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Short communication

# Mortality among injecting drug users in Melbourne: A 16-year follow-up of the Victorian Injecting Cohort Study (VICS)

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#### **Abstract**

Multiple factors affect injecting drug-related mortality, many of which will vary over time and between jurisdictions. There are relatively few studies of mortality among injecting drug users (IDU) in Australia. We aimed to provide data comparable to those reported internationally on the rate of mortality among IDU in Australia. We retrospectively examined mortality among participants (N=220) from the first Australian cohort study of IDU by linking coded personal identifier records with a national death register. The overall mortality rate among those followed-up was 0.83 per 100 PY (95% CI, 0.56–1.21 per 100 PY). This rate is lower than those reported internationally but comparable to the limited Australian data from other cohorts of IDU. Mortality was higher among males, most common among those aged in their early thirties and drug-related mortality occurred typically after substantial injecting careers. Extensive experience of incarceration (≥3 times) was associated with increased risk of mortality. These results suggest that rates of mortality among Australian IDU may be lower than those reported internationally, with low HIV prevalence and Australia's long-held harm reduction framework potentially contributing to this result. Further studies using defined cohorts followed over time are needed to examine long-term outcomes among IDU in Australia. © 2008 Elsevier Ireland Ltd. All rights reserved.

Keywords: Mortality; Injecting drug use; Cohort study; Data linkage

### 1. Introduction

Injecting drug users (IDU) are at considerably greater risk of morbidity and mortality than their non-injecting peers (Warner-Smith et al., 2001). Characteristics such as gender and age (Hickman et al., 2003), psychosocial factors such as unemployment and imprisonment (Brugal et al., 2005), dose and frequency of injection (van Ameijden et al., 1999), medical complications from injecting drugs (Warner-Smith et al., 2001), and healthcare and drug treatment utilisation (Langendam et al., 2001) are important factors determining mortality risk among IDU. Risk may also be affected by structural and environmental character-

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istics related to drug policy environments (Burris et al., 2004; Kerr et al., 2007).

Few studies of mortality among IDU cohorts have been conducted in Australia, with most research focused on coronial data. While these studies are important, they cannot determine IDU mortality rates as the size of the population at risk is unknown. Given the complexity of the factors described above and variations in the characteristics of IDU and drug using environments internationally, we would expect to see differences in rates of mortality between jurisdictions. Indeed, substantial variations in mortality rates have been reported between countries and over time (EMCDDA, 1999). For this reason it is important to understand IDU mortality in Australia, where harm minimisation is the overarching drug policy (Ritter et al., 2004).

We retrospectively examined mortality within the Victorian Injecting Drug Users Cohort Study (VICS) of Australian IDU recruited in the early 1990s. Our aim was to provide IDU mortality data comparable to those reported internationally and

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examine characteristics associated with mortality in an Australian context.

#### 2. Methods

#### 2.1. VICS

VICS was the first longitudinal study of IDU conducted in Australia. A detailed description of VICS is reported elsewhere (Crofts and Aitken, 1997). Briefly, VICS was a longitudinal study of 626 IDU recruited through the social networks of 'privileged access' interviewers (PAIs; former or continuing IDU with extensive experience of the IDU "scene") and 'snowballing' from these networks. VICS PAIs interviewed participants at approximately nine-month intervals between 1990 and 1995, recording detailed demographics, drug use characteristics and life events.

#### 2.2. Case ascertainment

Mortality was determined using National Death Index (NDI) matching of coded unique identifiers extracted from VICS records. These identifiers, a combination of letters of participants' first and second names, gender and dates of birth, were only available for 220 participants interviewed by two PAIs, hereafter referred to as the mortality cohort. The remaining participants were interviewed by other PAIs who had not kept the requisite records or were no longer contactable. The mortality cohort was recruited between 21st June 1990 and 5th September 1994 and final follow-up interviews were conducted between 19th November 1990 and 12th October 1995. The median number of interviews per participant was three (IQR 1–5), the median time between VICS interviews was 253 days (IQR 163–435), with an average length of VICS follow-up of 2 years.

