

# INCREASING DIVERSION OF METHADONE IN VANCOUVER, CANADA, 2005-2015

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## ABSTRACT

**Background and Aim:** Although methadone, an opioid agonist, has been an effective medication used to treat opioid use disorder for over 40 years, recent studies have found that methadone was identified in more than a quarter of prescription opioid-related deaths among people who use illicit drugs **in Vancouver, Canada**. Thus, we sought to longitudinally examine the availability of diverted methadone among people who inject drugs (PWID).

**Design and Methods:** Data were collected from three prospective cohorts of PWID in Vancouver, Canada between December 2005 and May 2015. Multivariable generalized estimating equation logistic regression was used to identify temporal trends in the immediate availability of diverted methadone (defined as the ability to acquire illicit methadone in <10 minutes).

**Results:** A total of 2092 participants, including 727 (34.8%) women, were included in the present study. In the multivariable analyses after adjusting for a range of potential confounders, later calendar year (adjusted odds ratio [AOR] = 1.21 per year; 95% confidence interval [CI]: 1.19–1.23) was independently and positively associated with reporting immediate availability of diverted methadone.

**Conclusions:** We observed a significant increase in the reported availability of diverted methadone among PWID over a ten-year follow-up period. Further research is needed to identify strategies to limit methadone diversion and assess the impact of alternative medications that are equally effective but safer, such as buprenorphine/naloxone.

**Word Count:** 221

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# 1. INTRODUCTION

In the past decade, opioid use disorder (OUD) has become a major public health challenge in Canada and the United States (Gomes et al., 2011; United Nations Office on Drugs and Crime, 2014). Increases in the availability of heroin and other illicit opioids, significant increase in opioid prescription, and diversion of prescription opioids have contributed to the morbidity and mortality associated with OUD (Carter, 2012; Compton, Jones, & Baldwin, 2016; King, Fraser, Boikos, Richardson, & Harper, 2014; Nosyk et al., 2012). Specific consequences of OUD include increased risk of blood-borne disease including viral hepatitis and HIV, as well as opioid related overdose and death (Peters et al., 2016; Suryaprasad et al., 2014; Zibbell, Hart-Malloy, Barry, Fan, & Flanigan, 2014) (Dart et al., 2015; Fischer, Jones, & Rehm, 2013; Gomes et al., 2014).

Methadone maintenance therapy (MMT) is a longstanding pharmacotherapy prescribed for OUD (Nosyk, Marsh, Sun, Schechter, & Anis, 2010). In British Columbia, Canada, MMT clinical practice guidelines were introduced in 1995 and have been expanded to include strategies to monitor and titrate daily dosing, treatment initiation, maintenance dosing, and take-home doses (College of Physicians and Surgeons of British Columbia, 2005; Payte, 1995). With an exemption under section 56 of the Controlled Drugs and Substances Act, primary care physicians can prescribe methadone that is dispensed through community pharmacies. Between 1996 and 2016, the number of patients receiving

methadone has increased nearly six-fold in British Columbia (Nosyk et al., 2010; Office of the Provincial Health Officer, 2017). MMT has been shown to effectively decrease illicit opioid use, reduce rates of hepatitis C and HIV infection among people who inject drugs (PWID) and improve antiretroviral adherence and virologic outcomes among people living with HIV (Gowing, Farrell, Bornemann, Sullivan, & Ali, 2011; Low et al., 2016; MacArthur et al., 2012; Perlman et al., 2015).

However, the risk of toxicity and adverse events associated with methadone is greater than other prescription opioids due to the narrow therapeutic index, long and highly variable half-life, and potential for drug-drug interactions (British Columbia Centre on Substance Use, 2017; Webster et al., 2011). In the United States, the rate of methadone related emergency room visits has been found to be approximately six times greater than prescription oxycodone and 23 times greater than prescription hydrocodone **after adjusting for the total number of prescriptions dispensed** (Substance Abuse and Mental Health Services Administration 2013; Webster et al., 2011). **While methadone prescription has been linked to diversion and methadone-related overdose in several countries, some settings have successfully expanded methadone programs without an increase in mortality risk** (Fugelstad, Lars, & Thiblin, 2010; Iwersen-Bergmann et al., 2014; Morgan, Griffiths, & Hickman, 2006; Strang, Hall, Hickman, & Bird, 2010). In the United States, methadone was identified in more than a third of opioid-related deaths in 2009 despite representing 5-19% of all opioid prescriptions per year (Centers for Disease & Prevention, 2012). **Although recent**

