Mortality in the Melbourne injecting drug user cohort study (MIX)

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Abstract

Background: There are few studies of mortality amongst people who inject drugs (PWID) in Australia. In this study, we estimate mortality in a cohort of PWID in Melbourne and examine predictors of mortality including health service use, demographic characteristics, drug use and personal wellbeing.

Findings: We linked identifiers from the Melbourne injecting drug use cohort study (MIX; n = 655) to the National Death Index from 2008 to 2012 to estimate standardised mortality ratios (SMRs). Cox regression was used to examine the bivariate relationship between exposures determined at baseline and subsequent mortality. There were 24 (3.6%) deaths over the study period. The mortality rate in the cohort was 1.0 per 100 PY (95% CI 0.71 – 1.57), with an SMR of 17.3 (95% CI 11.6 – 25.8). Baseline reports of four or more lifetime incarcerations (HR 3.65, 95% CI 1.16 – 11.52), past month ambulance attendance (HR 4.43, 95% CI 1.76 – 11.17), past month emergency department presentation (HR 3.44, 95% CI 1.47 – 8.03) and past 6-month self-reported heroin overdose (HR 3.14, 95% CI 1.24 – 7.96) were associated with increased mortality risk.

Conclusions: Contact with emergency services, particularly for drug overdose, remains a lost opportunity to provide referrals for harm reduction and naloxone training programmes to PWID at greater risk of mortality.

Keywords: Emergency services, Australia, Injecting drug use, Mortality, Cohort

Introduction

Estimates of mortality among people who inject drugs (PWID) in developed countries (based mostly on treatment samples [1]) range between 0.5 and 5 deaths per 100 person-years (PY). Stoové et al. [2] reported a mortality rate of 0.8 per 100 PY among PWID in Melbourne between 1990 and 2006, with most deaths related to drug overdose and other injecting-related causes; unlike other countries, HIV mortality was uncommon [3]. A range of factors increase mortality risk among PWID, including having a history of non-fatal overdose events [4]. PWID who overdose often come into contact with ambulance and emergency department (ED) services; however, the relationship between the use of these and other health services with mortality has not been previously explored.

We provide updated estimates of mortality among PWID in Australia where HIV prevalence is low and targeted health services for PWID are available [5]. We describe the relationship between mortality and demographic characteristics, patterns of drug use, measures of personal wellbeing and use of health services.

Methods

Data collection

Baseline data from the Melbourne injecting drug user cohort study (MIX) collected in Melbourne between November 2008 and March 2010 was linked to Australia’s National Death Index (NDI). MIX participants were recruited through a combination of respondent-driven sampling, snowball sampling and outreach. Eligible participants were aged 18 and over, reported injecting regularly for at least 6 months and had a valid Medicare card. The baseline MIX questionnaire included questions on socio-demographics, drug use, health service use, and self-reported health and wellbeing. Further details of the recruitment methods and the wider study are described elsewhere [6]. Probabilistic data linkage of
participant identifier codes based on letters from first
and last names, gender and date of birth was used to
link NDI data, with matches validated using full first
names, deaths known to the study team and date of last
contact. Deaths up to December 2012 were captured
across all states and territories. Cause-of-death codes are
reported where available.

The study was approved by the Human Research Eth-
ics Committee of the Victorian Department of Health
and the Monash University Human Research Ethics
Committee, and informed consent was obtained from all
participants.

Statistical analyses
Person-years (PY) were calculated as the time from
baseline interview until death or censorship at 31st
December 2012. Mortality rates were calculated using
the person-time method [7] and disaggregated by gen-
der. Standardised mortality ratios (SMRs) compared ob-
served age- and sex-specific mortality rates of the cohort
with age- and calendar-year-matched Australian popu-
lation estimates using indirect standardisation. Five-year
age groups were assigned. The 95 % confidence intervals
(CI) were calculated using the Poisson distribution.

