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Overdose deaths following previous non-fatal heroin overdose: Record linkage of ambulance attendance and death registry data

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Abstract

Introduction and Aims. *Experiencing previous non-fatal overdoses have been identified as a predictor of subsequent non-fatal overdoses; however, few studies have investigated the association between previous non-fatal overdose experiences and overdose mortality. We examined overdose mortality among injecting drug users who had previously been attended by an ambulance for a non-fatal heroin overdose.* ***Design and Methods.*** *Using a retrospective cohort design, we linked data on non-fatal heroin overdose cases obtained from ambulance attendance records in Melbourne, Australia over a 5-year period (2000–2005) with a national death register.* ***Results.*** *4884 people who were attended by ambulance for a non-fatal heroin overdose were identified. One hundred and sixty-four overdose deaths occurred among this cohort, with an average overdose mortality rate of 1.20 per 100 person-years (95% CI, 1.03–1.40). Mortality rate decreased 10-fold after 2000 coinciding with widely reported declines in heroin availability. Being male, of older age (>35 years) and having been attended multiple times for previous non-fatal overdoses were associated with increased mortality risk.* ***Discussion and Conclusions.*** *As the first to show a direct association between non-fatal overdose and subsequent overdose mortality, this study has important implications for the prevention of overdose mortality. This study also shows the profound effect of macro-level heroin market dynamics on overdose mortality.* [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]

Key words: overdose, mortality, injecting drug use, cohort study, data linkage.

Introduction

The health consequences of injecting drugs over an extended time period are profound. Dependent injecting drug users (IDU) are of considerable risk of morbidity [1], and substantially greater risk of mortality (estimated at between six and 20 times) compared with their non-injecting peers [2,3]. Over the past two decades heroin overdose has emerged as a major public health challenge. Opioid use constitutes the largest contributor to illicit drug deaths, driven largely by the injection of heroin [4,5].

Mortality among IDU is dependent on the complex interaction of precursors and sequelae associated with injecting drugs. Factors identified as increasing mortality risk among IDU include: drug toxicity, dose and frequency of injection [6,7]; psychosocial and environmental factors, such as imprisonment and homelessness [8,9]; medical complications resulting from injecting drugs [10,11]; and opioid pharmacotherapies (primarily during initial treatment periods; see [12,13]). In addition, demographic characteristics, such as being male and older age or longer duration of injecting, have been shown to be associated with greater overdose risk [1,2].

Fatal overdose, however, makes up only a small proportion of overdose events, estimated at between 2% and 4% [14]. Others have reported annual rates of non-fatal overdose among IDU of between 10% and 30% [15–19]. Non-fatal overdose results in significant morbidity [19,20] and recent studies have identified previous non-fatal overdose experiences as a significant

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predictor of subsequent non-fatal overdose [17,21,22]. However, to our knowledge, researchers are yet to report associations between previous non-fatal overdose and subsequent overdose mortality.

Australian studies show that most heroin overdose cases are attended by ambulance [19,23]. Ambulance service records are a rich source of information on the nature and prevalence of heroin overdose [24–26]. In this study, we linked a database of ambulance service records with a mortality database to examine trends in overdose mortality among people who had previously experienced a non-fatal heroin overdose. This retrospective cohort study design allowed us to examine overdose mortality among a cohort who had been previously attended by ambulance for a non-fatal heroin overdose between 2000 and 2005, as well as explore the effects of personal characteristics, such as age, sex and number of recorded overdoses on mortality rates.

