



Impact of binge alcohol on mortality among people who inject drugs



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ABSTRACT

Introduction: While the impacts of illicit drug use on mortality have been well described, the impact of poly-substance that includes alcohol has received less attention. We examined the impact of binge alcohol use on mortality among a cohort of people who inject drugs (PWID) in a Canadian setting.

Methods: Using data derived from a prospective cohort study of PWID in Vancouver, Canada recruited between May 1996 and November 2013. We ascertained dates and causes of death through a confidential linkage with the provincial registry and examined the impact of binge alcohol use. The primary outcome of interest was all-cause mortality. We used Cox proportional hazard regression to determine factors associated with mortality, including socio-demographic characteristics, drug use patterns and other risk behaviours.

Results: During the study period, 2550 individuals were followed (844 of whom were HIV positive at baseline) for a median of 75.4 months (interquartile range 37.9–113.2). Of these, 795 (31%) participants reported binge alcohol use at some time during the study period. In multivariable analyses, binge alcohol use remained independently associated with all-cause-mortality (adjusted hazard ratio = 1.41; 95% confidence interval: 1.06–1.88) after adjustment for other drug use patterns.

Conclusions: Binge alcohol use was associated with time to all-cause mortality among PWID in this setting. Since alcohol use is often overlooked as a risk factor for mortality among this population, these findings highlight the continued need to incorporate addiction treatment and public health interventions and policies that address binge alcohol use to reduce alcohol related-harms.

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1. Introduction

Approximately 11–21 million people inject drugs worldwide (Degenhardt & Hall, 2012). Injection drug use is a well established-risk factor for increased morbidity and mortality (Degenhardt, Bucello, et al., 2011; Mathers & Degenhardt, 2014; Mathers et al., 2013; Miller, Kerr, Strathdee, Li, & Wood, 2007) with previous studies demonstrating that the mortality for people who inject drugs (PWID) exceeds the general population by as much as 13 to 15 times (Hulse, English, Milne, & Holman, 1999; Mathers et al., 2013). Previous studies have denoted that fatal overdose accounts for the majority of deaths in the illicit drug using population (Degenhardt, Bucello, et al., 2011; Mathers

et al., 2013). Though other acute and chronic diseases also contribute to mortality for PWID the majority of non-overdose related deaths are attributable to preventable risk factors including infectious disease such as HIV as well as suicide (Miller et al., 2007).

Although alcohol consumption patterns vary geographically (Rehm et al., 2003), alcohol use disorder (AUD) is one of the most prevalent substance use disorders with an estimated 3.6% of adults affected globally (J Rehm et al., 2009). In Canada in 2012, 18.1% of the population met the criteria for AUD in their lifetime and 3.2% of the population met the same criteria over the last 12 months (Pearson, Janz, & Ali, 2013). AUDs inflict one of the largest burdens on mortality globally and are estimated to account for the largest years of life lost within mental health and substance use disorders at 44.4%, with the largest burden occurring among working age adults (Whiteford et al., 2013). AUD also has a large impact on the non-fatal burden of disease and is estimated to account for 9.6% of disability-adjusted-life years lost worldwide and an estimated 7.9% of years of life lived with disability (Whiteford et al., 2013). Individuals with AUD have a high mortality risk, with individuals in clinical settings estimated to be three to five times greater risk for death, with women at an increased risk in comparison to men (Roerecke & Rehm, 2013).

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Concurrent use of illicit drugs and alcohol is known to be a major contributor to overdose mortality. The impact of the use of central nervous system depressants such as alcohol on fatal and non-fatal overdose has been well described with opioid injection drug use (Degenhardt, Bucello, et al., 2011; Kerr et al., 2007; White, Hingson, Pan, & yi, 2011), with one study reporting an increased mortality risk by as much as 69% (Fischer et al., 2004). In New York City between 1990 and 1998, the combination of alcohol, opioids and cocaine was shown to be the most common cause of overdose death, accounting for 97.6% of all overdose deaths (Coffin et al., 2003). Another study in California showed a two-fold increase in nonfatal overdose for PWID who reported drinking alcohol 17 out of the last 30 days (Martinez, D'Amico, Kral, & Bluthenthal, 2012). In this study, 19% of participants reported drinking alcohol daily in the last 30 days (Martinez et al., 2012). Although this evidence suggests the importance of understanding the impact of alcohol on overdose mortality, there are limited data that explore the impact of binge alcohol use patterns on all-cause mortality among PWID. Therefore, the present study was undertaken to examine the effect of binge alcohol use on mortality in PWID in a Canadian setting.