### 2.3. Data matching

The NDI contains records of all deaths in Australia since 1980. The NDI compared identifier codes from the mortality cohort to those from all deaths occurring between 1990 and 18th September 2006. Date of death and cause of death codes (only primary underlying ICD9 codes prior to 1997, thereafter primary and all secondary ICD10 codes) from matched cases were merged into the VICS database. 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.

# 2.4. Analysis

Selection bias was assessed by comparing characteristics (e.g. sociodemographics, current/past injecting characteristics, incarceration history) of the mortality cohort with the rest of the VICS cohort using independent-sample *t*-tests for interval data and Wilcoxon–Mann–Whitney rank tests for ordinal data. Mortality was estimated with person-years (PY) of follow-up determined from first interview date to either death or censorship at 18th September 2006. Mortality rates were calculated using standard formulas and the standardised mortality ratio (SMR) was calculated indirectly using time-specific age and sex matched Australian population data. Characteristics associated with mortality were determined using bivariate and multivariate Cox regression. Criterion for the inclusion of predictors in regression models were based on a combination of bivariate results, theoretical importance in relation to mortality and the overall magnitude of regression coefficients.

This study was approved by the Human Research Ethics Committee of the Department of Human Services, State Government of Victoria.

### 3. Results

In assessing selection bias, there were few statistically significant differences between the mortality cohort and the remainder of the VICS participants, except that the mortality cohort was more likely to have drug treatment experience and less likely to report government benefits as their primary income source (neither of which were associated with mortality in the mortality cohort). Characteristics of the mortality cohort sample were generally similar to those of other samples of IDU recruited in Australia (e.g. NCHECR, 2007a). The mean age of the mortality cohort was 28 years (S.D. = 6.6), 57% were male, 34% reported previous incarceration, and 64% reported heroin as the drug they injected most at final VICS interview.

Twenty-six participants died during the follow-up period. The average age at death was 33 years (S.D. = 6.33, min. 21, max. 46). The overall mortality rate was 0.83 (95% CI, 0.56–1.21) per 100 PY, with an SMR of 6.08 (95% CI, 4.14–8.93), higher among males, and highest among those aged 30–34 years (Table 1).

Drug overdose was the most common cause of death (14/26), producing an overdose mortality rate of 0.44 (95% CI, 0.26–0.75) per 100 PY. A further four mortality cases were probably injecting-related – one each of endocarditis, air embolism, pulmonary embolism with thrombosis of deep lower extremity vessels, and open wound of hand (likely septicaemia); their addition produced a drug-related mortality rate of 0.57 (95% CI, 0.36–0.91) per 100 PY. The average length of injecting career at death was 17 years (S.D. = 7.05, min 3.86, max 29.79).

In bivariate analyses, being male (hazard ratio (HR) = 3.46; 95% CI, 1.30–9.16) and incarceration three times or more compared to not at all at baseline interview (HR = 2.96; 95% CI,

Overall mortality rates of the injecting drug user cohort

	Number in cohort	Deaths (%)	Person-years	Mortality rate per 100 person-years		Rate ratio	
				Overall	95% CI	RR	95% CI
Total rate	220	26	3151	0.83	0.56–1.21		
Sex							
Female	96	5 (19)	1430	0.35	0.15-0.84	1.00	
Male	124	21 (81)	1720	1.22	0.80-1.87	3.49	1.32-9.26
Age in years (	(baseline)						
<25	79	10 (38)	1123	0.89	0.48-1.66	1.00	
25-29	59	8 (31)	833	0.96	0.48-1.92	1.08	0.43 - 2.73
30-34	45	7 (27)	624	1.12	0.54-2.35	1.26	0.48-3.31
35+	37	1 (4)	571	0.18	0.03-1.24	0.20	0.03-1.54

