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Drastic elevations in mortality among female injection drug users in a Canadian setting

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Abstract
The health and social conditions of women living in Vancouver's Downtown Eastside has recently been the focus of substantial international attention. Since few studies have examined rates and correlates of death among addicted women in Canada, we have characterized patterns of mortality among female injection drug users (IDUs) in Vancouver. The Vancouver Injection Drug Users Study (VIDUS) is a prospective open cohort study of IDUs. The analyses presented here, were restricted to women enrolled between May 1996 and May 2002 and who were aged 14 years or older. We estimated cumulative mortality rates using Kaplan-Meier methods and Cox regression was used to calculate univariate and adjusted relative hazards. Between May 1996 and May 2002, 520 female IDUs have been recruited from the Vancouver area among whom 68 died during the study period. Elevated rates of mortality were observed among those who reported, baseline sex-trade involvement, those with HIV-infection at baseline, and those who lived in unstable housing at baseline (all log-rank: $p < 0.05$). In adjusted analyses, HIV infection (RH = 3.09 [95% CI: 1.86–5.11]; $p < 0.001$), unstable housing (RH = 1.74 [95% CI: 1.10–2.86]; $p = 0.029$) and sex-trade involvement (RH = 1.82 [95% CI: 0.95–3.45]; $p = 0.071$) were associated with the time to death. When the number of observed deaths was compared to the number of expected deaths based on the general female population of British Columbia using indirect standardization, the rate of death among female IDUs was elevated by a factor of 47.3 (95% CI: 36.1–58.5). In Vancouver, female IDUs have rates of mortality almost 50 times that of the province's female population. Our findings are consistent with a growing number of reports from other settings internationally, and demonstrate the need for an appropriate evidence-based strategy to address the health and social needs of addicted women.

> We're like the living dead down here, in the Eastside. We're on the news now . . . We're all dyin', we're fallin' off the face of the earth. . . it's bad, it's really bad.
>
> (Female sex-trade worker)

Introduction

While there has been much research into mortality among injection drug users (Gossop et al., 2002; Hickman et al., 2003; Selwyn, 1991) few studies focus on mortality rates and causes of death among addicted women (Smith et al., 2003). In British Columbia, Canada the case of over sixty missing women who have disappeared from Vancouver's Downtown Eastside has garnered both national and international attention (BBC, 26 Feb 2002; *Guardian*, 11 Feb 2002; National Post, 3 Oct 2002). Media furore has been focused upon the search of a pig farm, the identification of DNA linked to a large number of missing women and the subsequent criminal case against the farm's owner in rural BC (BBC, Feb 26 2002; Guardian, Feb 11 2002; National Post, Oct 3 2002). However, emerging evidence suggests that the health and social crisis among addicted women in Vancouver is much larger than this single serial murder investigation. For example, while addicted women in Vancouver involved in sex work continue to be exposed to appalling levels of drug-related harm, predation, and violence (Lowman, 2004; Lowman & Fraser, 1996; Spittal et al., 2003) analyses conducted in Vancouver have also demonstrated that women (Spittal et al., 2002; Spittal & Schechter, 2001) particularly Aboriginal women (Benoit et al., 2003; Craib et al., 2003) are at markedly elevated risk of HIV infection. A recent analysis from the same setting has also demonstrated that HIV-infected women and Aboriginal persons are also less likely to ever receive the benefits of HIV treatment prior to death (Wood et al., 2003). Unfortunately, these observations are consistent with many settings internationally where addicted women suffer from elevated rates of violence and health-related harms

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(Fisher et al., 1995; Miller & Neaigus, 2002; Romero-Daza et al., 2003; Wechsberg et al., 2003).

Locally, recent cut backs and closing of services for women in British Columbia and concomitant threat of sweeping social welfare cuts (Globe & Mail, 21 Oct 2003) have resulted in increased scepticism from several international bodies, regarding the commitment of this provincial government to the health and social wellbeing of the most marginalized [Human Rights Watch, 2003; United Nations, 2003]. For instance, while praising the significant strides made in advancing the rights of women, a recent UN report was derisive of the high number of women who remain entrenched in poverty in Canada (United Nations, 2003).

Nevertheless, the intersecting epidemics of poverty, HIV/AIDS, violence and death that threaten the lives of addicted women in Canada remain poorly understood. We have been following a cohort of more than 1400 injection drug users in Vancouver since 1996 of whom approximately 35% are women. Follow up of the cohort now allows for an investigation aimed at examining predictors of mortality and careful examination of causes of death among women who used injection drugs in one of Canada's poorest neighbourhoods.

