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NON-FATAL OVERDOSE AS A RISK FACTOR FOR SUBSEQUENT FATAL OVERDOSE AMONG PEOPLE WHO INJECT DRUGS

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Abstract

Objectives—To examine the relationship between non-fatal overdose and risk of subsequent fatal overdose.

Methods—We assessed risk factors for overdose death among two prospective cohorts of persons who inject drugs (PWID) in Vancouver, Canada. Extended Cox regression was used to examine if reports of non-fatal overdose were associated with the time to fatal overdose while adjusting for other behavioral, social and structural confounders.

Results—Between May, 1996 and December, 2011, 2,317 individuals were followed for a median of 60.8 months. In total, 134 fatal overdose deaths were identified for an incidence density of 8.94 (95% confidence interval [CI]: 7.55 – 10.59) deaths per 1,000 person-years. During the study period there were 1795 reports of non-fatal overdose. In a multivariate model, recent non-fatal overdose was independently associated with the time to overdose mortality (adjusted hazard ratio [AHR] = 1.95; 95% CI: 1.17 - 3.27). As well, there was a dose response effect of increasing cumulative reports of non-fatal overdose on subsequent fatal overdose.

Conclusion—Reports of recent non-fatal overdose were independently associated with subsequent overdose mortality in a dose-response relationship. These findings suggest that individuals reporting recent non-fatal overdose should be engaged with intensive overdose prevention interventions.

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Contributions

EW and TK contributed to the study design. AC drafted the manuscript. KH, MM and EW reviewed and edited draft and contributed to development of discussion. HD performed statistical analyses. All authors edited and have approved the final article

Conflict of Interest

Alexander Caudarella - Conflicts of interest: none
Kanna Hayashi - Conflicts of interest: none
Huiru Dong - Conflicts of interest: none
MJ Milloy - Conflicts of interest: none
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Keywords

Mortality; Injection drug use; Vancouver; non-fatal overdose

1. INTRODUCTION

Globally, the nonmedical use of drugs represents a considerable public health burden and the human and financial costs have been a growing focus of research over the past decade. Of all the harms associated with illicit drug use, among the most direct and important consequences is fatal overdose. In the United States, for instance, accidental overdose has recently emerged as a leading cause of death (Mack, 2013; Murphy S, 2013). Similarly, overdose mortality has been a longstanding concern, particularly among persons who inject drugs (PWID; Mathers et al., 2013; Quan et al., 2011).

In this context, considerable research has been dedicated to identifying risk factors for overdose mortality with many past studies examining toxicology reports and other circumstances of overdose death (Preti et al., 2002; Zamparutti et al., 2011). Similarly, significant energy has gone into identifying risk factors associated with non-fatal overdose (Darke et al., 2005; Mathers et al., 2013). Substantially more common than fatal overdose (Warner-Smith et al., 2002), non-fatal overdoses are the cause of significant morbidity with a proportion of individuals suffering from hypoxia, aspiration or other negative health outcomes (Britton et al., 2010; Warner-Smith et al., 2002, 2001). The reported prevalence of non-fatal overdoses among illicit drug users has varied significantly based on geography and study population, with estimates ranging between 20% and 70% per lifetime (Darke et al., 1996; Kerr et al., 2007; Kinner et al., 2012; Ochoa et al., 2001; Silva et al., 2013).

One important question, which remains insufficiently addressed in the literature, is to what degree non-fatal overdose events are associated with the risk of subsequent fatal overdose. It may be that persons who experience non-fatal overdose may become more cautious in their future drug use thereby reducing the risk of future adverse events (Mathers et al., 2013), or that those experiencing non-fatal overdose are at higher risk of subsequent fatal overdose (Coffin et al., 2007; Stoové et al., 2009). Due to the urgent public health crisis surrounding fatal overdose mortality, the present study was undertaken to examine if self-reported non-fatal overdose was associated with subsequent fatal overdose among PWID in a Canadian setting

2. METHODS

Data for the present study were derived from the Vancouver Injection Drug Users Study (VIDUS) and AIDS Care Cohort to Evaluate Access to Survival Services (ACCESS), which are open prospective cohorts of persons who use drugs in Vancouver, Canada. The studies have been described in detail previously and are essentially identical in their recruitment, data collection and follow up procedures with the exception of HIV status and an eligibility criterion regarding injection drug use (Kerr et al., 2008; Strathdee et al., 1998; Wood et al., 2001). HIV-negative adult persons who have injected drugs in the previous month are eligible for VIDUS and HIV-positive adult persons who have used an illicit drug other than

cannabinoids in the previous month are eligible for ACCESS. Individuals who become HIV-infected while under follow up in VIDUS are offered recruitment into the ACCESS study.