Semi-parametric analysis using Cox regression was
used to describe baseline characteristics associated with
mortality, including socio-demographic, drug use and
health service use data. Validated tools included a vari-
ant of the AUDIT-C scale [8] to assess past month alco-
hol consumption (categorised as abstinent, 1–7, 8+) and
the SF8 quality of life scale summary measurements for
physical and mental health [9] as measures of health-
related quality of life (categorised as low (lower quartile
scores), average (second and third quartile scores) and
high (upper quartile scores) [10]). The small number of
events (deaths) restricted analyses to bivariate relation-
ships between exposures and mortality. Variables were
considered significant at \( p < 0.05 \). Associations were re-
ported using hazard ratios (HR); 95 % confidence inter-
vals (CIs) for crude mortality rates were calculated using
a Poisson distribution. We describe time-varying factors
associated with mortality using longitudinal data from
the MIX cohort as supplementary analyses to identify
missed opportunities for interventions [2, 7]. Analyses
were conducted using Stata Version 13.1 (StataCorp LP,
TX, USA).

Results
Baseline characteristics
We recruited 688 participants between 2008 and 2010,
of whom 23 (3.4 %) were excluded from analysis due to
incomplete data on exposures of interest such as past
month use of emergency, outpatient and ambulance ser-
VICES. No mortality cases were excluded in this way.

Participants with complete data (\( n = 665 \)) contributed
2277 PYs across a median of three interviews. Table 1
describes baseline characteristics of participants who
were young relative to other studies of Australian PWID
(median age 29, interquartile range (IQR) 17–40), pre-
dominantly male and unemployed. Participants had been
injecting for a median of 10 years (IQR 6–13) and over a
third were receiving OST. Participants were frequent
users of health services and almost one-third had poor
self-reported physical health.

Mortality rates, causes of death, and correlates of
mortality
There were 24 (3.6 %) deaths in study period; the me-
dian age at death was 28 years (range 19–31) and the
median time from the last interview to death was 257
days (range 7–1134 days). The estimated mortality
rate was 1.0 per 100 PY (95 % CI 0.7–1.6). The esti-
mated SMR was 17.3 (95 % CI 11.6–25.8) overall and
there was no evidence of a significant difference between
women (23.5, 95 % CI 10.5–52.3) and men (15.9, 95 %
CI 10.0–25.3).

Cause of death was available for 23 of the 24: 12 were
drug-related, involving opioids and multiple drug use,
four were suicides, four were due to physical assault,
two were from medical conditions not directly related to
injecting drug use, and one resulted from an accident-
related injury. Heroin was the most common drug de-
dected in the drug-related deaths (83 %), followed by
benzodiazepines (67 %). Most (83 %) drug-related deaths
involved multiple substances, including heroin, benzodi-
azeines, methadone, antidepressants, antipsychotics
and alcohol.

Bivariate Cox regression analyses of associations be-
tween mortality and exposures are presented in Table 1.
Increased mortality risk was associated with frequency
of past incarceration (four or more compared to none),
reporting past month ambulance attendance, reporting
past month ED presentation and reporting a heroin
overdose in the past 6 months. The supplementary ana-
lyses of time-varying exposures showed the same pat-
ttern, but some exposures failed to reach significance
(Additional file 1: Table S1).

Discussion
The excess mortality reported in this study was almost
ten times higher than previous Australian estimates in-
volving PWID and people on opioid substitution therapy
(OST) [2, 11]. The excess mortality was also higher than
reported in other countries with a low HIV prevalence
[12]. The heightened risk of mortality in this community-
based cohort might be due to systematic differences
beyond injecting drug use. The cohort was community-
recruited rather than treatment-recruited [11] and was