2. Materials and methods

Our study was performed using data from the Vancouver Injection Drug Users Study (VIDUS) and AIDS Care Cohort to Evaluate Access to Survival Services (ACCESS), which are longstanding prospective cohorts of PWID operating in the Downtown Eastside of Vancouver, Canada. Both studies share identical recruitment and follow-up procedures, allowing for pooling of the data, with the only variance between the cohorts being that the ACCESS cohort includes only HIV-positive individuals and includes injection and non-injection drug users whereas VIDUS includes only HIV-negative PWID. Detailed descriptions of sampling and recruitment procedures for both cohorts have been described elsewhere (Milloy et al., 2012; Strathdee, Palepu, Cornelisse, et al., 1998; Tyndall et al., 2003).

Eligibility criteria included participants aged 18 years or older, any illicit drug use other than cannabinoids in the previous month (for ACCESS) or any injection drug use in the previous month (for VIDUS) and a current resident of the Greater Vancouver Regional District. All participants provided written and informed consent and are compensated (\$20) their time and transportation for each study visit. These cohorts receive annual approval from the University of British Columbia/Providence Healthcare Research Ethics Board.

At baseline and semi-annually thereafter, participants complete an interviewer-administered questionnaire and provide blood samples. Questionnaires ascertain a range of data including demographic characteristics, injection and non-injection drug use and sexual risk behaviours. All interviews occur in a private space with pre- and post-test counselling provided by trained study nurses. Participants who test positive for antibodies to HIV or Hepatitis C virus (HCV) are referred for ongoing health care. Individuals known to be HIV-positive provide blood samples for ongoing HIV disease monitoring.

Using a confidential linkage with the British Columbia Vital Statistics Agency, we ascertained dates and causes of death among study participants and through ongoing locator contacts provided by study participants. The Vital Statistics database recorded causes of death according to International Classification of Diseases (ICD), 10th edition. Both studies are observational and do not include any active study interventions. Participants in the VIDUS cohort that seroconvert during the study period are offered continued study participation in the ACCESS (HIV-positive) cohort.

The present study was restricted to individuals with a history of injecting drugs who were recruited between May 1996 and November 2013. To avoid potential bias relating to long durations between the last date of study visit where behavioural information was assessed and the date of death (i.e., loss to regular follow up), individuals who

were identified as deceased more than 24 months after the last follow-up visit were censored on the date of the last follow up.

Our primary outcome of interest was time to death (all-cause). The primary explanatory variable of interest was binge alcohol use, defined by answering "Yes" to the question, "Have you binged on alcohol in the last 6 months (that is when you used alcohol more than usual)?" We also considered a number of substance use behaviours in the previous six months including \geq daily heroin injection (yes vs. no), \geq daily cocaine injection (yes vs. no), \geq daily crack cocaine smoking (yes vs. no) and \geq daily amphetamine injection (yes vs. no). Other variables included: age (per 10 years older); gender (male vs. female); ethnicity (Caucasian vs. non-Caucasian); living in unstable housing (yes vs. no); HIV serostatus (positive vs. negative) and enrolment in methadone maintenance treatment (yes vs. no). These time-updated variables referred to exposures occurring in the six-month period prior to each study interview. As previously defined, unstable housing includes living in single room occupancy hotels, shelters or other transitional housing or living on the street (Spittal et al., 2002; Wood et al., 2007).

First, we examined baseline characteristics of the study sample, stratified by self-reported binge alcohol use in the previous 6 months. The initial analysis included the Chi-square test for dichotomous variables and the Wilcoxon rank sum test for continuous variables. All-cause mortality rate and 95% confidence intervals [CI] were calculated using the Poisson distribution.

Next, we used bivariable Cox proportional hazard regression to examine the relationship between each explanatory variable and time to death. All behavioural variables were treated as time-varying variables. To fit the multivariable model, we employed a conservative stepwise backward selection approach, as previously described in full (Lima et al., 2012; Milloy et al., 2011). In brief, we included all variables found to be significantly associated with time to death in bivariable analyses at $p < 0.10$ in a multivariable model, and used a stepwise approach to fit a series of reduced models. After comparing the value of the coefficient associated with binge alcohol use in the full model to the value of the coefficient in each of the reduced models, we dropped the secondary variable associated with the smallest relative change. We continue this iterative process until the minimum change exceeded 5%. Remaining variables were considered as potential confounders in a final multivariable model.