At baseline and semiannually, participants provide blood samples for serologic testing for HIV and hepatitis C virus and complete an interviewer-administered questionnaire. Participants receive $20 CAD for each study visit. The questionnaire items are essentially identical in both studies and elicit demographic data as well as information about drug use, HIV risk behavior, and drug treatment. The studies have been approved by the University of British Columbia/Providence Health Care Research Ethics Board.

The outcome of interest in this analysis was overdose mortality derived from a confidential record linkage with the provincial Vital Statistics Agency, with the provincial Coroner's office and other tracking procedures. The cause of death for each case is coded in accordance with the International Classification of Diseases, Tenth Revision (ICD -10).

The primary explanatory variable of interest was non-fatal overdose in the previous 180 days. As part of the study's baseline and semi-annual follow up questionnaires, participants were queried about recent non-fatal overdose experiences. The question specifically asked: “In the last six months, have you overdosed by accident (i.e., where you had a negative reaction from using too much drugs)?” The questionnaire did not ask participants if they had previously intentionally overdosed. Socio-demographic characteristics and behavioral factors were also considered as secondary explanatory variables. These included: age (per 10 years older), gender (male vs. female), ethnicity (Caucasian vs. other), homelessness (yes vs. no), incarceration (yes vs. no), daily cocaine injection (yes vs. no), daily heroin injection (yes vs. no), daily crack smoking (yes vs. no), enrolment in methadone maintenance treatment (yes vs. no), HIV serostatus (positive vs. negative) and HCV serostatus (positive vs. negative). All behavioral variables referred to the six months prior to the interview and were treated as time-updated. Unless otherwise specified, variable definitions are consistent with those described in previous studies.

The present analyses were restricted to those participants who completed baseline and at least one follow-up visit between May, 1996 and December, 2011. To avoid potential confounding due to long durations between the last study visit and the date of death, individuals who were deceased more than 24 months after the last follow-up visit were censored on the last follow-up date in December, 2011.

As an initial analysis, we summarized the baseline characteristics of participants, stratified by recent non-fatal overdose status at baseline. Comparisons of baseline characteristics for participants with and without report of recent non-fatal overdose were made using the Chi-square test (for binary measures) and Wilcoxon rank sum test (for continuous measures). Overdose mortality rate and 95% confidence interval (CI) were calculated using the Poisson distribution. Deaths from other causes were censored as non-events and treated as competing risks for the occurrence of fatal overdose. Therefore, cumulative incidence function was applied to estimate the cumulative probabilities of fatal overdoes for participants with and without a recent non-fatal overdose at baseline, and the difference between groups was

tested using Gray's method (Gray, 1988). Survival probabilities were also estimated using the complement of cumulative incidence function.

We then used extended Cox regression model (Kleinbaum DG, 1996) to examine bivariate associations between each explanatory variable and time to overdose mortality. To fit the multivariate model, we used a previously described backwards selection process (Maldonado and Greenland, 1993; Maldonado et al., 2008). In brief, we began with all explanatory variables of interest in a full model, then generated a series of reduced models by removing each secondary explanatory variable one at a time. For each of these models we assessed the relative change in the coefficient for non-fatal overdose. The secondary explanatory variable that resulted in the smallest absolute relative change in the coefficient for non-fatal overdose was then removed. Secondary variables continued to be removed through this process until the smallest relative change exceeded 5%. Remaining variables were considered confounders and were included in the final multivariate model. As a sub-analysis, we also used extended Cox regression to examine if the number of recent non-fatal overdose events is associated with the time to fatal overdose in a dose-dependent fashion. A multivariate model was used and adjusted for age and hive serostatus. Here, zero overdoses was the reference category and we compared this to individuals having had 1, 2–3, 4–7 and 8 or greater 6-month observation periods where the individual reported at least one overdose during the entire cohort observation period.

All p-values were two-sided. All statistical analyses were performed using SAS software version 9.3 (SAS, Cary, NC).

