Received: 2 May 2021 | Accepted: 19 May 2022

DOI: 10.1111/add.15975

RESEARCH REPORT

ADDICTION SSA

Mortality in the SuperMIX cohort of people who inject drugs in Melbourne, Australia: a prospective observational study

Penelope L. Hill[1,2,3,4] | Mark Stoové[1,2] | Paul A. Agius[1,2] | Lisa Maher[1,5] | Matthew Hickman[6] | Sione Crawford[7] | Paul Dietze[1,2,8]

[1]Behaviours and Health Risks, Burnet Institute, Melbourne, VIC, Australia

[2]School of Public Health and Preventative Medicine, Monash University, Melbourne, VIC, Australia

[3]The National Centre for Clinical Research on Emerging Drugs (NCCRED), Sydney, NSW, Australia

[4]National Drug and Alcohol Research Centre (NDARC), The University of New South Wales, Sydney, NSW, Australia

[5]Faculty of Medicine, Kirby Institute for Infection and Immunity, UNSW Sydney, NSW, Australia

[6]Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK

[7]Harm Reduction Victoria, North Melbourne, VIC, Australia

[8]National Drug Research Institute, Curtin University, Melbourne, VIC, Australia

Correspondence
Paul Dietze, Burnet Institute, Behaviours and Health Risks, 85 Commercial Road, Melbourne 3004, Victoria, Australia.
Email: paul.dietze@burnet.edu.au

Funding information
Colonial Foundation Trust, Grant/Award Number: 545891; National Health and Medical Research Council, Grant/Award Number: 1126090

Abstract

Aims: To measure mortality rates and factors associated with mortality risk among participants in the SuperMIX study, a prospective cohort study of people who inject drugs.

Design: A prospective observational study using self-reported behavioural and linked mortality data.

Setting: Melbourne, Australia.

Participants/cases: A total of 1209 people who inject drugs (67% male) followed-up between 2008 and 2019 for 6913 person-years (PY).

Measurements: We linked participant identifiers from SuperMIX to the Australian National Death Index and estimated all-cause and drug-related mortality rates and standardized mortality ratios (SMRs). We used Cox regression to examine associations between mortality and fixed and time-varying socio-demographic, alcohol and other drug use and health service-related exposures.

Findings: Between 2008 and 2019 there were 76 deaths in the SuperMIX cohort. Of those with a known cause of death (n = 68), 35 (51%) were drug-related, yielding an all-cause mortality rate of 1.1 per 100 PY [95% confidence interval (CI) = 0.88–1.37] with an estimated SMR of 16.64 (95% CI = 13.29–20.83) and overall accidental drug-induced mortality rate of 0.5 per 100 PY (95% CI = 0.36–0.71). Reports of recent use of ambulance services [adjusted hazard ratio (aHR) = 3.77, 95% CI =1.78–7.97] and four or more incarcerations (aHR = 2.78, 95% CI = 1.55–4.99) were associated with increased mortality risk.

Conclusions: In Melbourne, Australia, mortality among people who inject drugs appears to be positively associated with recent ambulance attendance and experience of incarceration.

KEYWORDS
Ambulance, drug-related deaths, injecting drug use, mortality, opioids, people who inject drugs

INTRODUCTION

People who inject drugs are at an elevated risk of premature mortality among most causes of death [1, 2]. A recent systematic review of mortality rates among people who use opioids extramedically [3] found, among people who inject drugs specifically, an all-cause mortality rate of 2.71 [95% confidence interval (CI) = 2.14–3.42] per 100 person-years (PY) and a pooled standardized mortality ratio (SMR) of 16.37 (95% CI = 10.92–24.55), which indicate much higher rates of excess deaths among people who inject drugs compared to the general population.

The largest contributors to mortality rates among people who inject drugs are related to overdose [4, 5], non-communicable diseases and infectious diseases [3]. Mortality risk among people who inject drugs has been associated with frequent heroin injection [6], previous overdose [7, 8], male gender [7] and frequency of incarceration [7, 8], but investigation of longitudinal associations between health-service utilization and mortality among people who use drugs is sparse, with few studies available that investigate associations recent ambulance attendance and emergency department utilization [8] and mortality within community-recruited cohorts of people who inject drugs. Risk of cause-specific mortality from drug-related/overdose deaths among people who inject drugs has been associated with recent prison release [9] and mental health service access [10].