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Table 1 Baseline socio-demographic, risk and health service utilisation factors associated with mortality among PWID in Melbourne (n = 665)

| Characteristics                                      | Baseline n (%) | Deaths N (%) | Hazard ratio (95% CI) | P value |
|------------------------------------------------------|----------------|--------------|-----------------------|---------|
| Gender                                               |                |              |                       |         |
| Male                                                 | 446 (67.1)     | 18 (4.0)     | 1.45 (0.58–3.66)      | 0.427   |
| Female                                               | 219 (32.9)     | 6 (2.7)      | 1                     |         |
| Employed                                             |                |              |                       |         |
| Yes                                                  | 91 (13.7)      | 2 (2.2)      | 0.57 (0.13–2.41)      | 0.444   |
| No                                                   | 574 (86.3)     | 22 (3.8)     | 1                     |         |
| Stable accommodation                                 |                |              |                       |         |
| Yes                                                  | 539 (81.0)     | 22 (4.1)     | 2.53 (0.59–10.77)     | 0.209   |
| No                                                   | 126 (18.9)     | 2 (1.6)      | 1                     |         |
| Current OST                                          |                |              |                       |         |
| Yes                                                  | 236 (35.5)     | 8 (3.4)      | 0.92 (0.39–2.16)      | 0.854   |
| No                                                   | 429 (64.5)     | 16 (3.7)     | 1                     |         |
| Attended emergency department in the past month      |                |              |                       |         |
| Yes                                                  | 88 (13.2)      | 6 (12.0)     | 3.44 (1.47–8.03)*     | 0.004   |
| No                                                   | 577 (86.8)     | 18 (2.9)     | 1                     |         |
| Attended PWID specific primary care services in the past month |     |              |                       |         |
| Yes                                                  | 116 (17.4)     | 22 (4.0)     | 0.43 (0.10–1.82)      | 0.249   |
| No                                                   | 549 (82.6)     | 2 (1.7)      | 1                     |         |
| Attended GP services in the past month               |                |              |                       |         |
| Yes                                                  | 387 (58.2)     | 16 (4.1)     | 1.44 (0.61–3.36)      | 0.403   |
| No                                                   | 278 (41.8)     | 8 (2.9)      | 1                     |         |
| Attended ambulance services in the past month        |                |              |                       |         |
| Yes                                                  | 50 (7.5)       | 6 (12.0)     | 4.43 (1.76–11.17)*    | 0.002   |
| No                                                   | 615 (92.5)     | 18 (2.9)     | 1                     |         |
| Past week heroin injecting frequency                 |                |              |                       |         |
| None                                                 | 10 (25.6)      | 6 (3.5)      | 1                     |         |
| Less than daily                                      | 297 (44.7)     | 12 (4.0)     | 1.14 (0.43–3.04)      | 0.794   |
| Daily or more                                        | 198 (29.8)     | 6 (3.0)      | 0.84 (0.27–2.60)      | 0.760   |
| AUDIT Alcohol Consumption Questions score            |                |              |                       |         |
| Abstinent                                            | 239 (35.9)     | 9 (3.8)      | 1                     |         |
| 1–7                                                  | 264 (39.7)     | 7 (2.6)      | 0.69 (0.26–1.87)      | 0.472   |
| 8 +                                                  | 162 (24.4)     | 8 (4.9)      | 1.35 (0.52–3.50)      | 0.537   |
| Arrested in the past 12 months                       |                |              |                       |         |
| Yes                                                  | 359 (54.0)     | 17 (4.7)     | 2.11 (0.88–5.09)$^+$  | 0.096   |
| No                                                   | 306 (46.0)     | 7 (2.3)      | 1                     |         |
| Frequency of past incarceration                      |                |              |                       |         |
| None                                                 | 271 (40.7)     | 7 (2.6)      | 1                     |         |
| 3 or less                                            | 339 (51.0)     | 12 (3.5)     | 1.39 (0.55–3.52)      | 0.491   |
| 4 or more                                            | 55 (8.3)       | 5 (9.1)      | 3.65 (1.16–11.52)*    | 0.027   |
relatively young compared to other cohorts [2, 11]. The excess mortality is comparable to results in contemporaneous cohorts of similar age [7], and the mortality rate might converge to estimates in the wider literature over a longer observation period potentially reflecting changes in risk behaviour with age and retention in drug treatment observed in other studies [11, 13].