3. RESULTS

In total, 2,598 participants were recruited and followed between May, 1996 and December, 2011. Overall, 281 (10.8%) individuals were excluded as a result of missing follow-up information or incomplete data. Those participants who were excluded were younger ($p < 0.05$), however, there was no difference in baseline reports of recent non-fatal overdose or any of the other variables considered.

For the 2,317 participants eligible for the present study, the median follow up time was 60.8 months (interquartile range: 33.5 – 112.9). Overall, 319 (13.8%) individuals reported a recent non-fatal overdose at baseline. The baseline characteristics of study participants stratified by fatal overdose are presented in Table 1. As shown, those who died from overdose during follow up were more likely to be HIV and/or HCV seropositive or report daily injection of cocaine at baseline (all $p < 0.05$).

During the study period, 883 participants experienced a total of 1,795 times of non-fatal overdose, the overall non-fatal overdose rate is 11.97 (95%CI: 11.21 - 12.80) events per 100 person-years. Similarly, there were 134 fatal overdoses with a rate of 8.94 (95% CI: 7.55 – 10.59) deaths per 1,000 person-years producing a crude rate ratio between non-fatal overdose and fatal overdose of 13.45.

Figure 1 presents the cumulative survival probabilities stratified by baseline recent non-fatal overdose. As shown here, the cumulative survival probability among participants reporting a

recent fatal overdose was 95.9% by 36 months of follow up compared to 97.9% among participants without reports of recent non-fatal overdose (p = 0.015). Among the 134 fatal-overdose participants, 66 (49.3%) of them reported at least once non-fatal overdose before death.

Table 2 provides results of bivariate and multivariate Extended Cox regression analyses. As shown, after adjusting for potential confounders, recent non-fatal overdose remained independently associated with overdose mortality (adjusted hazard ratio [AHR] = 1.95; 95% CI: 1.17 - 3.27). As shown in Figure 2, in the sub-analysis, there was a dose-response effect of increasing cumulative reports of non-fatal overdose on subsequent fatal overdose. Although one overdose event did not increase the risk of fatal overdose [AHR 1.15 (0.72-1.82)], 2–3 overdoses were independently associated with the time to fatal overdose with an AHR of 1.81 (95% CI: 1.19 – 2.27), 4-7 overdoses with an AHR of 2.12 (95 % CI: 1.11 – 4.04) and 8-11 overdoses with an AHR of 5.24 (95 % CI 1.56 – 17.01).

4. DISCUSSION

In the present study, we observed an elevated risk of death from overdose in individuals who had recently reported non-fatal overdose. In addition, a dose-response effect was observed with an increasing number of cumulative reports of non-fatal overdose associated with a greater risk of subsequent overdose death. This finding has significant implications for future research and public health practice.

Our study is among the few to investigate the relationship between non-fatal overdose events and fatal overdose. A recent systematic review and meta-analysis of studies examining mortality risk among PWID did not identify any studies reporting an association between mortality and non-fatal overdose (Darke et al., 2007; Mathers et al., 2013). One prior study examining overdose mortality following non-fatal overdose (Stoové et al., 2009). Here, the authors examined an ambulance register in Melbourne, Australia, for reports of non-fatal heroin overdose and compared it to death registry data. They identified an association between non-fatal overdoses and subsequent fatal overdose; an association which grew stronger as a greater number of non-fatal overdoses had been reported. This study was limited by the fact that the study only examined non-fatal overdoses for which an ambulance was called. More recently, findings from the Australian Treatment Outcome Study (ATOS), a cohort study of heroin users in Sydney, Australia, demonstrated history of overdose as a predictor of fatal overdose although no dose-response relationship was noted (Darke et al., 2011). Our study builds upon the ATOS research findings as their sample had an extensive addiction treatment history and was limited to opiate users. As well, whereas ATOS examined self-report of non-fatal overdose at baseline only, which could have been seven years before a participant deceased, the longitudinal nature of the VIDUS cohort allowed us to look at the effect of recent non-fatal overdose. Risk factors for non-fatal overdose have been carefully described across a range of geographical areas and demographic populations (Bergenstrom et al., 2008; Havens et al., 2011; Quan et al., 2011). In describing the association with future fatal overdose our analyses support and add value to the significant work done globally to identify individuals and populations at risk for non-fatal overdose (Darke et al., 2005; Warner-Smith et al., 2002). Our findings suggest that screening for