Methods

Case ascertainment

Cases were obtained from a database of ambulance service records collated by Turning Point Alcohol and Drug Centre in collaboration with the Melbourne Metropolitan Ambulance Service (MAS; see [27]). This database is a compilation of patient care records (PCR) that paramedics complete at the scene of attendance. PCR include descriptions of attendance and outcome details, basic patient demographics and relevant clinical details. All cases related to drug overdose or poisoning PCR are extracted by trained sorters from the entire pool of PCR and sent for data entry by trained coders. Although it is difficult to define the term heroin overdose adequately [3], the MAS database allows for a reasonably precise definition of overdose. To this end a heroin overdose was defined as a case where: (i) a positive response (increased respiration rate or Glasgow Coma Score) to the administration of naloxone was observed and there was no indication that the overdose resulted from another opioid, such as codeine or methadone; or (ii) heroin use is established through the assessment of the ambulance paramedic or by another person at the scene but naloxone was not administered. A more detailed description of the MAS drug overdose and poisoning database is reported elsewhere [27]. All persons recorded as experiencing a non-fatal heroin overdose attended by ambulance between 1 October 2000 and 31 September 2005 were included in the cohort.

Data matching

At data entry each case on the MAS database is given an alpha-numeric personal identifier code made up a letters from patient's first and second name, their date of birth and sex. The codes for our study cohort were sent to the National Death Index (NDI) for retrospective matching. The NDI is a data register containing information on all deaths occurring in Australia since 1980. The NDI is designed to facilitate the conduct of epidemiological studies and its use is strictly confined to medical research. The NDI matched personal identifier codes to all mortality cases recorded between 2000 and 2005. Matched cases were identified and date of death and International Classification of the Diseases (ICD) 10 cause of death codes were merged with the MAS dataset. Overdose deaths were defined as cases where accidental poisoning (ICD-10 X40-X49), intentional self-poisoning (ICD-10 X60-X64) and/or poisoning by drugs/toxic substances (ICD-10 T36-T65) were assigned as primary or secondary causes of death. Taking account of the polydrug use norms among heroin injectors and the imprecise nature of death registrations and identification of causes of death (particularly in drug-related mortality), a broad range of drug classes was included to ascertain drug overdose mortality among heroin injectors.

Analysis

Overdose mortality was estimated for all cases, with the person-years (PY) of follow-up determined from date of first overdose attendance to either death or finally censored at 31 December 2005 (the last date at which full mortality data were available at the time of data matching). Trends in mortality were described for the entire cohort and by sex, age at baseline and number of previous overdose events attended by ambulance between 1 October 2000 and 31 September 2005. Comparisons of mortality among these groups were analysed using Kaplan–Meier survival analyses (for baseline characteristics) and a continuous time Cox regression analysis. Non-fatal overdose events were treated as a continuously time-varying covariate, with follow-up time divided into periods between each non-fatal overdose event for each participant. All analyses were conducted using Intercooled STATA version 9.0 (StataCorp, College Station, TX, USA).

Results

A total of 4884 people were followed from the date of their first non-fatal heroin overdose ambulance attendance recorded after 1 October 2000 until the date of death or 31 December 2005, an average of 2.24 years between overdose events or censorship (minimum 0.003 years, maximum 5.25 years). The mean age of cases at ascertainment was 29 years (SD 8.28) with 1627 (33%) aged less than 25 years, 1238 (25%) aged

Table 1. *Mortality rate of injecting drug users that had previously experienced non-fatal overdose*

	Number in cohort[a]	Cumulative non-fatal heroin overdoses	Overdose deaths (%)	Person-years	Overdose mortality rate per 100 person-years	
					Overall	95% confidence interval
Annual rates						
2000	868	989	10 (6)	104	9.65	5.19–17.93
2001	1 619	1 875	15 (9)	1 280	1.17	0.71–1.94
2002	2 357	2 833	22 (13)	2 030	1.03	0.67–1.59
2003	3 321	4 172	33 (20)	2 639	1.25	0.89–1.76
2004	4 223	5 552	46 (28)	3 717	1.24	0.93–1.65
2005	4 699	6 445	38 (23)	4 427	0.86	0.63–1.18
Total rate	4 884		164	13 629	1.20	1.03–1.40
Sex						
Male	3 441	4 531	131 (80)	9 463	1.38	1.17–1.64
Female	1 443	1 914	33 (20)	4 167	0.79	0.56–1.11
Age group (years)						
<25	1 627	2 205	43 (26)	5 107	0.84	0.63–1.14
25–29	1 238	1 657	51 (31)	3 348	1.52	1.16–2.01
30–34	871	1 137	22 (13)	2 243	0.98	0.65–1.49
35+	1 150	1 446	48 (29)	2 932	1.64	1.23–2.17

