver Injection Drug Users Study. ARYS (At-Risk Youth Study).

[a] Denotes activities in the previous six months.

[b] Time-updated.

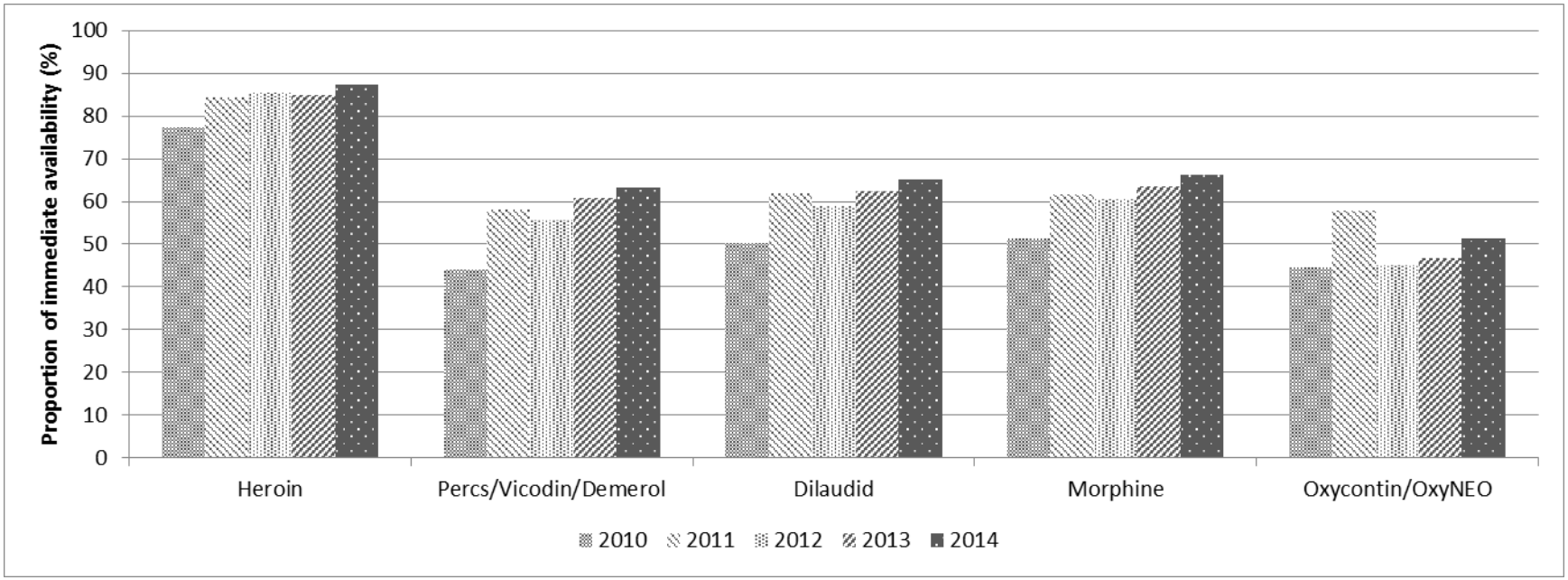

Figure 1. Proportion of ever-users of opioids in Vancouver, Canada indicating immediate availability (scoring within ≤10 minutes) from 2010-2014, n=1584

Table 4: Median retail price and unit of five groups of opioid between 2010 and 2014 reported by opioid users in Vancouver, Canada

Substance	Year	Median Price and Unit	Interquartile Range
Heroin	2010	10 CAD/half point	10 - 10
	2011	10 CAD/half point	10 - 10
	2012	10 CAD/half point	10 - 10
	2013	10 CAD/half point	10 - 10
	2014	10 CAD/half point	10 - 10
Percocet/Vicodin/Demerol	2010	3 CAD/pill	3 - 5
	2011	4 CAD/pill	3 - 5
	2012	4 CAD/pill	3 - 5
	2013	5 CAD/pill	3 - 5
	2014	5 CAD/pill	3 - 5
Dilaudid	2010	10 CAD/8mg pill	10 - 10
	2011	10 CAD/8mg pill	10 - 10
	2012	10 CAD/8mg pill	10 - 10
	2013	10 CAD/8mg pill	10 - 10
	2014	10 CAD/8mg pill	10 - 10
Morphine	2010	10 CAD/100mg pill	10 - 10
	2011	10 CAD/100mg pill	10 - 10
	2012	10 CAD/100mg pill	10 - 10
	2013	10 CAD/100mg pill	10 - 10
	2014	10 CAD/100mg pill	10 - 10
Oxycontin	2010	10 CAD/40mg pill	10 - 20
Oxycontin	2011	20 CAD/40mg pill	10 - 20
Oxycontin/OxyNEO	2012	20 CAD/40mg pill of oxycontin or 25mg pill of OxyNEO	10 - 20
OxyNEO	2013	20 CAD/25mg pill	10 - 20
OxyNEO	2014	20 CAD/25mg pill	10 - 20