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## Incidence and determinants of initiation into cocaine injection and correlates of frequent cocaine injectors

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### Abstract

**Purpose**—To investigate the incidence and correlates of cocaine injection initiation and the impacts of daily cocaine injection among a cohort of injection drug users.

**Methods**—Among 1603 participants, from May 1996 and December 2005, risk factors for initiation of cocaine injection among baseline heroin users were determined by Cox proportional hazards regression and correlates of daily cocaine injection by generalized estimating equations.

**Findings**—Of the 238 individuals who had never injected cocaine, 200 (84%) had at least one follow-up visit and 121 (61%) consequently initiated into cocaine injection yielding an incidence density of initiation into cocaine injection of 21.9% (95% Confidence Interval (CI) 17.9 – 25.8) per 100 person years. In a multivariate model, Downtown Eastside (DTES) residence (Adjusted Hazard Ratio (AHR) = 2.46, 95% CI: 1.68-3.60), incarceration (AHR = 1.50, 95% CI: 1.01-2.24), requiring help injecting (AHR = 1.57, 95% CI: 0.99 – 2.49), and binge drug use (AHR = 1.82, 95% CI: 1.22 - 2.73) remained associated with initiation into cocaine injection. DTES residence (adjusted odds ratio (AOR) = 1.99, 95% CI: 1.62 – 2.46), incarceration (AOR = 1.29, 95% CI: 1.04 – 1.60), unstable housing (AOR = 1.28, 95% CI: 1.04 – 1.53), sex trade involvement (AOR = 1.46, 95% CI: 1.15 – 1.85), requiring help injecting (AOR = 2.11, 95% CI: 1.73 – 2.58), borrowing syringes (AOR = 1.81, 95% CI: 1.35 – 2.43) and binge drug use (AOR = 2.16, 95% CI: 1.81 – 2.58) were independently associated with daily cocaine injection.

**Conclusions**—The baseline prevalence and subsequent incidence of initiation into cocaine injection was high. Daily cocaine injection was independently associated with a number of health and social harms including elevated HIV risk behavior.

### Keywords

Cocaine; injection drug use; risk factors; HIV

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## 1. Introduction

The use of injection cocaine has recently increased in a number of settings around the world. For example, a documented increase in cocaine use among injection drug users (IDU) in New South Wales, Australia, occurred (Hando et al., 1997), following a heroin drought that began at the end of December in the year 2000 (Weatherburn et al., 2003). This trend is of concern given that cocaine injection has been shown to be a potent risk factor for HIV acquisition (Chaisson et al., 1989; Kral et al., 1998; Spittal et al., 2002; Tyndall et al., 2003), and more recently HCV (Maher et al., 2006) and overdose (Galea et al., 2006).

To date, the vast majority of public health research specific to injection drug use has focused primarily on heroin using populations. In contrast, the growing use of injection cocaine has received significantly less attention. As a result, risk factors for initiation into cocaine injection and correlates of cocaine injection have not been well described. The present study was therefore undertaken to examine initiation into cocaine injection and correlates of frequent cocaine injection among a cohort of IDU in Vancouver, Canada.

## 2. Methods

### 2.1. Study Sample

Beginning in May 1996, persons who had injected illicit drugs in the previous month were recruited into the Vancouver Injection Drug User Study (VIDUS), a cohort study that is presently ongoing and has been described in detail previously (Miller et al., 2002; Spittal et al., 2002). In short, persons were eligible for VIDUS if they had injected illicit drugs at least once in the previous month, resided in the greater Vancouver region, and provided written informed consent. Participants were recruited through self-referral or street outreach from Vancouver's Downtown Eastside (DTES). For participants who moved away from the area or were living outside of the city during follow-up, phone interviews were undertaken. Alternatively, VIDUS staffs are able to travel to locations throughout the Greater Vancouver area to conduct face-to-face interviews. At baseline and semi-annually, study participants complete an interviewer-administered questionnaire on socio-demographic and behavioral factors as well as a nurse-administered questionnaire on health status. Participants also provided blood samples for diagnostic testing. Participants received \$20 for each study visit. The questionnaires elicited socio-demographic data as well as information about drug use, and behaviors associated with risk of blood born viruses. The study has been approved on an annual basis by the Providence Health Care/University of British Columbia Research Ethics Board.