Table 2 Unadjusted and adjusted Cox proportional hazard ratios

	Number	Deaths	Unadjusted hazard ratio	95% CI	Adjusted <sup>a</sup> hazard ratio	95% CI
Sex						
Female	96	5	1		1	
Male	124	21	3.42	1.29-9.07	3.94	1.41-11.04
Age in years (t	paseline)					
<25	69	10	1		1	
25-29	51	8	1.08	0.43 - 2.73	0.62	0.23 - 1.68
30-34	37	7	1.24	0.47 - 3.26	0.57	0.18 - 1.80
35+	36	1	0.20	0.03-1.52	0.07	0.08-0.61
Times incarcer	ated in prison (basel	line)				
0	148	15	1		1	
1–2	48	5	1.09	0.39-3.03	0.93	0.33 - 2.62
>2	24	6	2.96	1.14-7.71	3.36	1.10-10.25

<sup>&</sup>lt;sup>a</sup> Adjusted for variables in the table.

1.13–7.71) were the only variables associated with greater mortality risk.

Differences in survival were explored using Cox proportional hazards modelling. Table 2 shows adjusted HRs for factors associated with mortality. Being male, aged less than 35 years at baseline and incarceration three times or more at baseline were associated with higher mortality risk. HIV status was not associated with mortality (HR = 0.87 (base HIV negative); 95% CI, 1.13–7.71) and the inclusion of HIV status had no effect on the coefficients of other variables included in the model.

# 4. Discussion

Overall and overdose mortality rates in this cohort were lower than those reported in Europe and the USA, where overall mortality among IDU over comparable years range largely between 1–5 per 100 PY, but were typically in the order of 3 per 100 PY (e.g. EMCDDA, 1999; Langendam et al., 2001; Vlahov et al., 2004). A few previous Australian studies also show relatively low mortality rates. A follow-up of methadone patients (1976–1991) produced an overall mortality rate of 1.12 per 100 PY and an overdose mortality rate of 0.61 per 100 PY (Caplehorn et al., 1996). The only other Australian cohort study of mortality retrospectively followed amphetamine and heroin users admitted to hospital and psychiatric institutions between 1985 and 1998 and reported an overall mortality rate of 1.57 per 100 PY (Bartu, 2006; Bartu et al., 2004).

One possible reason for the relatively low mortality rate found in this and other Australian studies is low HIV prevalence among Australian IDU (NCHECR, 2007b). Studies in Europe (Brugal et al., 2005; EMCDDA, 1999) and the USA (Vlahov et al., 2004) over comparable periods report considerable proportions of AIDS deaths among IDU. However, even after removing AIDS deaths from these studies, mortality rates from other causes remain higher than those reported here. The low mortality rate found in this study might result from high participation rates in pharmacotherapy (Berbatis et al., 2000). Maintenance pharmacotherapies have been widely available and well-utilised in Victoria since the late 1980s (VGDHS, 2007). Research consistently demonstrates the protective effect of methadone

maintenance treatment on mortality (e.g. van Ameijden et al., 1999) and studies in Europe have reported mortality rates similar (Langendam et al., 2001) or lower (Brugal et al., 2005) than those reported here among IDU enrolled in methadone maintenance. While it is difficult to draw conclusions regarding relationships between broader ecological factors and IDU mortality, a harm reduction framework and public health responses to injecting drugs, established early in the epidemic cycle, possibly underpin the relatively low IDU mortality rates in Australian studies.

Consistent with previous research (e.g. Hickman et al., 2003) mortality rates were higher among males and those aged in their early to mid-thirties. Drug-related mortality also typically occurred after lengthy injecting careers. However, as shown in the proportional hazards model, those aged 35 years and over at VICS recruitment were at substantially lower mortality risk over the follow-up period compared to younger participants. It is likely that many of these older participants either reduced their injecting frequency or ceased injecting at some point over the post-VICS follow-up period, so much of their significant period of risk had passed.