recent non-fatal overdose events may also help identify individuals who are at a heightened risk of fatal overdose. Therefore, overdose prevention interventions should ensure to include these individuals. Further, interventions at the time of non-fatal overdose could be highly effective in motivating people to access addiction treatment. Previous research has demonstrated that individuals treated for non-fatal overdoses were more likely to seek drug treatment if health care workers took this opportunity to discuss substance abuse (Pollini et al., 2006a, 2006b). Although risk of overdose can increase upon discharge from abstinence-based treatments, gains made in terms of reduced drug use following treatment may limit the future risk of overdose. Further, referral to appropriate substitution therapies, including methadone maintenance treatment, has been shown to reduce overdose risk.

The present study has limitations. Although previous studies have indicated that the study sample is highly representative of PWID in Vancouver, neither VIDUS nor ACCESS is a random sample. Therefore, generalizability is limited. Secondly, non-fatal overdose represents a subjective experience and is subject to the limitations of self-report with participants asked only about accidental non-fatal overdoses. However, it is important to note that participants volunteered this information prior to subsequent overdose. Third, as with all observational studies, the relationships between the explanatory variables and outcome assessed may be under the influence of unobserved confounding. While we sought to address this bias with multivariate adjustment of the key demographic and behavioral predictors of survival, residual confounding may have persisted. Fourth, mortality rates may have been underestimated, as participants who died outside of the province were not included in the provincial registry and were thus not accounted for. However, previous studies have shown that migration rates among drug users are relatively low in this setting. As well, as we relied on a provincial death registry, we cannot exclude the possibility that some of the noted overdose deaths were in fact suicides. As well, although it was not possible for this study, it would be of value to evaluate the relationship between non-fatal overdose and all-cause mortality in future research.

In summary, reports of recent non-fatal overdose were independently associated with subsequent overdose mortality in a dose dependent fashion. These findings build on numerous studies identifying risk factors for non-fatal overdose and suggest that individuals reporting recent non-fatal overdose should be engaged with intensive overdose prevention interventions in order to reduce subsequent overdose mortality among PWID.

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REFERENCES

Bergenstrom A, Quan VM, Van Nam L, McClausland K, Thuoc NP, Celentano D, Go V. A cross-sectional study on prevalence of non-fatal drug overdose and associated risk characteristics among out-of-treatment injecting drug users in North Vietnam. Subst. Use Misuse. 2008; 43:73–84. [PubMed: 18189206]

Britton PC, Wines JD, Conner KR. Non-fatal overdose in the 12 months following treatment for substance use disorders. Drug Alcohol Depend. 2010; 107:51–55. [PubMed: 19828263]

Coffin PO, Tracy M, Bucciarelli A, Ompad D, Vlahov D, Galea S. Identifying injection drug users at risk of nonfatal overdose. Acad. Emerg. Med. 2007; 14:616–623. [PubMed: 17554010]

Darke S, Mills KL, Ross J, Teesson M. Rates and correlates of mortality amongst heroin users: findings from the Australian Treatment Outcome Study (ATOS), 2001-2009. Drug Alcohol Depend. 2011; 115:190–195. [PubMed: 21130585]

Darke S, Ross J, Hall W. Overdose among heroin users in Sydney, Australia: I. Prevalence and correlates of non-fatal overdose. Addiction. 1996; 91:405–411. [PubMed: 8867202]

Darke S, Ross J, Teesson M. The Australian Treatment Outcome Study (ATOS): what have we learnt about treatment for heroin dependence? Drug Alcohol Rev. 2007; 26:49–54. [PubMed: 17364836]

Darke S, Williamson A, Ross J, Teesson M. Non-fatal heroin overdose, treatment exposure and client characteristics: findings from the Australian treatment outcome study (ATOS). Drug Alcohol Rev. 2005; 24:425–432. [PubMed: 16298837]

Gray R. A class of K-sample tests for comparing the cumulative incidence of a competing risk. Ann. Stat. 1988; 16:1141–1154.