### 2.2. Initiation into Cocaine Injection

**2.2.1. Variables of Interest**—The primary outcome of the first analysis was initiation into cocaine injection. Study participants who had not injected cocaine at baseline, but had injected other illicit drugs (e.g., heroin, amphetamine, talwin and ritalin, tranquilizers, barbiturates, steroids, crystal methamphetamine, and methadone), were followed prospectively to examine subsequent rates of initiation into cocaine injection either alone or in combination with heroin in what is often referred to on the street as a “speedball”. As in prior analyses (Tyndall et al., 2003), the date of initiation was treated as the mid-point between the last injection cocaine-naïve and the first post-cocaine injection visit.

Socio-demographic variables included in this analysis included: sex (female versus (vs.) male), age, ethnicity (Aboriginal vs. other), Downtown Eastside (DTES) residence (yes vs. no), current unstable housing (yes vs. no), and incarceration (yes vs. no). Risk behavior information included sex trade involvement (yes vs. no), requiring help injecting (yes vs. no), syringe borrowing (yes vs. no), syringe lending (yes vs. no), binge drug use (yes vs. no), daily heroin

injection (yes vs. no), having a casual sex partner that injects drugs (yes vs. no) and ever being in drug treatment (yes vs. no). Variables considered referred to activity that occurred in the last six months unless otherwise specified. Unstable housing was defined as living in a single-room occupancy hotel, shelter or being homeless (Corneil et al., 2006). Binge drug use refers to using drugs more often than usual (Miller et al., 2006).

**2.2.2. Statistical analysis**—To examine changes in socio-demographic and behavioral variables over time, the unadjusted and adjusted relative hazard of initiation into cocaine injection were calculated using Cox Proportional Hazard regression. All behavioral variables were treated as time-updated covariates based on semi-annual follow-up data. For each participant, relevant socio-demographic and behavioral variables were examined in the questionnaire prior (i.e., questionnaire directly before reporting initiation) to when the individual reported initiating cocaine injection. Ties were handled using Breslow's method. To be eligible for this analysis, baseline injection cocaine-naïve participants had to have at least one follow-up visit to assess subsequent cocaine injection.

### 2.3. Correlates of frequent cocaine injection

**2.3.1. Variables of Interest**—The primary outcome in the second analysis was frequent cocaine injection. As in our previous work (Tyndall et al., 2003), frequent injection was defined as injecting a drug once or more daily. This cut-off was defined based on prior literature showing that daily use of cocaine was among the strongest determinants of HIV seroconversion (Tyndall et al., 2003). In addition to examining predictors of initiating into cocaine injection, we also were interested in gaining an understanding of correlates of frequent cocaine injection as this behavior is considered to be an important risk factor for infectious disease spread in our setting (Tyndall et al., 2003). Socio-demographic and behavioral variables included in this analysis were identical to those considered in the primary analysis and described above.

**2.3.2. Statistical Analysis**—Generalized estimating equations (GEE) for the binary outcomes with a logit link for the analysis of correlated data was used to determine the factors independently associated with frequent cocaine injection over time. These methods provided standard errors adjusted by multiple observations per person using an exchangeable symmetry correlation structure (Diggle et al., 1996).

In both analyses described above, multivariate models were fit using an *a priori* defined model building protocol involving adjustment for all variables that were statistically significant at the  $p < 0.05$  level in the univariate analyses. All statistical analyses were conducted with SAS software version 8.0 (SAS, Cary, NC) and  $p$ -values were two sided. We considered all participants recruited between May 1996 and December 2005.

## 3. Results

During the study period, 1603 IDU were enrolled into the VIDUS cohort. The median number of follow-up visits was 10 (Inter-quartile range (IQR): 4 – 16) for a median of 60 months (IQR: 24 – 96). The median age of the cohort at baseline was 30 years (IQR = 22 – 41). The proportion of study participants reporting daily cocaine injection declined from approximately 40% in 1996 to approximately 20% in 1999, and then remained fairly stable. The proportion of VIDUS participants at baseline who reported heroin injection was 1196 (75%) and 553 (35%) reported at least one injection per day of heroin. Among VIDUS participants at baseline, 658 (41%) reported injection of speedball, 107 (7%) reported injection of amphetamine, and less than 5% reported injection of talwin and ritalin, tranquilizers, barbiturates, steroids, crystal methamphetamine, or methadone. The proportion of VIDUS participants at baseline who reported a casual sex partner also being a person who injected drugs was 787 (49%).