**data have shown a decrease in methadone-related overdose deaths in the United States, they still accounted for 3400 overdose deaths in 2014 (Jones, Baldwin, Manocchio, White, & Mack, 2016). A recent study from British Columbia, Canada, reported similar results and found that methadone was involved in 25% of opioid-related deaths (Gladstone, Smolina, & Morgan, 2016). Thus, there seems to be regional differences in whether or not methadone prescription is associated with increases in overdose mortality.**

Many factors have been consistently associated with methadone-related overdose. These factors include non-prescribed, diverted and illicit use of methadone, as well as polysubstance use involving alcohol and benzodiazepines (Duffy P, 2014; Jones et al., 2016; Strang et al., 2010; Tjagvad et al., 2016). However, few studies have examined the diverted methadone market. **A recent study from the United States indicated methadone prescription for pain, as opposed to treatment for OUD, was the primary source of diversion, although other evidence indicates that this may be moderated by regional differences in prescription programs and the accessibility of methadone (Johnson & Richert, 2015b; Jones et al., 2016). While the primary source of methadone diversion in Vancouver, Canada is uncertain, previous studies reported that there were 344 active prescribers of methadone for OUD in 2012, compared to 685 who were authorized to prescribe methadone for analgesia, with a significant proportion being pain or palliative care specialists (Hawley, 2012; Office of the Provincial Health Officer, 2017). Given the association between methadone diversion and**

**methadone-related overdose**, we sought to longitudinally examine the availability of diverted methadone among three community-recruited prospective cohorts of PWID in Vancouver, British Columbia.

## 2. METHODS

### 2.1 Study Procedure

The data for this investigation were obtained from three ongoing open prospective cohort studies of people who use drugs: the Vancouver Injection Drug Users Study (VIDUS), the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS), and the At-Risk Youth Study (ARYS). These studies have been described in detail previously (Tyndall et al., 2003; Wood, Stoltz, Montaner, & Kerr, 2006). To provide a brief overview, VIDUS enrolls HIV-negative people who inject drugs, ACCESS enrolls HIV-positive people who use illicit drugs other than or in addition to cannabis (Strathdee et al., 1998; Wood et al., 2009) and ARYS enrolls street-involved youth who use illicit drugs, other than or in addition to cannabis, and are 14-26 years old (Wood et al., 2006). Participants in all three studies have to reside in the Greater Vancouver region and provide informed consent at study enrollment.

Data related to sociodemographic information, substance use patterns, HIV risk behavior and engagement with health and social services including addiction treatment were collected through an interview-administered questionnaire at baseline and semi-annually over follow-up. All three studies applied harmonized

recruitment and data collection methods to facilitate pooled analyses. Participants are remunerated \$30 CAD for each study visit. These studies have been approved by the University of British Columbia/Providence Health Care Research Ethics Board.

## 2.2 Participants and Outcome Measure

This study included all VIDUS, ACCESS and ARYS participants aged  $\geq 18$  years who had reported ever injecting drugs or initiated injecting during follow-up, completed at least one study visit between December 2005 and May 2015, had ever used heroin or any prescription opioid by injection or non-injection, and provided a valid answer to questions regarding the availability of diverted methadone. **The sample was restricted to people who inject drugs or people with a history of injection drug use since they are at a high risk of experiencing harms associated with diverted methadone such as overdosing (Kerr et al., 2007).** The primary outcome of interest was diverted methadone availability from street-based sources, which was derived from a question, “How difficult would it be for you to get street methadone right now in the area where you typically obtain your drugs?” The five response options included (1) within 10 minutes; (2) within 90 minutes; (3) within a day; (4) in more than a day; (5) could not access this drug. These categories were collapsed to create a three-level categorical variable for this study: (1) immediate availability (within 10 minutes); (2) delayed availability (i.e.,  $> 10$  minutes); and (3) not available. **Since very few participants selected responses (2)-(4) (i.e., within 90 minutes; within a day; in more than a day),** these

categories were collapsed to create a three-level categorical variable for this study: 1) immediate availability (within 10 minutes); (2) delayed availability (i.e., > 10 minutes); and (3) not available. **Retaining response options with small sample sizes can lead to unstable effect estimates, and combining these response options mitigated this issue (MacCallum, 1999).** We examined correlates of immediate and delayed availability of diverted methadone, respectively, against no availability.