[a]Participant numbers for annual rates denote sample size at the end of each calendar year.

between 25 and 29 years, 871 (18%) aged 30–34 years and 1150 (24%) aged 35 years and over. The majority (71%) of non-fatal overdose cases were male.

A total of 164 people died of an overdose during the follow-up period. Of these, 131 (80%) were male, 101 (62%) had been previously attended to by an ambulance for one heroin overdose, 36 (22%) had twice been attended to for a previous heroin overdose and 27 (17%) had been attended to more than twice for previous heroin overdoses (maximum six) during the follow-up period. The overall overdose mortality rate was 1.20 (95% CI, 1.03–1.40) per 100 PY. However, this varied dramatically across the follow-up period; from 9.65 per 100 PY in 2000 to around 1 per 100 PY for subsequent years. Mortality rates were higher for males and those aged 25–29 years and over 35 years (Table 1).

Differences in survival were assessed using Kaplan–Meier survival curves and Cox proportional hazards modelling. Figure 1 shows Kaplan–Meier curves by the baseline characteristics of sex and age. Table 2 shows unadjusted and adjusted hazard ratios by sex, age and number of previous non-fatal overdoses experienced during the follow-up period. Being male, aged 25–29 and over 35 years and having been attended by ambulance multiple times for previous non-fatal heroin overdoses was associated with greater risk of overdose mortality.

Discussion

This is the first study to provide a detailed examination of overdose mortality among a cohort who had previously been attended by ambulance for a non-fatal heroin overdose. During a follow-up period of 5 years and 3 months, 4884 individuals were identified (cumulative PY of 13 629) accounting for 6445 cases of non-fatal heroin overdose ambulance attendances and 164 overdose deaths. Our data showed a ratio of non-fatal to fatal overdose of 39.3:1 or that 2.6% of overdoses result in mortality—findings consistent with previously reported Australian data (3.1%, see [14]) and anecdotal reports from Australian heroin users (5%, see [23]).

The overall annual rate of mortality was 1.20 per 100 PY, but fluctuated approximately 1 per 100 PY across most of the follow-up period. Overdose mortality rates reported elsewhere vary across time, location and other factors, such as recruitment sites (e.g. treatment vs. emergency department) and prevalence of HIV among IDU. However, in all years other than 2000 our estimates of rates of overdose mortality are largely consistent with other Australian and international studies of heroin-related mortality [2,7,8,28,29]. In light of the case ascertainment used in this study and findings presented here and in other research of an increased overdose risk associated with previous overdose events (e.g. [17]), we might have expected rates of mortality in this study to be comparably higher than those reported in other studies.

Our estimated annual mortality for 2000 was 9.65 per 100 PY, some 9–10 times higher than that observed in subsequent years. This figure stresses the effects of the heroin 'glut' [30] of the late 1990s and the subsequent heroin 'drought' [31]. The glut condi-