### 3.1. Initiation into Cocaine Injection

Among 1603 participants, the proportion of individuals who reported *ever* injecting cocaine at baseline was 81% (n = 1299), with 41% (n = 658) reporting injecting of speedballs and 15% (n = 238) reporting that they had never injected cocaine or speedballs. Of the 238 individuals who had never injected cocaine, 200 (84%) had at least one follow-up visit and 121 (61%) consequently initiated into cocaine injection yielding an incidence density of initiation into cocaine injection of 21.9% (95% Confidence Interval (CI) 17.9 – 25.8) per 100 person years. To investigate whether the potential loss to follow-up bias between the 38 VIDUS participants who did not return for follow-up and the 200 that did, we examined baseline differences of sex, aboriginal ethnicity, unstable housing and age. Age was the only socio-demographic variable that differed significantly between the 38 VIDUS participants who did not return for follow-up and the 200 that did (median age 24 [IQR: 22-31] vs. 31 [IQR: 22-41],  $p < 0.001$ , respectively). The proportion of study participants reporting daily cocaine injection declined from approximately 40% in 1996 to approximately 20% in 1999, and then remained fairly stable. Table 1 displays the results of the unadjusted and adjusted Cox proportional hazard regression regarding initiation into cocaine injection. In the unadjusted model, DTES residence, incarceration, requiring help injecting, borrowing and lending of syringes, and binge drug use were associated with initiation into cocaine injection. In the adjusted model, DTES residence (Adjusted Hazard Ratio (AHR) = 2.46 [95% CI: 1.68-3.60]), incarceration (AHR = 1.50 [95% CI 1.01 – 2.24]), and binge drug use (AHR = 1.82 [95% CI: 1.22 - 2.73]) remained independently associated with subsequently initiating cocaine injection. Requiring help injecting (AHR = 1.57 [95% CI: 0.99 – 2.49]) was marginally associated with initiating into cocaine injection.

### 3.2. Correlates of Frequent Cocaine Injection

Overall, 77% (n = 1237) of IDU reported injecting cocaine at least once during the follow-up period. Approximately one third of VIDUS participants reported daily cocaine injection at baseline (34%, n = 549). As displayed in Table 2, baseline socio-demographic and behavioral variables associated with frequent cocaine injection included female gender, unstable housing, incarceration, syringe lending, binge drug use, and sex trade involvement. The results of the univariate and multivariate GEE analyses of factors associated with frequent cocaine injection over time are shown in Table 3. In unadjusted analyses, younger age, DTES residence, incarceration, unstable housing, sex trade involvement, requiring help injecting, syringe borrowing, syringe lending and binge drug use were significantly associated with frequent cocaine injection. Also shown in Table 3, in adjusted analyses DTES residence [adjusted odds ratio (AOR) = 1.99, [95% CI: 1.62 – 2.46]], incarceration (AOR = 1.29 [95% CI: 1.04 – 1.60]), unstable housing (AOR = 1.28, [95% CI: 1.04 – 1.53]), sex trade involvement (AOR = 1.46 [95% CI: 1.15 – 1.85]), requiring help injecting (AOR = 2.11 [95% CI: 1.73 – 2.58]), syringe borrowing (AOR = 1.81, [95% CI: 1.35 – 2.43]), and binge drug use (AOR = 2.16, [95% CI: 1.81 – 2.58]) remained significantly associated with frequent cocaine injection over time.

## 4. Discussion

In this study, the prevalence and incidence of cocaine injection was high and associated with a number of aspects of social harms and risk behaviors that elevate the possibility of infectious disease transmission. Over three quarters (81%) of study participants at baseline reported ever injecting cocaine and among those who had not, the majority (61%, n=121) subsequently initiated into cocaine injection (incidence density of 21.9% per 100 person years). In time to event analyses, DTES residence, incarceration, requiring help injecting and binge drug use were associated with subsequently initiating into cocaine injection. In multivariate GEE analyses, DTES residence, incarceration, unstable housing, sex trade involvement, requiring

help injecting, syringe borrowing and binge drug use were independently associated with frequent cocaine injection over time.