The mortality rate reported here is comparable to that in a recent Australian cohort of PWID recruited from prison settings and followed post-release [14]. Over half the MIX cohort reported a history of incarceration at baseline and we found that frequent incarceration was associated with mortality. Multiple events of incarceration indicate a particularly vulnerable group with an over-representation of low levels of education and socio-economic status, and unsafe injecting practices [15]. The primary overdose prevention tools potentially available through the criminal justice system are the pre- to post-release continuation of OST and the provision of naloxone at prison release. The impact of such programmes can be enhanced through a continuum of care between prison and community health services that facilitates programme retention.

Ambulance and ED attendance reported in the month prior to the last interview were associated with increased risk of mortality, as was reporting a heroin overdose in the previous 6 months. For three of the five deaths for which a previous ambulance attendance was reported, the attendance related to an overdose (data not shown). Frequent contact with emergency and ambulance services could be used to identify PWID at greater risk of fatal overdoses. Multiple overdose events may indicate reduced tolerance, interactions with other substances and the presence of other comorbidities [16]. Contact with emergency services is an opportunity to provide targeted harm reduction initiatives, such as take-home naloxone.

**Limitations**

Our study was limited by a small number of mortality events which affected the precision of estimates and limited adjusted mortality models. In most cases there was only a short observation period available for participants who died which limited our ability to observe the effect of time-varying risk factors, although this strengthens the temporal relevance of the observations in relation to mortality. The quality of the linkage was dependent on the accuracy of participant-provided identifier data. Exposures in cohort studies such as this are assumed to be fixed between interviews or censorship; however, this assumption is not always valid and means the predictors of mortality reported here should be interpreted with caution.

**Conclusions**

This analysis of mortality in community-recruited Australian PWID found significantly higher excess mortality than previous Australian studies and studies in comparable developed countries. These results highlight the importance of tailored interventions prioritising

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**Table 1** Baseline socio-demographic, risk and health service utilisation factors associated with mortality among PWID in Melbourne (n = 665) (Continued)

| Duration of injecting career (years) | Less than 3          | 3–9          | Greater than 10      |
|-------------------------------------|----------------------|--------------|----------------------|
|                                    | 77 (11.6)            | 243 (36.5)   | 345 (51.9)           |
| Overdose in the past 6 months       | 4 (5.2)              | 8 (3.3)      | 12 (3.5)             |
| Yes                                 | 10 (1.5)             | 6 (9.2)      | 3.14 (1.24–7.96)*    |
| No                                  | 655 (98.5)           | 18 (3.0)     | 1                     |
| SF8 physical health score in the past month |
| High (>56)                          | 161 (24.1)           | 4 (2.5)      | 1                     |
| Average (45–56)                     | 330 (49.6)           | 10 (3.0)     | 1.23 (0.39–3.93)     |
| Low (<45)                           | 174 (26.2)           | 10 (5.7)     | 2.39 (0.75–7.63)*†   |
| SF8 mental health score in the past month |
| High (>53)                          | 181 (27.2)           | 8 (4.4)      | 1                     |
| Average (31–53)                     | 327 (49.2)           | 9 (2.7)      | 0.63 (0.24–1.64)     |
| Low (<31)                           | 157 (23.6)           | 7 (4.5)      | 1.03 (0.37–2.85)     |

*p < 0.05
†p < 0.1
overdose prevention to young PWID. Our findings point to prison and emergency settings as ideal opportunities to deliver interventions such as harm reduction messages and referrals for naloxone training and prescribing to reduce mortality [17].

Highlights

- We describe mortality in a cohort of young, community-based Australian PWID
- Excess mortality in the cohort was higher than other local estimates and settings where HIV prevalence is low
- Recent use of emergency services such as emergency departments and ambulances was associated with mortality
- Opportunities remain in prisons and emergency settings to deliver overdose-related interventions

Additional file

Additional file 1: Table S1. Time-varying socio-demographic, risk and health service utilisation factors associated with mortality among PWID in Melbourne (n = 6655). (DOC 99 kb)

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

DN, MS and PD developed the study concept; DN, MS and PA developed the analysis plan; DN conducted the analysis and drafted the manuscript; PA and MH contributed to the analysis; MH, MS and PD contributed to the interpretation of the results and revisions of the final manuscript. All authors read and approved the final manuscript.

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