3. Results

A total of 2854 individuals were recruited during the study period between and May 1996 and November 2013. Among these 304 (10.7%) participants were excluded as a result of only having a baseline study visit, lacking of either follow-up visit or death date within 24 months from baseline. In comparison to those included in the present study, those excluded were younger ($p < 0.001$) but had no significant differences in gender, ethnicity and binge alcohol use ($p > 0.05$).

Overall, the study sample was followed for a median of 75.4 months (inter-quartile range [IQR]: 37.9–113.2). At baseline, 1687 were male (66.2%), 1541 reported Caucasian ethnicity (60.4%), the median age was 37.7 years (IQR: 29.9–44.2) and 381 (15%) reported binge alcohol use in the previous six months. At baseline, 971 (36%) individuals reported \geq daily heroin injection in the previous six months, 735 (28.8%) reported \geq injected cocaine daily, 614 (24.1%) reported \geq daily crack cocaine smoking and 44 (1.7%) injected amphetamines \geq daily. As shown in Table 1, at baseline, those who reported binge alcohol use were more likely to be younger (median age: 34.6 years vs. 38.3 years, $p < 0.001$), less likely to be enrolled in methadone maintenance treatment (odds ratio [OR] = 0.19; 95% CI: 0.12–0.29) and less likely to be HIV positive (OR = 0.63; 95% CI: 0.49–0.81). In terms of drug use patterns, binge alcohol use was negatively associated with \geq daily heroin injection (OR = 0.60; 95% CI: 0.47–0.76) and \geq daily crack cocaine smoking (OR = 0.50; 95% CI: 0.37–0.67) and positively associated with \geq daily cocaine injection (OR = 1.61; 95% CI: 1.28–2.02).

Table 1
Baseline characteristics of 2550 people who use injection drugs, stratified by binge alcohol use in the last 6 months, in Vancouver, Canada, 1996–2013.

Characteristic	Total N = 2550 (%)	Binge alcohol n = 381	No binge alcohol n = 2164	Odds ratio (95% CI)	p-Value
Gender					
Male	1687 (66.2)	252 (66.1)	1432 (66.2)	1.00 (0.79, 1.26)	0.990
Female	863 (33.8)	129 (33.9)	732 (33.8)		
Age [†]					
Median (IQR)	37.7 (29.9–44.2)	34.6 (27.0–41.3)	38.3 (30.6–44.8)		<0.001
Caucasian ethnicity					
Yes	1541 (60.4)	174 (45.7)	1363 (63.0)	0.49 (0.40, 0.62)	<0.001
No	1009 (39.6)	207 (54.3)	801 (37.0)		
Unstable housing*					
Yes	1770 (69.4)	254 (66.7)	1512 (69.9)	0.87 (0.69, 1.10)	0.233
No	759 (29.8)	123 (32.3)	635 (29.3)		
HIV serostatus*					
Positive	844 (33.1)	95 (24.9)	746 (34.5)	0.63 (0.49, 0.81)	<0.001
Negative	1705 (66.9)	285 (74.8)	1418 (65.5)		
Enrolment in MMT*					
Yes	594 (23.3)	24 (6.3)	569 (26.3)	0.19 (0.12, 0.29)	<0.001
No	1946 (76.3)	357 (93.7)	1586 (73.3)		
≥Daily heroin injection*					
Yes	917 (36.0)	101 (26.5)	814 (37.6)	0.60 (0.47, 0.76)	<0.001
No	1627 (63.8)	279 (73.2)	1345 (62.2)		
≥Daily cocaine injection*					
Yes	735 (28.8)	143 (37.5)	590 (27.3)	1.61 (1.28, 2.02)	<0.001
No	1799 (70.5)	235 (61.7)	1561 (72.1)		
≥Daily crack cocaine smoking*					
Yes	614 (24.1)	56 (14.7)	557 (25.7)	0.50 (0.37, 0.67)	<0.001
No	1933 (75.8)	325 (85.3)	1604 (74.1)		
≥Daily amphetamine injection*					
Yes	44 (1.7)	1 (0.3)	43 (2.0)	0.13 (0.02, 0.94)	0.010†
No	2500 (98.0)	380 (99.7)	2115 (97.7)		

Note: CI = confidence interval; IQR = interquartile range; MMT = methadone maintenance treatment.