To our knowledge, this is the first study that has examined risk factors for initiation into cocaine injection using longitudinal methods. Among the most interesting findings is that incarceration predicted subsequent initiation of cocaine injection. Although high rates of drug use in Canadian prisons has been reported (Wood et al., 2005), further research is required to shed light on this association. However, it is possible that incarceration as well as DTES residence in this model were acting as proxies for marginal lifestyle and are not directly related with our outcome variables. Future qualitative research could help discern whether the association between recent incarceration and cocaine injection was directly related to the outcome or whether incarceration was acting as a proxy for other factors related to lifestyle.

Of particular concern is that most factors associated with frequent cocaine injection in this analysis, such as borrowing syringes (Durante et al., 1995), requiring help injecting (Kral et al., 1999; Wood et al., 2003) and sex trade involvement (Tyndall et al., 2002; Wood et al., 2007) are also behaviors that have been shown to increase the risk for HIV infection in our setting and others (Bux et al., 1995; Kral et al., 2000; Wood et al., 2002; Tyndall et al., 2006). Cocaine injectors, when compared to heroin injectors, are known to exhibit elevated sexual risk behavior (Hudgins et al., 1995). Social cognitive theory – based, individually catered interventions have found to be feasible and effective at reducing high risk sexual behaviors (Patterson et al., 2005). Collectively, these results suggest that both sexual and injection risk behavior should be incorporated into interventions geared towards cocaine injectors.

In addition, location (e.g., DTES residence and incarceration) was associated with frequent cocaine injection. There is growing recognition of the important role that place and location plays in mediating the harms associated with injection drug use (Darke et al., 2001). Our findings, reinforce the reported need to expand our understanding of risk by moving beyond analyses of individual factors to investigations of the broader ‘risk environment’ of IDU (Rhodes, 2002; Rhodes et al., 2006). Integrating harm reduction services into the DTES, such as North America's first supervised injection facility (SIF), may play a role in mediating the risk environment in the DTES as it has been reported to have reached high risk injectors, including daily cocaine injectors (Wood et al., 2005). This may occur by providing not only a safer place to inject with clean injecting paraphernalia, but also by putting these injectors in contact with health service providers who can provide safer injecting education (Wood et al., 2004). Further, use of the SIF has been independently associated with reduced syringe sharing (Kerr et al., 2005). The DTES is Vancouver's HIV epicenter (Kerr et al., 2003). Since there has been an elevated risk of HIV seroconversion among frequent cocaine injectors (Tyndall et al., 2003) it is not particularly surprising that cocaine injection is associated with DTES residence. To further clarify the role of DTES residence, Vancouver's IDU HIV epicenter, in relation to cocaine injection, future studies could employ multi-level analyses comparing rates of frequent cocaine injection in the DTES and other surrounding neighborhoods. In light of our findings and given the elevated risk of HIV transmission among cocaine injectors, safer routes of drug administration may be a viable harm reduction message to prevent the initiation into injection drug use. Further research is also needed to determine the factors that lead an individual to initiate into injection cocaine given the known elevated risk for infectious disease.

Currently, there are few existing interventions for cocaine use and there are no well-described “gold standard” substitution treatments for injection cocaine use (de Lima et al., 2002). Pharmacotherapies investigated as potentially beneficial in the management of cocaine dependence include, antidepressants, anticonvulsants and dopaminergics (de Lima et al., 2002). However, the evidence concerning pharmacotherapies for cocaine dependence has been

equivocal (Shearer et al., 2003). It has also been suggested that due to the intrinsic medical danger of pharmacotherapy, prescriptions should be limited to individuals with serious cocaine dependence (Shearer and Gowing, 2004). In addition, considering pharmacotherapy within a larger comprehensive addiction treatment strategy is vital to improving the lives of individuals dependent on cocaine (de Lima et al., 2002). There has been some research on the role of cognitive behavioral therapy with or without contingency management to treat individuals with cocaine addiction, but these results are not conclusive (Epstein et al., 2003). It is evident that continued developments of new interventions for cocaine users combined with rigorous evaluation are warranted. In our setting, a supervised injecting facility has recently been opened and high utilization by cocaine injectors has been observed (Tyndall et al., 2005). Given existing evidence (Kerr et al., 2005), it may be that the supervised injection facilities may have potential to address the elevated risk of syringe sharing observed among cocaine injectors in this study. Similarly, there is debate regarding the initiation of stimulant maintenance trials, and it is hoped that these data may help to inform this debate and reinforce the need for the ongoing development of novel interventions for cocaine injectors.