Methods

The Vancouver Injection Drug User Study (VIDUS) is a prospective cohort study of injection drug users recruited through self-referral and street outreach from Vancouver's Downtown Eastside that was initiated in May 1996 (Strathdee et al., 1997). Persons were eligible to participate in the VIDUS study if they were 14 years of age or older, had injected illicit drugs at least once during the month prior to enrolment, and resided in the greater Vancouver region. All participants provided written informed consent. Participants were given a stipend ($20 CDN) at each study visit in order to compensate them for their time and to facilitate transportation. The study was approved by the University of British Columbia/Providence Healthcare Research Ethics Board.

VIDUS study protocol participants are followed semi-annually; at baseline and at each visit, participants completed interviewer administered questionnaires that elicited data regarding demographic characteristics, injection and non-injection drug use, injection practices, and sexual risk behaviours. In addition, venous blood samples were drawn at each visit, and tested for HIV and hepatitis C Virus (HCV) antibodies. All study volunteers had private interviews, were offered both pre- and post-test counselling with trained nurses, and referral for HIV/AIDS care was provided to those who tested positive.

The present study was restricted to female IDUs recruited since 1 May, 1996 and who were followed until 31 May, 2002. Transsexual IDUs (male to female) were excluded. As an initial analysis we evaluated the baseline demographic characteristics of female IDUs. Due to the well-known association of sex-trade work and premature mortality on the harms of sex trade, we stratified this analysis by sex-trade involvement at baseline (Lowman & Fraser, 1996; Spittal et al., 2003). Sex trade was defined as exchanging sex for money, drugs, or anything else including food or shelter. Variables of interest included: baseline age, Hepatitis C (HCV) status, HIV status, unstable housing, having ever been sexually abused, incarceration in the last six months, having sought but been denied addiction treatment, shooting gallery use, emergency room use, and having ever attempted suicide. As previously, unstable housing was defined as living in one of the Downtown Eastside's single room occupancy hotels (SROs), shelters or other transitional housing, or living on the street (Craib et al., 2003; Spittal et al., 2002).

We determined all cause mortality rates among VIDUS participants through ongoing follow-up with contacts provided by participants and through a confidential record linkage with British Columbia Vital Statistics. In addition, because of the large number of women who have disappeared from Vancouver's Downtown Eastside, we also examined how many women in the cohort were on the official missing women list compiled by the Royal Canadian Mounted Police (RCMP) (RCMP, 2003).

For the primary analysis of time to death, we examined variables that we *a priori* hypothesized may be associated with elevated risk of mortality. Here, we examined age, sex-trade involvement, unstable housing, HIV and HCV infection, years injecting, incarceration, historical sexual abuse, methadone maintenance therapy, requiring help injecting, binge drug use, recent non-fatal overdose, frequency of heroin and cocaine injection and crack cocaine use, and condom use. Methadone maintenance (MMT) was defined as accessing methadone maintenance therapy in the last six months. As in previous work (Spittal et al., 2002; Wood et al., 2001), clients who reported injecting cocaine or heroin once or more per day were defined as frequent cocaine and frequent heroin users respectively. Bingeing was defined as periods when drugs were injected more frequently than usual. Always using condoms with regular partners, casual partners and clients were evaluated as markers of sex-related risk.

Cumulative all cause mortality rates were calculated using Kaplan-Meier methods. In these analyses, time zero was defined as the date of enrolment into the study. Participants who did not die during follow-up were censored as of 31 May, 2002. Participants were stratified upon baseline characteristics and mortality rates were compared by the log-rank test. In addition, in order to evaluate the impact of time varying characteristics, such as sex-trade involvement and drug use patterns in the last six months, Cox proportional hazards regression was used to assess the independent effect of both fixed and time-dependent covariates on time to death. Values for time-dependant variables were included from all available visits. Age was treated as a continuous variable without transformation. The multivariate model was fitted using an *a priori* defined protocol of adjusting for all variables that were statistically significant at the $p < 0.1$ level in bivariate analyses. All statistical analyses were performed using SAS software version 8.0 (SAS, Cary, NC).