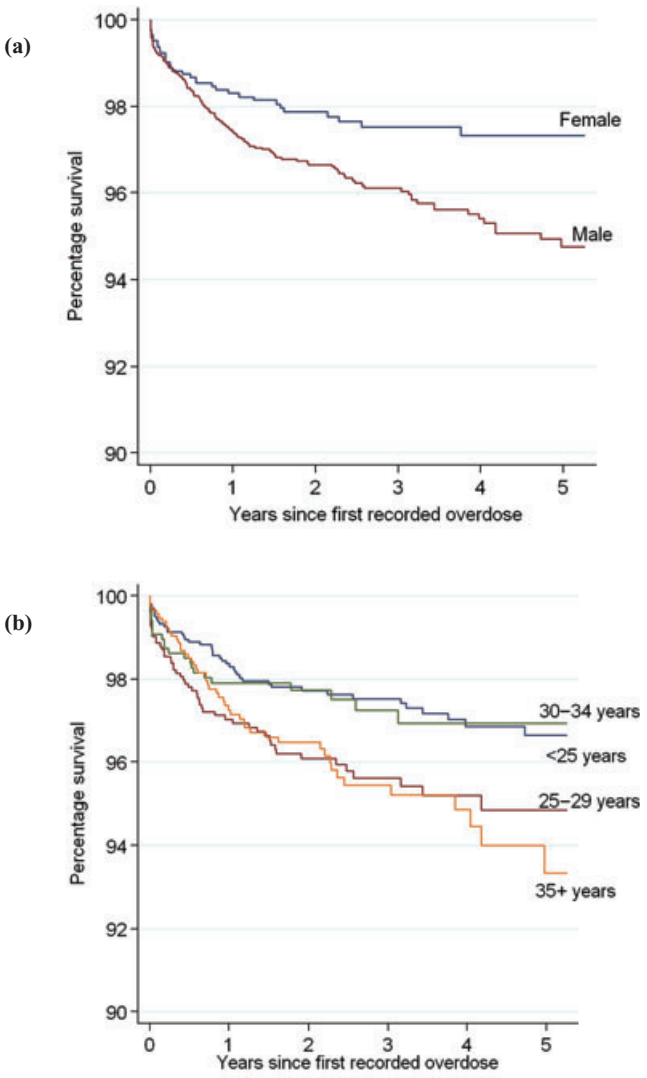

Figure 1. *Kaplan–Meier survival curves of overdose mortality by (a) sex and (b) age at cohort entry.*

tions of heroin supply of high purity and ready availability of the late 1990s appear to have driven the extraordinarily high rates of overdose mortality we observed in 2000. The effect of the heroin drought, where indicators of heroin purity and availability fell sharply in Melbourne, was to reduce rates of heroin overdose mortality and morbidity by approximately 80% [31]. These effects were evident in our cohort with mortality rates among our sample more consistent (even somewhat less than) with those previously reported, perhaps reflecting more 'normal' heroin market conditions in Melbourne following the onset of the heroin drought [30]. The effects are important in an international context as the heroin drought was not unique to Australia with researchers in western Canada also reporting similar market disruptions that produced comparable, if less dramatic, reductions in heroin overdose mortality [32]. This considerable fluctuation in mortality also has implications for indirect prevalence estimates of IDU populations, given that mortality multipliers remain a popular method to estimate the size of this 'hidden' population.

Consistent with previous research findings [2,4,7,26,28], males were over-represented in both non-fatal and fatal overdose cases, and showed an increased mortality risk. Also consistent with previous findings was the association between older age and increased risk of fatal overdose. Although contrary to popular belief, it is well documented elsewhere that fatal heroin overdose is not concentrated among younger, novice or inexperienced users. Rather overdose mortality occurs on average among those in their late twenties and early thirties with generally considerable experience of heroin use [1,8,33].

Our study has shown, for the first time, the profound effect of previous non-fatal overdoses on subsequent risk of overdose fatality. After controlling for age and sex, those who had been attended by an ambulance for two non-fatal overdoses in the follow-up period were at more than three and half times the risk of a fatal overdose compared with those who had experienced only one overdose in this period. This figure climbed alarmingly to more than seven times the risk for those who had experienced more than two non-fatal overdoses. This result suggests that the risk of overdose among heroin users is not attenuated through knowledge obtained from previous overdose experiences. Indeed, overdose risk appears to increase considerably following previous events.