Havens JR, Oser CB, Knudsen HK, Lofwall M, Stoops WW, Walsh SL, Leukefeld CG, Kral AH. Individual and network factors associated with non-fatal overdose among rural Appalachian drug users. Drug Alcohol Depend. 2011; 115:107–112. [PubMed: 21126831]

Kerr T, Fairbairn N, Tyndall M, Marsh D, Li K, Montaner J, Wood E. Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. Drug Alcohol Depend. 2007; 87:39–45. [PubMed: 16959438]

Kerr T, Small W, Johnston C, Li K, Montaner JS, Wood E. Characteristics of injection drug users who participate in drug dealing: implications for drug policy. J. Psychoactive Drugs. 2008; 40:147–152. [PubMed: 18720663]

Kinner SA, Milloy MJ, Wood E, Qi J, Zhang R, Kerr T. Incidence and risk factors for non-fatal overdose among a cohort of recently incarcerated illicit drug users. Addict. Behav. 2012; 37:691–696. [PubMed: 22385733]

Kleinbaum, DG.; K.M.. Survival Analysis: A Self-Learning Text. Springer-Verlag; New York: 1996.

Mack KA. Drug-induced deaths - United States, 1999-2010. MMWR Surveill. Summ. 62 Suppl. 2013; 3:161–163.

Maldonado G, Greenland S. Simulation study of confounder-selection strategies. Am. J. Epidemiol. 1993; 138:923–936. [PubMed: 8256780]

Maldonado G, GS.; Lash, TL. Modern Epidemiology. Lippincott Williams & Wilkins; New York: 2008.

Mathers BM, Degenhardt L, Bucello C, Lemon J, Wiessing L, Hickman M. Mortality among people who inject drugs: a systematic review and meta-analysis. Bull. World Health Organ. 2013; 91:102–123. [PubMed: 23554523]

Murphy S, XJ.; Kochanek, K. Deaths: Final Data for 2010. National Centre for Health Statistics. National Vital Statistics Reports; Hyattsville: 2013.

Ochoa KC, Hahn JA, Seal KH, Moss AR. Overdosing among young injection drug users in San Francisco. Addict. Behav. 2001; 26:453–460. [PubMed: 11436937]

Pollini RA, McCall L, Mehta SH, Vlahov D, Strathdee SA. Non-fatal overdose and subsequent drug treatment among injection drug users. Drug Alcohol Depend. 2006a; 83:104–110. [PubMed: 16310322]

Pollini RA, O'Toole TP, Ford D, Bigelow G. Does this patient really want treatment? Factors associated with baseline and evolving readiness for change among hospitalized substance using adults interested in treatment. Addict. Behav. 2006b; 31:1904–1918. [PubMed: 16483724]

Preti A, Miotto P, De Coppi M. Deaths by unintentional illicit drug overdose in Italy, 1984-2000. Drug Alcohol Depend. 2002; 66:275–282. [PubMed: 12062462]

Quan VM, Minh NL, Ha TV, Ngoc NP, Vu PT, Celentano DD, Mo TT, Go VF. Mortality and HIV transmission among male Vietnamese injection drug users. Addiction. 2011; 106:583–589. [PubMed: 21054619]

Silva K, Schrager SM, Kecojevic A, Lankenau SE. Factors associated with history of non-fatal overdose among young nonmedical users of prescription drugs. Drug Alcohol Depend. 2013; 128:104–110. [PubMed: 22974490]

Stoové MA, Dietze PM, Jolley D. Overdose deaths following previous non-fatal heroin overdose: record linkage of ambulance attendance and death registry data. Drug Alcohol Rev. 2009; 28:347–352. [PubMed: 19594787]

Strathdee SA, Palepu A, Cornelisse PG, Yip B, O'Shaughnessy MV, Montaner JS, Schechter MT, Hogg RS. Barriers to use of free antiretroviral therapy in injection drug users. JAMA. 1998; 280:547–549. [PubMed: 9707146]

Warner-Smith M, Darke S, Day C. Morbidity associated with non-fatal heroin overdose. Addiction. 2002; 97:963–967. [PubMed: 12144598]

Warner-Smith M, Darke S, Lynskey M, Hall W. Heroin overdose: causes and consequences. Addiction. 2001; 96:1113–1125. [PubMed: 11487418]

Wood E, Tyndall MW, Spittal PM, Li K, Kerr T, Hogg RS, Montaner JS, O'Shaughnessy MV, Schechter MT. Unsafe injection practices in a cohort of injection drug users in Vancouver: could safer injecting rooms help? CMAJ. 2001; 165:405–410. [PubMed: 11531048]

Zamparutti G, Schifano F, Corkery JM, Oyefeso A, Ghodse AH. Deaths of opiate/opioid misusers involving dihydrocodeine, UK, 1997-2007. Br. J. Clin. Pharmacol. 2011; 72:330–337. [PubMed: 21235617]

Highlights

- We assessed risk factors for overdose death among two prospective cohorts of persons who inject drugs (PWID).
- Recent non-fatal overdose was independently associated with subsequent overdose mortality.
- A dose-dependent relationship was found between fatal overdose and number of previous overdoses.