Results

A total of 1,478 participants were recruited and completed an enrolment questionnaire between 1 May 1996 and 31 May 2002, among whom 520 (35.2%) were women. The characteristics of the entire cohort have been described elsewhere (Strathdee et al., 1997). The median age of women at enrolment was 32 (Inter-quartile range: 24–38), 204 (39.2%) were Aboriginal, and at baseline the median number of years injecting was 9 (Inter-quartile range: 3–18).

Table I shows the baseline socio-demographic and risk behaviour characteristics of the cohort of female stratified by sex-trade involvement at baseline. As shown here, those who reported sex-trade work at baseline were more likely to be HCV-positive ($p < 0.001$), HIV-positive ($p = 0.007$), to reside in unstable housing ($p < 0.001$), to have experienced lifetime sexual abuse ($p < 0.001$), to have been recently incarcerated ($p = 0.044$), to have recently used a shooting gallery ($p < 0.001$), and were more likely to inject cocaine daily ($p < 0.001$). Sex-trade workers were more likely to have attempted suicide ($p < 0.060$) but this did not attain conventional statistical significance. Baseline age and daily heroin injection were similar between both groups, and having sought but been denied addiction treatment in the last six months was also similar at approximately 20% at baseline.

Ongoing follow-up with contact information provided by participants and a confidential record linkage with British Columbia Vital Statistics revealed that there were 61 deaths among women. In addition, from the RCMP's missing women task force, we determined that there were seven female VIDUS participants for which murder charges have been laid due to the discovery of DNA evidence (RCMP, 2003). Together the 68 events among female participants produced a crude all-cause mortality rate of 13.1%. When the age-specific death rates observed among female participants were compared to the female population of British Columbia aged 18 to 64 (BC Vital Statistics Agency, 1991–1999), using indirect standardization (Shyrock & Siegal, 1976), the standardized mortality ratio was 47.3 (95% CI: 36.1–58.5). By way of comparison, the corresponding SMR among male participants was 20.7 (95% CI: 17.2–24.2). The specific causes of death are shown in Table II.

Table I. Causes of death among female IDUs stratified by history of sex-trade during follow-up.

Cause of Death	No History of Sex-Trade $n = 10$	History of Sex-Trade $n = 58$
Non-HIV-related		
Overdose Fatalities	1	13
Homicide	–	12
Accidental causes	2	3
Cardiac	–	3
Other*	3	10
HIV-related		
Advanced HIV/wasting	1	3
Pneumoncystic carinii pneumonia	2	7
Mycobacterium avium Complex	–	1
HIV unclassified	–	2
Tuberculosis	1	3
Meningitis	–	1

Notes: *Includes 1 alcohol related death, 1 brain haemorrhage, 2 GI bleed, 1 liver disease, 2 unknown causes, 2 suspected overdose, 2 respiratory disease, 1 salmonella, 1 bacterial infection.

Figure 1 shows the Kaplan-Meier cumulative mortality estimates. As shown in Panel (a), the mortality rate at 48 months among women who reported sex-trade involvement at baseline was 15.1% vs 7.0% among non-sex-trade workers (log-rank: $p = 0.046$). As shown in Panel (b), the mortality rate among those with HIV infection at baseline was 21.9% vs 9.1% among those who were not HIV infected at baseline (log-rank: $p < 0.001$). Finally, as shown in Panel (c), the mortality rate among those with unstable housing at baseline was 15.0% vs 9.8% among those who lived in stable housing (log-rank: $p = 0.037$).

We then considered fixed and time-updated variables in Cox regression analyses as shown in Table III. With the exception of age, number of years injecting, history of sexual abuse and previous non fatal overdose that were fixed at baseline, all other variables were time dependant. In univariate analyses, the number of years injecting (relative hazard

Table II. Baseline characteristics of female injection drug users stratified by sex-trade involvement at baseline.