### 2.3 Explanatory Variables

In order to examine temporal trends of the availability of diverted methadone, we included calendar year of interview (per year later) as the primary explanatory variable. The selection of additional explanatory variables that may impact the association between the primary explanatory variable and the availability of diverted methadone was based on existing literature (Hadland et al., 2010; Lake et al., 2015; Nosyk et al., 2012). These variables included socio-demographic factors such as age (per 10 years older), sex (male vs. female), ethnicity/ancestry (white vs. others), residing in the Downtown Eastside (DTES) neighborhood of Vancouver which contains a large open drug scene (yes vs. no), cohort designation (ARYS vs. ACCESS vs. VIDUS [the reference category]) and homelessness (yes vs. no). Drug use patterns included: crack smoking ( $\geq$  daily vs. < daily); injection heroin use ( $\geq$  daily vs. < daily); injection cocaine use ( $\geq$  daily vs. < daily); injection crystal methamphetamine use ( $\geq$  daily vs. < daily); injection of prescription opioids ( $\geq$  daily vs. < daily); and non-fatal overdose (yes vs. no).



Variables related to health and social service utilization included: enrollment in MMT (yes vs. no), and having tried but been unable to access addiction treatment services (yes vs. no or never tried). Other social and structural exposures included: incarceration (yes vs. no); involvement in drug dealing (yes vs. no); and involvement in sex work (yes vs. no). Variable definitions were consistent with previous studies and all behavioral variables referred to the previous 6 months (Wood et al., 2001).

## **2.4 Statistical Analysis**

As a first step, we analyzed the baseline sample characteristics stratified by availability of diverted methadone (immediate vs. delayed vs. no availability), using Cochran-Armitage trend test for categorical variables and Kruskal-Wallis test for continuous variables. We also graphically illustrated temporal trends in the availability during the study period. Since repeated measures were available for each participant, we applied generalized estimating equation (GEE) logistic regression for the analysis of correlated data. By using an exchangeable correlation structure that adjusts for multiple observations for each participant, this method identified factors associated with the outcome across the entire study period. The initial multivariable model included all explanatory variables associated with diverted methadone availability at the level of  $p < 0.10$  in bivariable analyses. Through a manual stepwise approach, reduced models were built by removing one secondary explanatory variable at a time that produced the smallest relative change in the calendar year coefficient. This process was repeated until the

minimum change in the calendar year coefficient surpassed five percent. The objective of this technique is to retain covariates with a larger relative impact on the association between the primary explanatory variable and the outcome (Maldonado & Greenland, 1993).

We also performed a sub-analysis to examine changes in the self-reported price of diverted methadone during the study period. The median price of diverted methadone was presented for each calendar year. All statistical analyses were performed using SAS version 9.4 (SAS Institute, USA). All tests of significance were two sided.

### **3. RESULTS**

During the study period (December 2005 and May 2015), a total of 2092 participants enrolled in the VIDUS, ACCESS or ARYS were eligible for the present study. The median age of participants was 37.3 (interquartile range [IQR] = 26.2-45.9) years at baseline. Seven hundred and twenty-seven (34.8%) were females and 1324 (63.3%) were white. Participants completed a median of six study visits (IQR = 2-12) and the median observation time per participant was 49.0 months (IQR = 12.0-92.0). At baseline, 601 (28.7%) participants reported having immediate access to diverted methadone, 387 (18.5%) individuals reported delayed availability, and 1104 (52.8%) participants were not able to access diverted methadone.

Baseline characteristics of the study sample stratified by diverted methadone availability are shown in Table 1. Factors that differed across diverted

methadone availability strata included age, sex, homelessness, DTES residence, involvement in drug dealing, prescription opioid injection, participation in MMT and being unable to access addiction treatment (all  $p < 0.05$ ). Unadjusted temporal trends in the availability of diverted methadone are illustrated in Figure 1.

Table 2 includes two models showing the bivariable and multivariable GEE analyses of the temporal trends of the availability of diverted methadone. Model 1 analyzed trends of the immediate availability (vs. not available) and the adjusted analysis revealed that calendar year remained independently and positively associated with immediate availability (adjusted odds ratio [AOR] = 1.21; 95% confidence interval [CI]: 1.19–1.23). Model 2 analyzed trends of the delayed availability (vs. not available) and in the adjusted model, the calendar year (AOR = 1.21; 95% CI: 1.19–1.23) was also independently and positively associated with delayed availability. The median **self-reported** price of diverted methadone remained at \$10 CAD per 100mg in every calendar year of follow-up.