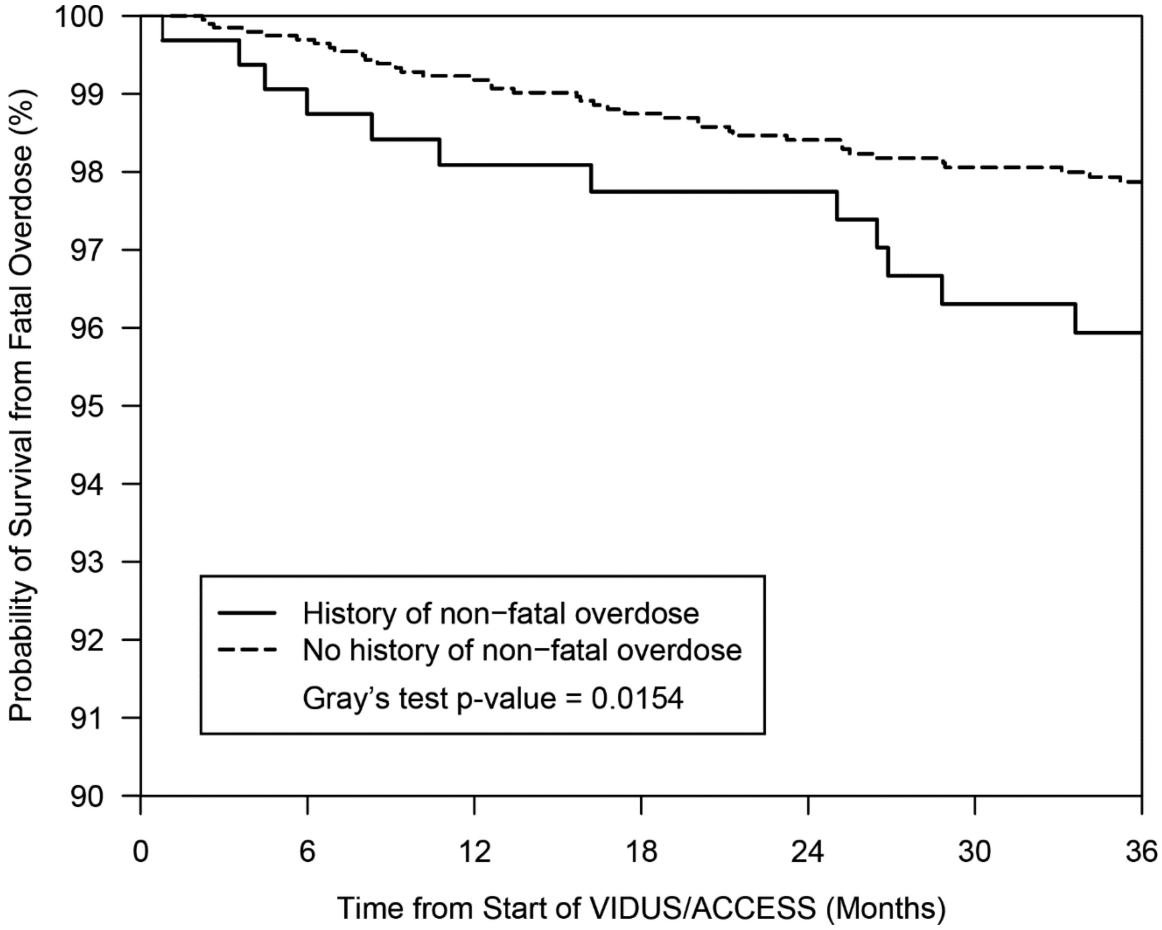

Figure 1.
Time to overdose mortality stratified by reporting non-fatal overdose in the last six months at baseline.