These results have implications for overdose prevention. Overdose prevention initiatives are numerous, mostly focussing on education programs of factors associated with overdose risk [34]. Such programs have attracted criticism because they fail to acknowledge contextual factors associated with overdose that impede the uptake of risk reduction advice, such as not injecting alone or avoiding polydrug use [26,35]. Calls for structural interventions that control risk environments for IDU, such as the introduction of supervised injection facilities (SIF) are motivated in part by the aim to reduce overdose incidence. Indeed, studies of SIF suggest that they are effective in managing overdose and reducing the effect of overdose on drug-related mortality and morbidity [22]. Furthermore, in findings similar to ours, a study of North America's first SIF in Vancouver showed that having a history overdose was a significant independent predictor of time to overdose among the 336 on-site overdoses observed [6]. The fact that none of these overdoses in Vancouver was fatal suggests the importance of SIF in reducing overdose fatality and creating environments protective against overdose mortality. Indeed, our results suggest that

Table 2. *Cox proportional hazard ratios: unadjusted and adjusted[a] analyses*

	Unadjusted		Adjusted	
	Hazard ratio	95% confidence interval	Hazard ratio	95% confidence interval
Sex				
Female	1	—	1	—
Male	1.70	1.16–2.50	1.67	1.14–2.45
Age group (years)				
<25	1	—	1	—
25–29	1.68	1.12–2.53	1.63	1.09–2.45
30–34	1.05	0.63–1.76	1.03	0.62–1.73
35+	1.75	1.16–2.64	1.79	1.19–2.72
Number of previous overdoses				
1	1	—	1	—
2	3.60	2.45–5.26	3.71	2.54–5.45
>2	7.20	4.69–11.04	7.38	4.81–11.32

[a]Adjusted for variables in the Table.

those with a history of non-fatal overdose would benefit most from the use of such facilities.

There are a number of limitations associated with this study primarily related to cohort ascertainment. First, the cohort was derived from records of ambulance attendances at overdose events between 2000 and 2005. Although we believe that most overdose events in Melbourne are attended by ambulance, and heroin users are not reluctant to call ambulances in this jurisdiction [19,36,37], it is possible that some cases had also experienced overdoses that were not attended by an ambulance. However, overdose events attended by ambulance are likely to identify more severe non-fatal overdose events and perhaps indicative of individuals using heroin in particularly risky ways. In the context of survival, it is this group of injectors that we might reason to be of greatest interest. It is also of interest that, despite experiencing multiple overdoses of sufficient severity to require ambulance attendance, lessons are perhaps not being learned from these events to minimise later overdose mortality risk. Second, the finite period of follow-up means that overdose events occurring before October 2000 could not be determined. Before October 2000, case identifiers contained only the five letter alpha-code and year of birth (considered insufficient to reliably match data with the NDI). Both these limitations have particular implications for the associations between cumulative overdose experiences and subsequent overdose mortality. Third, approximately 10% of cases did not or could not provide ambulance paramedics with personal identifying information, thus limiting the number of individuals included in the dataset or limiting the number of overdoses attributed to individuals included in the analyses. It is plausible that this group might be most at risk of overdose if the severity of their overdose event was such that they were unable to provide identifying information with sufficient clarity. Finally, the classification of a heroin overdose is difficult and some misclassification might have occurred in ascertaining cases for this study.

Conclusions

Independent of sex and age, the results of this studied showed for the first time that experiencing a non-fatal overdose substantially increases the risk of subsequent overdose mortality. Annual overdose mortality reported in this study corresponded well with known changes in heroin market dynamics. Following a period of high heroin purity and availability and high mortality rates, overdose mortality stabilised at levels comparable with those reported in other studies in Australia and internationally. These findings provide salient evidence of personal and temporal factors that contribute to increased risk of fatal overdose events. Strategies to effectively reduce overdose mortality should consider personal drug use histories and drug market dynamics as important factors in determining overdose risk.

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