Characteristic	No Sex-trade	Sex-trade	Odds Ratio (95% CI)	*p* value
Age				
Median (IQR)	33 (24–39)	31 (25–37)	0.9 (0.7–1.1)	0.150
Baseline HCV-positive				
No	51 (35.2)	67 (17.9)		
Yes	94 (64.8)	308 (82.1)	2.5 (1.6–3.8)	<0.001
Baseline HIV-positive				
No	119 (82.1)	264 (70.4)		
Yes	26 (17.9)	111 (29.6)	1.9 (1.2–3.1)	0.007
Unstable Housing*				
No	80 (55.2)	133 (35.5)		
Yes	65 (44.8)	242 (64.5)	2.2 (1.5–3.3)	<0.001
Sexual Abuse†				
No	72 (49.7)	91 (24.3)		
Yes	73 (50.3)	284 (75.7)	3.1 (2.1–4.6)	<0.001
Recently incarcerated*				
No	112 (77.2)	256 (68.3)		
Yes	33 (22.8)	119 (31.7)	1.6 (1.0–2.5)	0.044
Denied drug treatment*				
No	114 (78.6)	293 (78.1)		
Yes	31 (21.4)	82 (21.9)	1.0 (0.6–1.6)	0.904
Shooting gallery use*				
No	112 (77.2)	228 (60.8)		
Yes	33 (22.8)	147 (39.2)	2.2 (1.4–3.4)	<0.001
Emergency room use*				
No	75 (51.7)	177 (47.2)		
Yes	70 (48.3)	198 (52.8)	1.2 (0.8–1.8)	0.355
Attempted suicide†				
No	86 (59.3)	188 (50.1)		
Yes	59 (40.7)	187 (49.9)	1.5 (1.0–2.1)	0.060
Daily heroin injection†				
No	76 (52.4)	190 (50.7)	1.1 (0.7–1.6)	0.721
Yes	69 (47.6)	185 (49.3)		
Daily cocaine injection†				
No	100 (69.0)	164 (43.7)	2.9 (1.9–4.3)	<0.001
Yes	45 (31.0)	211 (56.3)		

Notes: IQR = interquartile range. *Refers to last six months; †refers to lifetime history.

[RH] = 1.03 [95% CI: 1.00–1.06]; $p = 0.025$), age (RH = 1.11 [95% CI: 1.02–1.07]; $p = 0.002$), HIV-infection (RH = 2.99 [95% CI: 1.81–4.92]; $p < 0.001$), and unstable housing (RH = 1.77 [95% CI: 1.09–2.88]; $p = 0.022$) were significantly associated with the time to death. Both sex-trade involvement (RH = 1.76 [95% CI: 0.91–3.36]; $p = 0.087$) and condom use with regular partners (RH = 0.44 [95% CI: 0.19–1.02]; $p = 0.057$) were marginally associated with the hazard of death and were therefore considered in the multivariate analysis. HCV-infection, history of sexual abuse, recent incarceration, methadone use, frequent heroin use, and frequent cocaine use, and previous non-fatal overdose were all non-significant.

In adjusted analyses shown in Table III, age (adjusted relative hazard [ARH]: 1.06 [95%CI: 1.02–1.09]; $p < 0.001$), HIV infection (RH = 3.09 [95% CI: 1.86–5.11]; $p < 0.001$), and unstable housing (RH = 1.74 [95% CI: 1.00–2.86]; $p = 0.029$) were independently associated with the hazard of death. Sex-trade involvement (RH = 1.82 [95% CI: 0.95–3.45]; $p = 0.071$) just failed to reach conventional statistical significance after adjustment for the above covariates as well as condom use with regular partners, which was not statistically significant ($p > 0.05$).

Discussion

In the present study we found that deaths among female injection drug users were almost 50 times higher than deaths exhibited by the general female British Columbia population. Elevated rates of mortality in the cohort was associated with unstable housing, and HIV-infection. Causes of death were