#### 4. DISCUSSION

In the present study, we observed a significant increase in the reported availability of diverted methadone among a community-recruited sample of PWID in Vancouver between 2005 and 2015 even after adjustment for a range of potential demographic, behavioural and social-structural confounders. The price of diverted methadone remained consistent at \$10 CAD per 100mg over the ten-

year follow-up period, with a median price of \$10 CAD per 100mg reported at every year of the study period. This price was substantially less than that identified from studies in the United States, which reported a price of approximately \$20 US per 80mg dose (Gwin Mitchell et al., 2009).

A number of existing studies have contextualized the illicit market for methadone and buprenorphine (Cicero & Inciardi, 2005; Spunt, 1986). This market is different from the trafficking of other illicit opiates such as heroin, in that it consists of several individuals, primarily, patients undergoing opioid agonist therapy, who are selling small quantities of their prescription medication (Agar, 1977; Fountain, Strang, Gossop, Farrell, & Griffiths, 2000). A number of individual, social and structural risk factors for diversion have also been identified. Three consistently recognized risk factors for a patient diverting their medication include current illicit drug use, previous experience of purchasing illicit methadone or buprenorphine and socializing with active drug users (Johnson & Richert, 2015b). Supervised dosing and strict collection routines were associated with a decreased risk of diversion in some studies, yet other studies did not report this association to be significant (Dale-Perera, 2012; Duffy & Baldwin, 2012; Spunt, 1986; Winstock, Lea, & Sheridan, 2008). Specific diversion methods have been understudied, but obtaining more than one prescription (multiple prescription) and exaggerating the severity of drug addiction to receive a higher dose (overprescription) have been reported as strategies by methadone patients (Fountain, 1998). The two primary motives for

diversion include a financial need, which may or may not involve supporting existing drug use, and altruistic motives to support others who are experiencing withdrawal. Ethnographic researchers have identified that people who use drugs often develop a norm system where it is considered unethical to not share drugs with friends or acquaintances who are suffering from withdrawal. This has been termed 'a moral economy of sharing' that is based on empathizing with others in withdrawal and can also be influenced by the expectation that the recipient will pay for the medication (Bourgois, 1998; Bourgois, & Schonberg, 2009; Havnes, Clausen, & Middelthon, 2013). The altruistic motive may be a more significant factor since a previous study reported 'helping others' was cited as a motive for diversion by 90% of participants while only 40% reported 'financial need' as the purpose (Johnson & Richert, 2015c)

Increased diversion of methadone from opioid agonist therapy has been associated with methadone-related fatalities in several countries (Jones et al., 2016; Morgan et al., 2006; Seymour et al., 2003; Strang et al., 2010). Our results suggest that methadone diversion may have increased between 2005 and 2015, coinciding with a steady expansion of MMT programs in this setting during this period (College of Physicians and Surgeons of British Columbia, 2014). **During the study period, the total number of patients receiving methadone in British Columbia increased from approximately 8,000 in 2005, to 16,900 in 2015 (Office of the Provincial Health Officer, 2017) (Office of the Provincial Health Officer, 2013).** However, between 2006/2007 and 2007/2008, the number of active

methadone prescribers decreased from over 400 to less than 300. This may be reflected in our trend data (Figure 1), which indicate a plateau in the availability of illicit methadone from 2007 to 2011. Between 2011 and 2015, the number of active opioid agonist therapy prescribers increased from 328 to 401 (Office of the Provincial Health Officer, 2013; Office of the Provincial Health Officer, 2017).