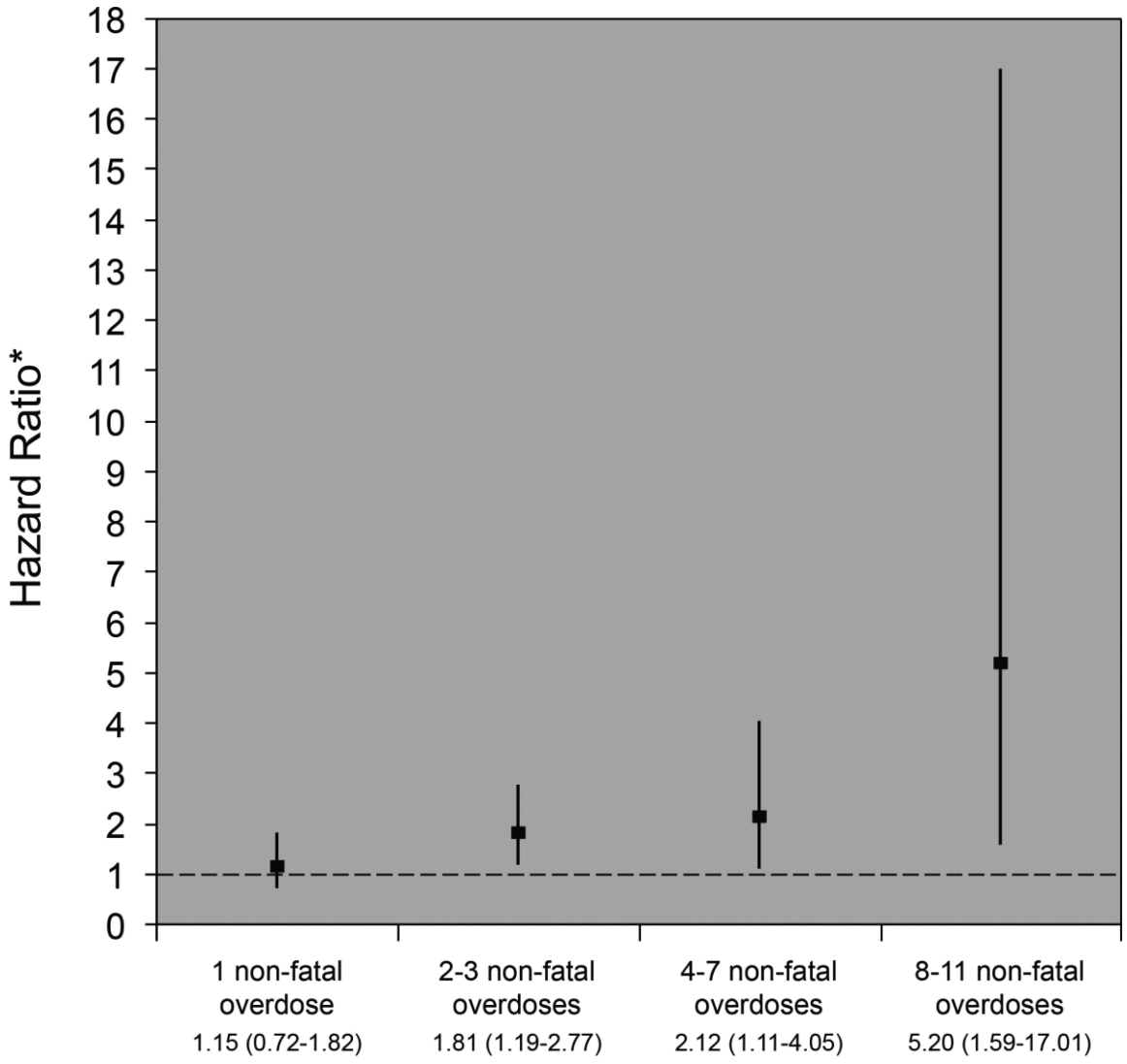

Figure 2.

Dose-response effect of reporting non-fatal overdose on subsequent fatal overdose

*Hazard ratios adjusted for age and HIV serostatus.

TABLE 1

Baseline demographics of study participants stratified by fatal overdose (n = 2317).