Our study has limitations inherent to working with large observational cohort data. First, regarding the self reporting bias, while some studies have suggested that self reports of IDU are valid (Latkin et al., 1993), the risk behaviors measured are stigmatized behaviors, and therefore it is possible that some of these behaviors were underestimated in the present study (Greenfield et al., 1995). However, we do not know of a reason why this concern would be differentially distributed among cocaine users and non-cocaine users. Second, regarding sampling bias, VIDUS is not a random sample. Although we have previously shown that VIDUS is representative of IDU in the community (Tyndall et al., 2003). Thirdly, this study focused on cocaine injection, although we appreciate that physical and psychological harm among injecting and non-injecting cocaine users occurs irrespective of route of administration and frequency of use (Kaye and Darke, 2004). Fourthly, we did not have more precise information on the date of transitioning into injection cocaine, which is why the midpoint between the last non cocaine injecting visit and the first cocaine injecting visit was used. However, our follow-up period was over a decade; therefore, we do not believe that this limitation has largely impacted our results.

In summary, the prevalence and incidence of cocaine injection was high and associated with a number of well-known risks for HIV infection and other adverse health outcomes, including syringe borrowing, requiring help injecting, binge drug use, sex trade involvement, and incarceration. In light of our findings and given the elevated risk of HIV transmission among cocaine injectors, safer routes of drug administration may be a viable harm reduction message. Further research is needed in determining the factors that lead an individual to initiate into injection cocaine given the known elevated risk for infectious disease.

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**Table 1**  
**Univariate and multivariate Cox proportional hazard analyses of the time to cocaine initiation among injection drug users who did not inject cocaine at baseline (n = 200)**

Variable	RH	Unadjusted Relative Hazard (RH) (95% CI)	p-value	RH	Adjusted** Relative Hazard (RH) (95% CI)	p-value
<b>Sex</b> (Female vs Male)	0.94	(0.66 – 1.35)	0.744			
<b>Age</b> (per year older)	0.99	(0.98 - 1.01)	0.504			
<b>Ethnicity</b> (Aboriginal vs Other)	1.16	(0.76 – 1.76)	0.491			
<b>DTEs residence*</b> (Yes vs No)	2.38	(1.65 – 3.44)	<0.001	2.46	(1.68 – 3.60)	<0.001
<b>Incarceration*</b> (Yes vs No)	1.66	(1.11 – 2.47)	0.013	1.50	(1.01 – 2.24)	0.045
<b>Unstable housing*</b> (Yes vs No)	1.00	(0.70 – 1.45)	0.987			
<b>Sex trade involved*</b> (Yes vs No)	1.37	(0.84 – 2.26)	0.212			
<b>Require help injecting*</b> (Yes vs No)	1.94	(1.25 - 3.03)	0.003	1.57	(0.99 – 2.49)	0.055
<b>Syringe borrowing*</b> (Yes vs. No)	2.00	(1.27 - 3.16)	0.003	1.70	(0.92 – 3.17)	0.093
<b>Syringe lending*</b> (Yes vs. No)	1.77	(1.12 – 2.81)	0.015	1.35	(0.73 – 2.51)	0.346
<b>Binge drug use*</b> (Yes vs. No)	2.17	(1.46 - 3.24)	<0.001	1.82	(1.22 – 2.73)	0.004
<b>Daily heroin injection*</b> (Yes vs. No)	1.30	(0.90-1.88)	0.160			
<b>IDU casual sex partner*</b> (Yes vs. No)	1.47	(0.98 – 2.18)	0.059			
<b>Ever in drug treatment</b>						

Variable	Unadjusted Relative Hazard (RH)		Adjusted** Relative Hazard (RH)	
	RH	(95% CI)	RH	(95% CI)
(Yes vs. No)	0.76	(0.52-1.11)		
				p-value
				0.152