In addition to concerns regarding methadone diversion, the risk of toxicity and adverse events associated with methadone provoked policy change for the treatment of OUD. In 2017, health authorities in British Columbia also released new OUD treatment guidelines, which recommended replacing methadone with buprenorphine-naloxone as the preferred first-line opioid agonist therapy due to the improved public safety profile with similar treatment efficacy (British Columbia Centre on Substance Use, 2017; Dunlap & Cifu, 2016). This guideline also proposed a range of more stringent guidelines including urine drug screening and unannounced medication checks for those with take home dosing as a strategy to reduce diversion. **While our findings provide support for such change, the control and support measures should incorporate existing evidence from illicit methadone markets. Increased dosing supervision significantly reduced methadone-related mortality among methadone programs in Scotland and England, yet stringent supervision can also decrease the autonomy of patients, be perceived as an indignity and create an obstacle to gainful employment (Johnson & Richert, 2015b; Morgan et al., 2006; Strang et al., 2010). Patients who**

are regular diverters also seem to be relatively unaffected by the threat of sanctions, which suggests that broad increases in controls may have little effect on these diverters and impose unnecessary restrictions on rule following patients (Johnson & Richert, 2015b). A more promising strategy for minimizing diversion may be improved management of comorbid psychological and physical health issues among opioid agonist therapy patients. Ongoing illicit drug use and heavy alcohol consumption are associated with diversion, and may represent forms of self-medication for unmanaged psychological and physical symptoms. Sustained follow-up with patients to evaluate dosing protocols and side effects is also recommended since these issues are potential triggers for diversion (Johnson & Richert, 2015b). Increasing the accessibility of buprenorphine-naloxone in opioid agonist therapies is also likely to improve health outcomes among patients with OUD.

Buprenorphine-naloxone is generally viewed to be equally effective for reducing illicit opioid use and sustaining treatment enrolment as methadone (Kakko et al., 2007; Mattick, Breen, Kimber, & Davoli, 2014; Nielsen et al., 2016). The advantages of buprenorphine-naloxone include a decreased risk of overdose due to its partial agonist effect, reduced public-health risk with diversion and injection based on the naloxone component, milder side effect profile and fewer drug-drug interactions (Bell, Butler, Lawrance, Batey, & Salmelainen, 2009; Chou, Weimer, & Dana, 2014; D'Amore et al., 2011). In addition, buprenorphine-naloxone may be more cost effective than methadone since the shorter induction

period and more flexible take-home dosing schedules reduce pharmacy dispensing costs and require fewer clinical visits to achieve a stable dose (Auriacombe, Franques, & Tignol, 2001; CADTH Rapid Response Reports, 2013). **Although there is a decreased risk of diversion with buprenorphine-naloxone due to a lower abuse potential and lower street value, diversion and misuse of buprenorphine-naloxone is still a concern for opioid agonist therapy programs (Johnson & Richert, 2015a).** A recent study of patients receiving buprenorphine for opioid detoxification found that sharing medication was perceived as a normative behaviour and 50% of the patients studied reported sharing their medication in the past (Kenney, Anderson, Bailey, & Stein, 2017). There is evidence that methadone may be preferable to buprenorphine-naloxone for individuals at a high risk of dropout or for those who continue to experience withdrawal symptoms despite receiving an optimal buprenorphine-naloxone dose (Srivastava, Kahan, & Nader, 2017). Buprenorphine-naloxone induction can also produce severe precipitated withdrawal if the induction is done incorrectly, which does not occur with methadone treatment (Rosado, Walsh, Bigelow, & Strain, 2007). However, the partial agonist effect of buprenorphine-naloxone makes it more manageable for patients to switch from buprenorphine-naloxone to methadone if needed, which supports buprenorphine-naloxone as the preferred first-line option if contraindications are not present (Breen et al., 2003; Walsh et al., 1995). Based on the many advantages of buprenorphine-naloxone over



methadone, these guidelines may help to alleviate morbidity and mortality among PWID living with OUD in our setting.

The major strength of this study is the prospective cohort design, which permitted the analysis of multiple independent correlates of diverted methadone availability over a ten-year follow-up period. This study also has several limitations. Since the participants were not randomly recruited, these results may not be generalizable to PWID in this and other settings. While self-report methods generally provide valid and reliable measurements among PWID, socially desirable responding and recall bias remain concerns (Darke, 1998). Lastly, there is a possibility that residual confounding may have impacted the associations with diverted methadone availability since this is an observational design.

In summary, we found that the availability of diverted methadone among PWID significantly increased between 2005 and 2015. Given the increasing concerns of diverted methadone and methadone-related overdose, it is encouraging that buprenorphine-naloxone has been endorsed as a preferred first-line treatment for OUD. Since methadone is still recommended for patients who are ineligible for buprenorphine-naloxone, interventions to reduce methadone diversion must consider how treatment access for those seeking treatment for OUD will be affected. Local guidelines have recently recommended strategies to reduce diversion, and future evaluation should examine the impacts of these changes (British Columbia Centre on Substance Use, 2017).