Many studies that investigate mortality in broader populations at risk of opioid overdose, such as opioid-dependent people and those receiving opioid treatment, link administrative databases of specialist drug treatment [11–15], health [10,16–21] or prison data [22–24] with mortality records. In these studies, injecting drug use is identified as a key risk factor, as are related issues such as HIV status [25, 26], with opioid agonist treatment (OAT) typically protective [27]. However, individual studies do not always provide specific rates or SMRs [2, 11] among people who inject drugs, meaning that contemporary specific mortality estimates are sparse.

In our study we explored mortality among the largest, longest running and only active cohort of people who inject drugs in Australia. We aimed to:

- estimate mortality rates and report causes of mortality and
- estimate associations of mortality risk by fixed and time-varying self-reported socio-demographic, drug-related and health service utilization characteristics.

METHODS

Study design and setting

Our data were drawn from the Melbourne Injecting Drug Use Cohort Study (MIX), a prospective observational study described in detail in previous work [12] and its extension, SuperMIX. SuperMIX participants were recruited from eight areas with historically high levels of street-based drug use across Melbourne and Greater Geelong, through a combination of respondent-driven sampling, snowball sampling and outreach. Baseline data were collected through three recruitment periods between 2008 and 2010, 2011 and 2017–19, with 40% of participants recruited between July 2017–July 2019. Further details on SuperMIX recruitment can be found elsewhere [12]. Participants were interviewed at baseline using a structured questionnaire that includes questions on socio-demographic, drug use, health service use and general health and wellbeing, with follow-up surveys completed annually using a modified version of the questionnaire. Outcome data were collected through data linkage.

Participants

Eligible participants were aged 18 years and over, reported injecting at least monthly for at least 6 months at baseline and had a valid Medicare card (available to all Australian citizens and permanent residents, enabling access to Australia's universal health-care system).

Measures

Linkage and outcome measurement

The National Death Index (NDI) contains records of all deaths occurring in Australia since 1980 [20]. Either a medical practitioner or a coroner is required to certify a cause of death, which is classified according to ICD-10 codes on death certificates. Probabilistic linkage of self-report questionnaire data to participant data from the NDI was undertaken by the Australian Institute of Health and Welfare (AIHW). A fully identified SuperMIX data file was created with identifier data and study identification number (SID) for each participant, which was sent to the AIHW where probabilistic linkage with the NDI was performed by the AIHW. Deaths were captured between the beginning of the study, 18 April 2008, to 31 May 2019 across all states and territories of Australia. Cause of death codes are reported, where available, up to 19 October 2017, with such codes sometimes delayed for 2–3 years due to ongoing coroner investigations. The linked data file was subsequently merged with self-report databases on the basis of SID and housed at the secure data laboratory of the Australian Institute of Family Studies, and was then later securely transferred to a remote access secure environment at the AIHW for analysis.

Exposures

We examined a range of exposures drawn from socio-demographic, drug use and other risk factor variables drawn from self-report data collected as part of annual participant interviews. Variable selection was based on previous literature, including previous analyses of the SuperMIX cohort [8]. These variables included baseline socio-demographic variables, including sex (male/female), education

level completed (≤ 9 years of education/10–11 years of education/≥ 12 years of education/tertiary education/trade qualification); and time-varying exposures, including: current employment (yes/no), current accommodation (stable/unstable), current income (< AU $400/≥ AU$400 per week), and number of times previously incarcerated (never/one to three times/≥ four times). Drug use and other risk factor exposures were time-varying and included time since first injection (less than 3 years, 3–9 years, ≥ 10 years), experiencing an opioid overdose since last interview (yes/no) and heroin injecting in past week (none/less than weekly/weekly or more). A variant of the alcohol use disorders identification test–consumption (AUDIT-C) scale was used to assess past month alcohol consumption [categorized as abstinent/less than 8 (moderate)/8+ (high risk)] [13]. Recent use of health service variables were also examined as time-varying exposures, including past month use of an emergency department (yes/no), ambulance services (yes/no), a general practitioner (GP) for non-mental health or OAT reasons (yes/no) and mental health services (yes/no), which included seeing a GP, a psychologist or a psychiatrist for mental health reasons, together with current enrolment in OAT (yes/no). The SuperMIX questionnaire is described in more detail elsewhere [12].