† p-Value Fisher's exact test report as 'yes' sample N = 1.

* Behaviours and status in the last 6 months.

A total of 795 (31%) of all individuals followed reported binge alcohol use at any follow-up visit. Overall, 530 individuals died for an incidence density of 2.9 (95% CI: 2.7–3.2) deaths per 100 person years. The primary causes of death included HIV related mortality (23.4%), accidental poisonings (22.1%), unspecified causes (13.8%) and cardiovascular disease (6.3%).

Table 2 shows the bivariable and multivariable Cox regression results examining for a potential association between binge alcohol use and time to death. In the bivariable analyses, binge alcohol use was positively associated with mortality with a (hazard ratio of 1.38 [95% CI: 1.05–1.83]). After adjusting for potential confounders including age, HIV serostatus, daily cocaine injection and enrolment in methadone maintenance treatment, in the multivariable model binge alcohol use remained independently and positively associated with time to all-cause mortality (adjusted hazard ratio [AHR] = 1.41 [95% CI: 1.06–1.88]).

4. Discussion

In the present analysis, we found that binge alcohol use was independently associated with an increased risk for all-cause mortality after adjusting for potential confounders including demographic and drug use characteristics. These variables are known risk factors and were included to adjust for their potential confounding effects (Mathers et al., 2013). The most common causes of death were HIV/AIDS-associated mortality and overdose.

Our findings that binge alcohol use is associated with an increased risk for mortality is unique as we are unaware of any study that specifically examined binge alcohol use and all-cause mortality risk for PWID. Nevertheless, our findings are congruent with existing literature that focuses on fatal and non-fatal overdose mortality for PWID, particularly for opioid users with alcohol use, although such results have varied across geographic regions in their prediction of morbidity and mortality (Coffin et al., 2003; Darke, Ross, & Hall, 1996; Fischer et al., 2004; Kaye &

Table 2

Bivariable and multivariable analyses of time to all-cause death among 2550 people who use injection drugs, Vancouver, Canada, 1996–2013.

Variable	Unadjusted hazard ratio		Adjusted hazard ratio [†]			
	HR	(95% CI)	p-Value	HR	(95% CI)	p-Value
Binge alcohol use* (Yes vs. no)	1.38	(1.05–1.83)	0.023	1.41	(1.06–1.88)	0.018
Gender (Male vs. female)	1.08	(0.91–1.30)	0.372			
Age (Per 10-year older)	1.26	(1.15–1.38)	<0.001	1.29	(1.17–1.42)	<0.001
Ethnicity (Caucasian vs. non-Caucasian)	1.07	(0.90–1.28)	0.421			
Unstable housing* (Yes vs. no)	1.34	(1.13–1.60)	<0.001			
HIV serostatus* (Positive vs. negative)	2.49	(2.10–2.96)	<0.001	2.53	(2.12–3.01)	<0.001
Enrolment in MMT* (Yes vs. no)	0.80	(0.68–0.95)	0.013	0.80	(0.67–0.95)	0.010
≥Daily heroin injection* (Yes vs. no)	0.81	(0.65–1.02)	0.069	1.44	(1.15–1.80)	0.002
≥Daily cocaine injection* (Yes vs. no)	1.46	(1.17–1.82)	<0.001			
≥Daily crack cocaine smoking* (Yes vs. no)	0.89	(0.73–1.08)	0.250			
≥Daily amphetamine injection* (Yes vs. no)	0.24	(0.06–0.96)	0.043			

Note: CI = confidence interval; HR = hazard ratio; MMT = methadone maintenance treatment.

* Behaviours and status in the last six months.

† Model was adjusted for age, HIV serostatus, daily cocaine injection and enrolment in methadone maintenance treatment.