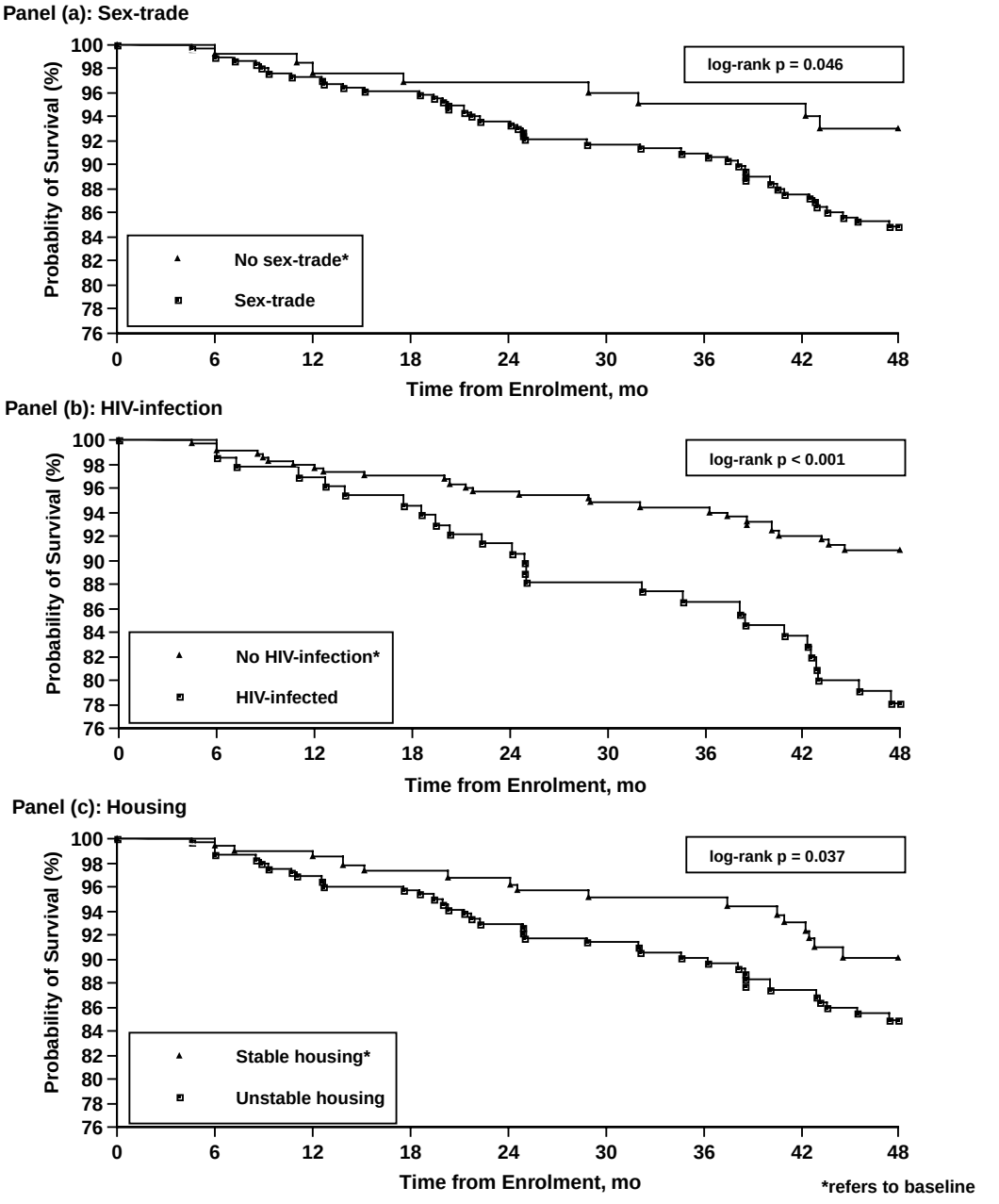

Figure 1. Kaplan-Meier product limit cumulative all cause mortality estimates stratified by: (Panel a) sex-trade involvement; (Panel b) HIV status; (Panel c) housing status.

primarily related to overdose, homicide, and HIV/AIDS.

The fact that so many addicted women are dying in Vancouver from non-AIDS related conditions is an indicator of their extreme vulnerability (Cohen et al., 2002). Previous studies have demonstrated that homelessness and living in shelters is associated with elevated frates of violence, rape, recruitment into the sex-trade and injection drug use among women (Fisher et al., 1995; Wechsberg et al., 2003). We recognize that unstable housing was independently associated with mortality in our analyses because it is likely a marker for these underlying risk factors which are highly prevalent in this setting (Kushel et al., 2003). While our findings would suggest that shelters, low-income housing, and other interventions known to potentially prevent these deaths should be expanded, it is noteworthy that in British Columbia, funding for services for at risk women have recently been markedly reduced (United Nations, 2003). Further, studies have demonstrated that, in such environments, women may trade sex for basic necessities including food and shelter (Miller & Neaigus, 2002; Spittal et al., 2003). Sex trade involvement was associated with death in our setting although this did not attain statistical significance.

Table III. Univariate and multivariate* Cox proportional hazard analyses of the time to death among 520 female injection drug users recruited between May, 1996 and May, 2002.