\* Refers to previous six months, DTES = Downtown Eastside., IDU = injection drug user

**Table 2**  
**Baseline socio-demographic and behavioural variables associated with frequent cocaine injection (n = 1603)**

Variable	Not Freq. Cocaine Inject n = 1054 (%)	Freq. Cocaine Inject n = 549 (%)	Odds Ratio (95% CI)	p-value
<b>Sex</b>				
Female	361 (34)	223 (41)	1.31 (1.06 – 1.62)	0.012
Male	693 (66)	326 (59)		
<b>Age</b>				
Median (IQR)	33 (24-40)	33 (26 – 40)	1.00 (0.99 – 1.01)	0.834
<b>Ethnicity</b>				
Aboriginal	270 (26)	162 (30)	1.25 (0.99 – 1.58)	0.058
Other	784 (74)	384 (70)		
<b>DTES residence*</b>				
Yes	550 (52)	369 (67)	1.88 (1.51 – 2.33)	< 0.001
No	504 (48)	180 (33)		
<b>Unstable housing*</b>				
Yes	602 (57)	395 (72)	1.93 (1.54 – 2.41)	< 0.001
No	452 (43)	154 (28)		
<b>Incarceration*</b>				
Yes	318 (30)	218 (40)	1.52 (1.23 – 1.89)	< 0.001
No	736 (70)	331 (60)		
<b>Syringe borrowing*</b>				
Yes	378 (36)	212 (39)	1.13 (0.91 – 1.39)	0.278
No	676 (64)	337 (61)		
<b>Syringe lending*</b>				
Yes	356 (34)	216 (39)	1.27 (1.03 – 1.57)	0.027
No	698 (66)	333 (61)		
<b>Require help injecting*</b>				
Yes	439 (42)	228 (42)	1.00 (0.81 – 1.23)	0.963
No	615 (58)	321 (58)		
<b>Binge drug use*</b>				
Yes	478 (45)	294 (54)	1.39 (1.13 – 1.71)	0.002
No	572 (55)	255 (46)		
<b>Sex trade involved*</b>				
Yes	259 (25)	201 (37)	1.77 (1.42 – 2.22)	< 0.001
No	795 (75)	348 (63)		

\* Refers to previous six months, DTES = Downtown Eastside Residence, Freq. = frequent.

**Table 3**  
**Univariate and multivariate GEE analysis of frequent cocaine injection (n = 1603)**

Variable	OR	Unadjusted Odds Ratio (OR) (95% CI)	p-value	AOR	Adjusted** Odds Ratio (AOR) (95% CI)	p-value
<b>Sex</b> (Female vs. male)	0.97	(0.84-1.12)	0.698			
<b>Age</b> (per year older)	0.99	(0.98-1.00)	0.037	1.00	0.99 – 1.01	0.985
<b>Ethnicity</b> (Aboriginal vs. other)	1.13	(0.97 – 1.31)	0.107			
<b>DTES residence*</b> (Yes vs. No)	2.10	(1.88 – 2.32)	<0.001	1.99	(1.62 – 2.46)	<0.001
<b>Incarceration*</b> (Yes vs. No)	1.81	(1.63 – 2.00)	<0.001	1.29	(1.04 – 1.60)	0.022
<b>Unstable housing*</b> (Yes vs. No)	1.62	(1.49 - 1.77)	<0.001	1.28	(1.07 – 1.53)	0.006
<b>Sex trade involvement*</b> (Yes vs. No)	2.37	(2.07 – 2.70)	<0.001	1.46	(1.15 – 1.85)	0.002
<b>Requiring help injecting*</b> (Yes vs. No)	2.18	(1.96 - 2.42)	<0.001	2.11	(1.35 – 2.58)	<0.001
<b>Syringe borrowing*</b> (Yes vs. No)	2.11	(1.90 - 2.36)	<0.001	1.81	(1.35 – 2.43)	<0.001
<b>Syringe lending*</b> (Yes vs. No)	2.09	(1.88 – 2.32)	<0.001	1.10	(0.78 – 1.55)	0.605
<b>Binge drug use*</b> (Yes vs. No)	2.36	(2.16 - 2.57)	<0.001	2.16	(1.81 – 2.58)	<0.001

\* Refers to previous six months, DTES = Downtown Eastside Residence