Analyses

PY were calculated as the time from baseline interview until death or censorship at 31 May 2019. Mortality rates were calculated using the person–time method and disaggregated by age [8, 14]. SMRs were calculated to observe age- and sex-specific mortality rates of the cohort with age- and calendar-year-matched Australian population estimates from the Australian Bureau of Statistics (accessed 31 August 2019) using indirect standardization [15]. Five-year age groups were assigned; 95% CIs were calculated using the Poisson distribution. Participants with missing baseline data were excluded case-wise from analyses.

Semi-parametric survival analysis using Cox regression [16] was used to estimate associations between fixed and time-varying exposures and mortality. Variables were considered significant at $P < 0.05$ and included in the final model if $P < 0.05$ in unadjusted analysis. Associations are reported using unadjusted and adjusted hazards ratios (HR and aHR). In the Cox regression, we assessed the proportional hazards assumption using Kaplan–Meier curves and Schoenfeld residuals. We found no violation of proportionality in the Cox model. The low number of accidental drug-induced deaths precluded cause-specific analysis of exposure effects.

Analyses were conducted using Stata version 15.1 (Statacorp LP, College Station, TX, USA). The Strengthening the Reporting of Observational Studies in Epidemiology (collaboration) (STROBE) checklist for observational studies was utilized for this paper, presented as Supporting information, Table S2. We did not pre-register our analysis plan and results should be considered exploratory.

Ethics statement

The study was approved by the Human Research Ethics Committee of the Victorian Department of Health and Human Services and the Australian Institute of Health and Welfare.

RESULTS

Cohort characteristics

Following exclusion of participants without complete exposure data (n = 35, 3%), 1209 participants were included in the current analysis. SuperMIX participants had a median age of 31 years [interquartile range (IQR) = 26–35 years] at baseline, were predominantly male (67.1%), unemployed (87.0%) and in stable accommodation (80.7%). Most participants had been injecting for a median of 13 years with more than one-third receiving OAT (36.0%) at baseline. Rates of self-reported recent general and emergency health service use were high, with almost two-thirds (63.4%) reporting recent visits to general practitioners (GP), one-fifth (19.2%) to mental health practitioners, 12.7% to emergency departments and 8.5% receiving care from an ambulance prior to their last interview. Rates of incarceration in the cohort were also high, with only 34.6% of participants having not been incarcerated previously, and 13.0% being incarcerated four or more times.

Mortality rates and causes of mortality

All included SuperMIX participants at 31 May 2019 (n = 1209) had contributed 6913.17 PY with a mean of 5.73 PY per participant (IQR = 0.89–9.86). Due to a complete case approach, 35 (3%) SuperMIX participants were excluded from the original cohort (n = 1244) for this analysis due to missing follow-up data. The median age of the cohort was 34.5 (IQR = 29.6–39.4), and there were 76 (6.3%) deaths in the study period; the median age at death was 30.3 years (IQR = 26.9–24.7). The all-cause mortality rate was 1.1 per 100 PY (95% = CI = 0.88–1.37). The estimated SMR was 16.64 (95% CI = 13.29–20.83).

Cause of mortality was available for 68 of the 76 cases: 35 (51%) were classified as accidental drug-induced deaths, 14 (21%) as occurring by other means (including physical assault, traffic-related incidents and undetermined intent), 13 (19%) as occurring from other medical conditions and six (9%) were classified as suicide intentional deaths (drug-induced and non-drug induced suicides). Further detail on ICD-10 codes related to these subgroups is provided in Supporting information, Table S1. Fewer than five deaths were classified as due to hepatitis C or causes related to HIV. Drug-induced mortality was 0.5 per 100 PY (95% CI = 0.36–0.71).