	Unadjusted Relative Hazard (RH)			Adjusted* Relative Hazard (RH)		
Variable	RH	(95% CI)	*p*-value	RH	(95% CI)	*p*-value
Age (per year older)	1.11	(1.02–1.07)	0.002	1.05	(1.02–1.09)	<0.001
HIV Infected (Yes vs No)	2.99	(1.81–4.92)	<0.001	3.09	(1.86–5.11)	<0.001
Sex-trade (Yes vs No)	1.76	(0.91–3.36)	0.087	1.82	(0.95–3.45)	0.071
Housing Status (Unstable vs Stable)	1.77	(1.09–2.88)	0.022	1.74	(1.10–2.85)	0.029

Note: *Model was also adjusted for condom use with regular partners and years fixing which were both non-significant in the final model.

However, we had diminished power to detect such an association as more than 82% of women in our study reported sex trade involvement. Any association of sex trade with mortality is likely due, in part, to the fact that street level sex trade workers are often forced to work in environments, such as remote and unlit areas, that leave them particularly vulnerable to predation and violence (Fisher et al., 1995; Wechsberg et al., 2003). Presently, sex workers have very limited opportunity to access adequate services at night and in appropriate locations where they may be at highest risk (Spittal & Schechter, 2001). In order to reduce harm experienced by sex-trade workers, innovative models that have been effective elsewhere need to be implemented in consultation with experiential women (Ellen et al., 2001; Lowman, 2004; Lowman & Fraser, 1996). In addition, others have noted that unless an evidence-based socio-legal environment is created that puts the safety of sex-trade workers first, ongoing harms will persist (Lowman, 2004).

Fatal overdose and HIV-related mortality are well recognized to be preventable causes of death (Tyndall et al., 2001). The number of deaths due to overdose is of grave concern. However, it is noteworthy that these data were derived prior to the opening of North America's first supervised injection facility and it is hoped that this intervention will help to reduce the burden of avoidable deaths among addicted women (Kerr & Palepu, 2001). However, it has been previously demonstrated that there are substantial gender differences in risk of HIV-infection and overdose death, and it has been noted that there must be continued efforts to mainstream gender based concerns into overall drug strategies (Remis, 2002; Spittal et al., 2002). Equally distressing are the numbers of women who are dying from AIDS related illness despite access to free antiretroviral therapy. Over 5 years ago, Strathdee et al. conducted a study exploring the barriers to the use of free antiretrovirals among IDU in British Columbia and found that women were half as likely to receive HIV treatment (Strathdee et al., 1998). Subsequently, we demonstrated that women and Aboriginal people continue to die from HIV/AIDS related illness without ever accessing the benefits of HIV treatment and care (Wood et al., 2003b). In light of these data, progress must be made in addressing the barriers to HIV care for women, particularly for those who remain addicted and engaged in prostitution (Wood et al., 2003a). The challenges faced by women must be incorporated into culturally appropriate training programmes for HIV clinicians and alternative models of the delivery of sustained care must be urgently considered (Burke et al., 2003; Mellins et al., 2003; Wood et al., 2003). We have also recently demonstrated the substantial harms of limited access to addiction treatment in our setting (Wood et al., 2004), and it is noteworthy that while use of methadone was protective for male IDUs, the use of methadone was not associated with reduced mortality among female IDUs. Future studies will be required to examine barriers addiction treatment for addicted women, and why methadone was not protective against mortality in our setting.

As previously discussed, although we have previously demonstrated that the cohort appears to be highly representative of IDUs in the Downtown Eastside, VIDUS is not a random sample. We should also note that we used a crude definition of unstable housing that included single room occupancy hotels (SROs), shelters or other transitional housing, or living on the street. Similarly, sex-trade was similarly loosely defined as trading sex for money, drugs, shelter, or anything else in exchange. However, previous studies have demonstrated that all definitions of housing and sex-trade generally have limitations, and it is noteworthy that if misclassification existed due to our broad definitions, this would have biased our analyses towards no association (Culhane et al., 2001; Spittal et al., 2003). In Vancouver, women injection drug users have rates of mortality almost 50 times that of the general British Columbian population, and sex-trade, unstable housing, and HIV-infection were associated with mortality. International experts in the area of drug policy and public health have argued that rates of avoidable mortality among drug users is a barometer of the effectiveness of drug strategies (Hickman et al.,

2003). As such, our data suggest that Canada's drug strategy is desperately failing addicted women. Without supportive access to voluntary HIV testing, counselling and treatment services, and increased availability of safe housing more women will die. Our findings reinforce the need for an appropriate evidence-based drug strategy (Oscapella, 1995), and demonstrate that further inaction on the part of policy-makers will likely result in continued elevated mortality rates among women in this setting (Lowman, 2004).

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