Darke, 2004; Kerr et al., 2007; McGregor, Darke, Ali, & Christie, 1998; Sergeev, Karpets, Sarang, & Tikhonov, 2003). One Canadian study, which focused on overdose mortality, identified alcohol use as a predictor of overdose in the unadjusted model, however the adjusted model was not significant (Fischer et al., 2004). Another Canadian study that looked at non-fatal overdose among polysubstance users found an independent association between daily alcohol use and non-fatal overdose (OR 1.32 CI: 1.09–1.60) (Kerr et al., 2007). Our other multivariable findings are consistent with published literature on increased mortality for PWID including HIV serostatus (Degenhardt, Bucello, et al., 2011; Hayden et al., 2014; Lappalainen et al., 2015) and daily cocaine injection (Degenhardt, Singleton, et al., 2011; Hayden et al., 2014), while participation in a methadone maintenance therapy was associated with a negative time to all cause mortality. This suggests the need for a multi-pronged approach to intervention, including harm reduction strategies, to address morbidity and mortality among PWID. Such an approach should also include screening and treatment for binge or excessive alcohol use.

There are multiple ways that alcohol use is categorized in the literature; AUDs, alcohol abuse, alcohol dependence, excessive drinking and binge alcohol use, with a lack of consensus internationally on a standardized guideline for low risk drinking (Carmen, Angeles, Ana, & María, 2004). In the United States, binge alcohol use can be defined as a consuming 5 or more (for males) and 4 or more drinks in 2 h, which can also be defined as 'excessive' drinking (Services, 2004). In Canada, a set of low risk drinking guidelines were adopted in 2012, which advise 0–2 standard drinks per day for women (≤ 10 per week) and 0–3 standard drinks per day for men (≤ 15 per week) (Stockwell, Butt, Beirness, Gliksman, & Paradis, 2012). Excessive or binge drinkers are at increased risk for developing an AUD (Dawson, 2000) and approximately 9–10% of binge drinkers will develop an AUD in their lifetime (Esser et al., 2014). The prevalence of an AUD increases with the frequency of binge drinking episodes (Esser et al., 2014). Interestingly, an earlier study from our setting, which examined a range of drug use patterns including daily alcohol use, did not find an independent association between daily alcohol use and increased mortality (Hayden et al., 2014). In contrast, the present study may suggest that binge alcohol use rather than regular daily use may be an important and distinct from people who identify as daily drinkers including those who have not been diagnosed with an AUD but engage in binge or high risk types of alcohol use. However, additional research with more robust measures of binge alcohol use is needed to fully elucidate the impact this predictor of mortality among PWID.

Population-based studies have shown that only 5% of the population is able to accurately describe low-risk drinking guidelines and short and long-term harms related to alcohol use (De Visser & Birch, 2012; Livingston, 2012). This lack of knowledge may lead to an underestimation of alcohol consumption and drinking in excess of the guidelines. In addition to international standardization of low-risk drinking guidelines, addiction treatment and public health strategies are needed to enhance knowledge and prevention. There is a substantial evidence base in support of programmes and policies to reduce alcohol related-harms; for example generic psychosocial and developmental programmes (Foxcroft & Tsertsvadze, 2012) to reduce risk factors for drug and alcohol use; policies to tax alcohol and restrict its availability; as well as individually-focused interventions such as screening and brief interventions (Anderson, Chisholm, & Fuhr, 2009; O'Donnell et al., 2014).

There are several limitations to the study. Firstly, this sample was not recruited at random and this may affect the generalizability of the findings. Second, much of the data is ascertained through self-reported measures, particularly for patterns of drug use, and therefore may include some reporting biases. However, self-reported data has been previously used to control for potential confounding in observational studies involving PWID and has been found to be valid (Darke, 1998; Weatherby et al., 1994). Of note, our primary endpoint was based on mortality data obtained through the Vital Statistics database. Third,

binge alcohol use directly before or at the time of death are not described due to the method of self-reporting, which inhibits our ability to ascertain data as proximal at time of death. Fourth, although migration rates out of the province for PWID are low, mortality rates may be underestimated as participants who may have died outside of the province thus not included in the provincial registry. We also censored events that occurred following a long period (>24 months) between the final study interview and death. Fifth, the dichotomous nature of the question used to ascertain binge alcohol use as defined in this study does not provide data for numbers of drinks consumed or frequency of binge episodes. Finally, as this is a non-randomized study, there exists the possibility of residual confounding rather than a causal association between binge alcohol use and mortality. While this bias was addressed in part by using multivariable adjustment of key demographic and behavioural predictors of survival, there may be other unmeasured confounders.

In summary, in this setting, self-reported binge alcohol use was independently associated with higher rates of all-cause mortality among PWID. While these findings are limited by their observational nature, they reinforce the continued need to incorporate addiction treatment, public health interventions and policies that address binge alcohol use to reduce alcohol related-harms.

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