More extensive experience of incarceration was associated with increased mortality risk. Others have reported associations between cumulative length in detention and non-fatal overdose risk (Ochoa et al., 2005; Seal et al., 2001), and many studies have shown elevated overdose mortality risk among IDU during the immediate post-release period (e.g. Bird and Hutchinson, 2003; Seaman et al., 1998). This mortality has been largely attributed to the loss of drug tolerance (Seaman et al., 1998), although high rates of post-release non-drug-related mortality are also reported (Bird and Hutchinson, 2003). While we could not determine incarceration history between last VICS interview and censorship, or the temporal relationship between prison release and mortality, our findings suggest that causes other than drug overdose were primarily responsible for the association between imprisonment and mortality. We found a lower overdose mortality risk compared to all-cause mortality among those imprisoned three times or more, while most overdose deaths (71%) occurred among participants with no prison history at the time of VICS interviews. Others have argued that long-term health outcomes of IDU with an incarceration history go beyond mortality and morbidity directly attributable to drug use and include psychosocial factors related to poor health, such as socio-economic status, homelessness, and psychological stress associated with re-entry into the community (Galea and Vlahov, 2002).

Our study is limited in several ways. First, we were unable to include all VICS participants. The only selection biases apparent were that the mortality cohort was more likely to have a history of drug treatment and less likely to report government benefits as their primary income source compared to the remaining VICS participants. Both these factors are potentially protective of mortality, so mortality may have been higher among the remaining VICS participants. Second, we may have under-ascertained mortality cases because complete identifying information was not available. Using alpha-numeric identifier codes, this study was susceptible to incorrect identifying information (either reported by participants or recorded by researchers) affecting the reliability of data linkage. Third, in retrospective cohort studies such as this, events occurring between the last follow-up and censorship are unknown. This is particularly important when exploring correlates of mortality and means that the predictors of mortality reported here should be interpreted with caution. For example, given the association between illicit drug injecting and incarceration, some participants are likely to have had prison experience between the final interview and data linkage. Fourth, the precision of estimates in this study was affected by the small number of deaths. Finally, overdose and drug-related mortality rates may be under-estimated because prior to 1997 only the primary cause of death was recorded in the NDI register.

Few studies have reliably estimated mortality rates among Australian IDU. The scarcity of Australian prospective studies of IDU has produced deficiencies in our knowledge of the natural history and long-term outcomes of IDU within the Australian context. While cohort studies are expensive and are logistically difficult to conduct with this population, better use of record linkage methods offers a viable alternative. Our study suggests that mortality rates among Australian IDU are lower than those reported internationally. Further research with other Australian cohorts will establish the reliability of these findings.

# **Conflicts of interest**

The authors have no conflicts of interest to declare in relation to this study.

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Contributions: Mark Stoové was the principal investigator on this study, was responsible for data management, conducted the statistical analyses and was primarily responsible to the preparation of the manuscript. Paul Dietze contributed to the research design, provided advice on the conduct of the research and contributed to the writing of the manuscript. Campbell Aitken provided advice during the conduct of the research, provided VICS data, liaised with other VICS researchers and contributed to the writing of the manuscript. Damien Jolley provided advice and guidance on statistical analyses and contributed to the writing of the manuscript.

#### References

Bartu, A., Freeman, N.C., Gawthorne, G.S., Codde, J.P., Holman, D.J., 2004.
Mortality in a cohort of opiate and amphetamine users in Perth, Western Australia. Addiction 99, 53–60.

Bartu, A., 2006. Bartu et al., 2004: a correction. Addiction 101, 1523-1524.

Berbatis, C.G., Sunderland, V.B., Bulsara, M., Lintzeris, N., 2000. Trends in licit opioid use in Australia 1984–1998: comparative analysis of international and jurisdictional data. Med. J. Aust. 173, 524–527.

Bird, S.M., Hutchinson, S.J., 2003. Male drugs-related deaths in the fortnight after release from prison: Scotland 1996–99. Addiction 98, 185–190.