Of the 35 accidental drug-induced deaths, most (n = 29, 83%) involved two or more drug types, as shown in Table 1. Drug types were classified as: heroin, methadone, opioids other than heroin or

TABLE 1 Drug types involved in accidental drug-induced deaths (n = 35)

One drug type involved in death	6 (17%)
Two drug types involved in death	16 (46%)
Three or more drug types involved in death	13 (37%)

methadone (including codeine, morphine and pethidine), benzodiazepines, stimulants, other psychoactive substances and antipsychotics.

The most common combination for the 'two drug types involved' group was a combination of heroin and benzodiazepines, but due to conditions put in place to reduce re-identification, the combinations involved in these groups cannot be reported (with most combinations experienced by fewer than five participants). Thirty-two of the accidental drug-induced deaths (91%) involved opioids including heroin, methadone, morphine, codeine and pethidine, as determined through ICD-10 codes. Benzodiazepines were involved in 21 (60%) of accidental drug-induced deaths, stimulants were involved in 11 (34%) and fewer than five deaths involved antipsychotics or other psychoactive substances.

Associations between exposures and mortality

Associations between exposures and all-cause mortality are presented in Table 2. In unadjusted analyses, increased mortality risk was associated with recent attendance (in past month) of an emergency department (HR = 2.23, 95% CI = 1.28–3.88), recent utilization (past month) of ambulance services (HR = 3.98, 95% CI = 2.29–3.88), recent attendance of mental health services (past month) (HR = 1.70, 95% CI = 1.00–2.89) and experiencing four or more incarcerations (HR = 2.97, 95% CI = 1.66–5.32). Decreased mortality risk was associated with current employment (HR = 0.42, 95% CI = 0.19–0.91). After adjustment, reports of recent utilization of ambulance services (aHR = 3.77, 95% CI = 1.78–7.97) and four or more incarcerations (aHR = 2.78, 95% CI = 1.55–4.99) were associated with increased mortality risk.

DISCUSSION

In this sample of Melbourne-based community-recruited people who inject drugs, 6% of participants died, with participants enrolled into the study for an average of 6 years at the time of record linkage. Accidental drug-induced death was the reported cause of mortality in approximately half the cases. All-cause mortality was associated with recent utilization of ambulance services and experiencing four or more terms of incarceration.

Our mortality rate is consistent with studies of mortality among other Australian people who inject drugs, which range between 0.50 and 1.27 deaths per 100 PY [11], but is low on a global scale. The overall mortality rate of 1.1 per 100 PY is consistent with previous estimates [8] in the SuperMIX cohort (2008–12), but was higher than previous estimates of Australian people who inject drugs of 0.72 and 0.83 [7, 17] and opioid treatment-related cohorts of 0.65–0.92 [18–20]. With an SMR of 16.64, mortality was similar to global standardized mortality rates for people who use opioids [3]. However, this rate was greatly elevated compared to the general Australian population, and higher than other recent Australian estimates for people who inject drugs (11.09, 95% CI = 6.68–18.39) [17], although lower than previous MIX estimates from 2012 (17.3, 95% CI = 11.6–25.8) [8]. Proportions of cause-specific deaths remained similar to other Australian studies of people who inject drugs [7, 17] and previous MIX estimates [8]. However, in 2012, heroin and benzodiazepines were detected in 83 and 67% of these deaths, respectively, compared to 60 and 60% in 2019 estimates, indicating a shift in drugs associated with mortality.

Previous research findings, including those from the SuperMIX cohort [21], indicate frequent use of health services among people who inject drugs [22]. Recent self-reported ambulance and/or emergency department utilization was associated with mortality risk in our study, which accentuates the need to scale up interventions involving these emergency services that aim to reduce future mortality events—such as making take-home naloxone (THN) available from ambulance services, similar to recent efforts to make THN available through emergency departments [23], potentially with referrals to community THN providers for follow-up. Research among broader populations of frequent ambulance attendees [24] or people who inject drugs who use emergency departments [21] indicates that reasons for calling emergency services for non-urgent issues are complex and often misunderstood, and impacted by socio-economic deprivation and lower income [28]. Further work should be conducted to investigate reasons for frequent utilization of these services by people who inject drugs and the opportunities for overdose prevention and other mortality that they present. Similar to some of these emergency services, visits to mental health professionals were significantly associated with all-cause mortality in unadjusted analyses, indicating another potential intervention point for overdose and other mortality prevention.