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**Table 1: Baseline characteristics stratified by diverted methadone availability among opioid users in Vancouver, Canada, 2005-2015 (n = 2092).**

	Diverted methadone Availability			p-value
	Not Available (n=1104) n (%)	Delayed Availability (n=387) n (%)	Immediate Availability (n=601) n (%)	
<b>Age (per additional year)</b>				
Median	37.9	34.1	38.8	<b>&lt;0.001</b>
IQR	(26.8 – 45.9)	(23.7 – 44.3)	(28.3 – 46.9)	
<b>White</b>				
Yes	671 (50.7)	271 (20.5)	382 (28.9)	0.126
No	433 (56.4)	116 (15.1)	219 (28.5)	
<b>Female</b>				
Yes	412 (56.6)	119 (16.4)	196 (27.0)	<b>0.030</b>
No	692 (50.7)	268 (19.6)	405 (29.7)	
<b>Homeless<sup>A</sup></b>				
Yes	472 (49.9)	186 (19.6)	289 (30.5)	<b>0.022</b>
No	630 (55.3)	199 (17.5)	310 (27.2)	
<b>DTES residence<sup>A,B</sup></b>				
Yes	662 (49.8)	212 (16.0)	455 (34.2)	<b>&lt;0.001</b>
No	442 (57.9)	175 (22.9)	146 (19.2)	
<b>Dealing drugs<sup>A</sup></b>				
Yes	377 (44.8)	155 (18.4)	309 (36.8)	<b>&lt;0.001</b>
No	727 (58.1)	232 (18.5)	292 (23.4)	
<b>Sex work involvement<sup>A</sup></b>				
Yes	186 (53.7)	65 (18.8)	95 (27.5)	0.570
No	911 (52.5)	320 (18.4)	505 (29.1)	
<b>Prescription opioid injection<sup>A</sup></b>				
≥ daily	65 (44.5)	23 (15.8)	58 (39.7)	<b>0.006</b>
< daily	1036 (53.4)	364 (18.8)	541 (27.8)	
<b>Injection heroin use<sup>A</sup></b>				
≥ daily	346 (52.5)	111 (16.9)	201 (30.6)	0.491
< daily	756 (52.8)	276 (19.3)	400 (27.9)	
<b>Injection cocaine use<sup>A</sup></b>				
≥ daily	90 (53.6)	19 (11.3)	59 (35.1)	0.398
< daily	1010 (52.6)	368 (19.2)	542 (28.2)	
<b>Injection methamphetamine use<sup>A</sup></b>				
≥ daily	58 (40.6)	37 (25.8)	48 (33.6)	0.152
< daily	1042 (53.6)	350 (18.0)	552 (28.4)	
<b>Non-injection crack use<sup>A</sup></b>				

≥ daily	402 (52.3)	121 (15.8)	245 (31.9)	0.152
< daily	701 (53.0)	265 (20.1)	356 (26.9)	
<b>Non-fatal overdose<sup>A</sup></b>				
Yes	121 (48.7)	48 (19.4)	79 (31.9)	0.174
No	980 (53.3)	339 (18.4)	521 (28.3)	
<b>Participated in MMT<sup>A</sup></b>				
Yes	402 (48.2)	162 (19.5)	269 (32.3)	<0.001
No	697 (55.9)	223 (17.9)	328 (26.2)	
<b>Unable to access addiction treatment<sup>A</sup></b>				
Yes	83 (40.7)	49 (24.0)	72 (35.3)	0.001
No	1015 (54.1)	336 (17.9)	525 (28.0)	
<b>Incarceration<sup>A</sup></b>				
Yes	214 (50.8)	82 (19.5)	125 (29.7)	0.481
No	882 (53.1)	305 (18.3)	475 (28.6)	
<b>Cohort designation</b>				
ACCESS	301 (50.3)	114 (19.0)	184 (30.7)	0.307
ARYS	239 (49.4)	126 (26.0)	119 (24.6)	
VIDUS	564 (55.9)	147 (14.6)	298 (29.5)	