Brugal, M.T., Domingo-Salvany, A., Puig, R., Barrio, G., Garcia de Olalla, P., de la Fuente, L., 2005. Evaluating the impact of methadone maintenance programmes on mortality due to overdose and AIDS in a cohort of heroin users in Spain. Addiction 100, 981–989.

Burris, S., Blankenship, K.M., Donaghoe, M., Sherman, S., Vernick, J.S., Case, P., Lazzarini, Z., Koester, S., 2004. Addressing the "risk environment" for injection drug users: the mysterious case of the missing cop. Milbank Q. 82, 125–156.

Caplehorn, J.R., Dalton, M.S., Haldar, F., Petrenas, A.M., Nisbet, J.G., 1996.
Methadone maintenance and addicts' risk of fatal heroin overdose. Subst.
Use Misuse 31, 177–196.

Crofts, N., Aitken, C.K., 1997. Incidence of bloodborne virus infection and risk behaviours in a cohort of injecting drug users in Victoria, 1990–1995. Med. J. Aust. 167, 17–20.

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 1999.
Co-ordination of implementation, follow-up and analysis of cohort studies on mortality among drug users in European Union Member States, EMCDDA Scientific Report. Lisbon, Portugal.

Galea, S., Vlahov, D., 2002. Social determinants of the health of drug users: socioeconomic status, homelessness, and incarceration. Public Health Rep. 117 (Suppl. 1), s135–s145.

Hickman, M., Carnwath, Z., Madden, P., Farrell, M., Rooney, C., Ashcroft, R., Judd, A., Stimson, G., 2003. Drug-related mortality and fatal overdose risk: pilot cohort study of heroin users recruited from specialist drug treatment sites in London. J. Urban Health 80, 274–287.

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

Langendam, M.W., van Brussel, G.H.A., Coutinho, R.A., Van Ameijden, E.J.C., 2001. The impact of harm-reduction-based methadone treatment on mortality among heroin users. Am. J. Public Health 91, 774–780.

National Centre for HIV Epidemiology and Clinical Research (NCHECR), 2007a. Australian NSP Survey National Data Report, 2002–2006. NCHECR, Sydney.

NCHECR, 2007b. HIV/AIDS, Viral Hepatitis and Sexually Transmissible Infections in Australia: Annual Surveillance Report, 2007. NCHECR, Sydney.

- Ochoa, K.C., Davidson, P.J., Evans, J.L., Hahn, J.A., Page-Shafer, K., Moss, A.R., 2005. Heroin overdose among young injection drug users in San Francisco. Drug Alcohol Depend. 80, 297–302.
- Ritter, A., Wodak, A., Crofts, N., 2004. Reducing drug-related harm: Australia leads the way. Med. J. Aust. 181, 242–243.
- Seal, K.H., Kral, A.H., Gee, L., Moore, L.D., Bluthenthal, R.N., Lorvick, J., Edlin, B.R., 2001. Predictors and prevention of nonfatal overdose among street-recruited injection heroin users in the San Francisco Bay Area, 1998–1999. Am. J. Public Health 91, 1842–1846.
- Seaman, S.R., Brettle, R.P., Gore, S.M., 1998. Mortality from overdose among injecting drug users recently released from prison: database linkage study. Br. Med. J. 316, 426–428.
- van Ameijden, E.J.C., Langendam, M.W., Coutinho, R.A., 1999. Dose–effect relationship between overdose mortality and prescribed methadone dosage in low-threshold maintenance programs. Addictive Behav. 24, 559– 563.
- Victorian Government Department of Human Services, 2007. Victorian Drug Statistics Handbook, 2006. Victorian Government Department of Human Services, Melbourne.
- Vlahov, D., Wang, C., Galai, N., Bareta, J., Mehta, S.H., Strathdee, S.A., Nelson, K.E., 2004. Mortality risk among new onset injection drug users. Addiction 99, 946–954.
- Warner-Smith, M., Darke, S., Lynskey, M., Hall, W., 2001. Heroin overdose: causes and consequences. Addiction 96, 1113–1125.