Characteristic	Total (%) (*n* = 2317)	Overdose			
		Yes (%) (*n* = 134)	No (%) (*n* = 2183)	Odds Ratio (95% CI)	*p*-value
Age					
Median (IQR[£])	37.3 (29.4-43.7)	38.8 (31.6-42.8)	37.2 (29.2-43.9)	1.01 (0.99, 1.03)	0.305
Gender					
Male	1546 (66.7)	92 (68.7)	1454 (66.6)	1.10 (0.75, 1.60)	0.625
Female	771 (33.3)	42 (31.3)	729 (33.4)		
Ethnicity					
Caucasian	1419 (61.2)	83 (61.9)	1336 (61.2)	1.03 (0.72, 1.48)	0.864
Other	898 (38.8)	51 (38.1)	847 (38.8)		
Homelessness*					
Yes	417 (18.0)	22 (16.4)	395 (18.1)	0.89 (0.56, 1.42)	0.624
No	1900 (82.0)	112 (83.6)	1788 (81.9)		
Incarceration*					
Yes	351 (15.1)	28 (20.9)	323 (14.8)	1.52 (0.99, 2.34)	0.056
No	1965 (84.8)	106 (79.1)	1859 (85.2)		
Daily cocaine injection*					
Yes	263 (11.4)	23 (17.2)	240 (11.0)	1.68 (1.05, 2.68)	0.029
No	2054 (88.6)	111 (82.8)	1943 (89.0)		
Daily heroin injection*					
Yes	415 (17.9)	27 (20.1)	388 (17.8)	1.17 (0.75, 1.81)	0.486
No	1902 (82.1)	107 (79.9)	1795 (82.2)		
Daily crack smoking*					
Yes	563 (24.3)	33 (24.6)	530 (24.3)	1.02 (0.68, 1.53)	0.927
No	1754 (75.7)	101 (75.4)	1653 (75.7)		
Methadone Maintenance Treatment*					
Yes	1061 (45.8)	51 (38.1)	1010 (46.3)	0.71 (0.50, 1.02)	0.064
No	1256 (54.2)	83 (61.9)	1173 (53.7)		
HIV serostatus					
Positive	817 (35.3)	61 (45.5)	756 (34.6)	1.58 (1.11, 2.24)	0.010
Negative	1500 (64.7)	73 (54.5)	1427 (65.4)		
HCV serostatus					
Positive	2065 (89.1)	127 (94.8)	1938 (88.8)	2.29 (1.06, 4.97)	0.030
Negative	252 (10.9)	7 (5.2)	245 (11.2)		

[€]Odds ratio is associated with 10 years increase of age.

*Behaviours refer to activities in the last six months.

£IQR = Inter-quartile range.

Table 2

Bivariate and multivariate Extended Cox regression analyses of the time to fatal overdose among cohorts of persons who inject drugs in Vancouver, Canada (n = 2317).

	Unadjusted Hazard Ratio (HR)			Adjusted† Hazard Ratio (AHR)		
Variable	**RH**	**(95% CI)**	***p*-value**	**ARH**	**(95% CI)**	***p*-value**
Non-fatal Overdose*						
(yes vs. no)	1.85	(1.11 – 3.07)	0.018	1.95	(1.17 – 3.27)	0.011
Age						
(per 10 years older)	1.18	(0.99 – 1.40)	0.058	1.22	(1.02 – 1.45)	0.030
Gender						
(male vs. female)	1.27	(0.88 – 1.82)	0.206			
Ethnicity						
(Caucasian vs. other)	1.20	(0.85 – 1.70)	0.302			
Homelessness*						
(yes vs. no)	0.85	(0.54 – 1.34)	0.480			
Incarceration*						
(yes vs. no)	1.08	(0.70 – 1.66)	0.714			
Daily cocaine injection*						
(yes vs. no)	1.11	(0.71 – 1.74)	0.646			
Daily heroin injection*						
(yes vs. no)	0.81	(0.53 – 1.24)	0.327			
Daily crack smoking*						
(yes vs. no)	0.84	(0.57 – 1.24)	0.374			
Methadone Maintenance Treatment*						
(yes vs. no)	0.86	(0.61 – 1.21)	0.386			
HCV serostatus						
(positive vs. negative)	1.82	(0.85 – 3.90)	0.122			

*Behaviours refer to activities in the last six months.

†Model was also adjusted for HIV serostatus.