<sup>A</sup> denotes activities in the six months prior to follow-up interview

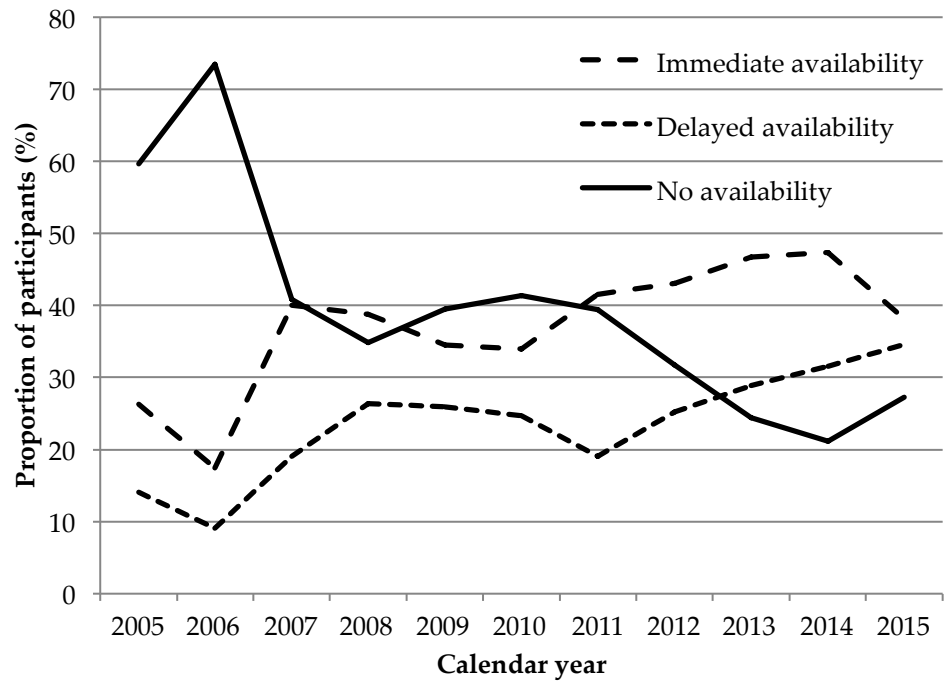
<sup>B</sup>DTES – Downtown Eastside; MMT – Methadone Maintenance Therapy; ACCESS – AIDS Care Cohort to Evaluate Exposure to Survival Services; VIDUS – Vancouver Injection Drug Users Study; ARYS – At-Risk Youth Study.



(≥ daily vs. <daily)	1.07 (0.92 – 1.25)	0.362			0.82 (0.69 – 0.98)	<b>0.032</b>
<b>Injection methamphetamine use<sup>A</sup></b>						
(≥ daily vs. <daily)	1.17 (0.98 – 1.41)	0.078			1.21 (0.99 – 1.47)	0.063
<b>Non-injection crack use<sup>A</sup></b>						
(≥ daily vs. <daily)	0.92 (0.84 – 1.01)	0.075			0.78 (0.70 – 0.87)	<b>&lt;0.001</b>
<b>Non-fatal overdose<sup>A</sup></b>						
(yes vs. no)	1.01 (0.88 – 1.17)	0.891			1.13 (0.96 – 1.33)	0.147
<b>Participated in</b>						
(yes vs. no)	1.51 (1.37 – 1.66)	<b>&lt;0.001</b>			1.57 (1.42 – 1.75)	<b>&lt;0.001</b>
<b>Unable to access addiction treatment<sup>A</sup></b>						
(yes vs. no)	1.03 (0.89 – 1.19)	0.695			1.19 (1.00 – 1.41)	<b>0.049</b>
<b>Incarceration<sup>A</sup></b>						
(yes vs. no)	0.82 (0.73 – 0.93)	<b>0.001</b>			0.89 (0.77 – 1.02)	0.101
<b>Cohort designation</b>						
(ACCESS vs. VIDUS)	0.98 (0.86 – 1.10)	0.710	0.85 (0.75 – 0.96)	<b>0.010</b>	0.98 (0.86 – 1.11)	0.721
(ARYS vs. VIDUS)	0.50 (0.42 – 0.60)	<b>&lt;0.001</b>	1.16 (1.08 – 1.24)	<b>&lt;0.001</b>	0.99 (0.84 – 1.17)	0.931

<sup>A</sup>Refers to the 6-month period before the interview.

<sup>B</sup>DTES – Downtown Eastside; 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.



**Figure 1.** Trends in diverted methadone availability over the study period.