GP attendance at baseline was high for the overall cohort, having increased from previous estimates from the initial round of recruitment for SuperMIX [29], but was not significantly associated with increased or decreased risk of mortality. Nevertheless, this high rate of attendance suggests willingness to attend primary and community health facilities and GP visits as important potential intervention points for broad harm reduction intervention. Finally, we found that current employment was associated with reduced mortality risk, highlighting the potential for employment and training programmes to not only address some of the social deprivation experienced by people who inject drugs, but also to potentially reduced mortality among these people. A stabilizing effect of employment has been reported in other cohorts of people who inject drugs, with strong calls to address barriers to employment among this population [30].

Incarceration-related exposures, including length of incarceration, have been associated with overdose and drug-related mortality in other longitudinal cohorts of people who use drugs [9, 31, 32], and we found a significant association between the frequency of

TABLE 2 Cohort characteristics at last interview by mortality status, and fixed and time-varying socio-demographic, risk and health service utilization factors associated with mortality among people who inject drugs in Melbourne (n = 1209)

Characteristics	Overall n = 1209	Deaths n = 76 (6.3%)	PYs	CMR per 1000	Unadjusted HR	P-value	Adjusted HR (< 0.05)	
Gender						0.090		
Male	813 (67.35%)	57 (75.00%)	4551.77	12.52 (9.65–16.23)	1.57 (0.93–2.63)			
Female	396 (32.75%)	19 (25.00%)	2361.39	8.05 (5.13–12.61)	1			
Age[a] (years)						0.686		
< 25	104 (8.60%)	13 (17.11%)	1057.32	12.29 (7.14–21.17)	1			
25–29	226 (18.69%)	21 (27.63%)	2221.43	9.45 (6.16–14.50)	0.76 (0.38–1.52)			
30 and above	879 (72.70%)	42 (55.26%)	3634.41	11.56 (8.54–15.64)	0.91 (0.49–1.72)			
Education level						0.226		
≤ 9 years	402 (33.25%)	31 (40.79%)	2262.72	13.70 (9.64–19.48)	1			
10–11 years	501 (41.44%)	33 (43.42%)	3102.81	10.6 (7.56–14.96)	0.77 (0.47–1.26)			
≥ 12 years	306 (25.31%)	12 (15.79%)	1547.64	7.75 (4.40–13.65)	0.57 (0.29–1.11)			
Currently employed[a]						0.027		0.086
No	1017 (84.12%)	69 (90.79%)	5590.70	12.34 (9.75–15.63)	1		1	
Yes	192 (15.88%)	7 (9.21%)	1322.47	5.29 (2.52–11.10)	0.42 (0.19–0.91)		0.50 (0.23–1.10)	
Stable accommodation[a]						0.062		
Unstable	285 (23.57%)	15 (19.74%)	892.23	16.81 (10.13–27.89)	1			
Stable	924 (76.43%)	61 (80.26%)	6020.94	10.13 (7.88–13.02)	0.58 (0.33–1.03)			
Weekly income[a]						0.126		
AU$400+/week	519 (42.93%)	19 (25.00%)	2279.56	8.33 (5.42–13.07)	1			
< AU$400 a week	690 (57.07%)	57 (75.00%)	4633.60	12.30 (9.49–15.95)	1.50 (0.89–2.53)			
Time since first injection (years)[a]						0.184		
Less than 3	67 (5.54%)	7 (9.21%)	421.43	16.61 (7.92–34.84)	1			
3–9	258 (21.34%)	19 (25.00%)	2314.82	8.21 (5.24–12.87)	0.46 (0.19–1.11)			
10 and above	884 (73.12%)	50 (65.79%)	4176.91	11.97 (9.07–15.79)	0.67 (0.30–1.49)			
Experienced a non-fatal opioid overdose[a]						0.947		
No	636 (52.61%)	36 (47.37%)	3899.22	9.23 (6.66–12.80)	1			
Yes	573 (47.39%)	40 (52.63%)	3013.94	13.27 (9.74–18.09)	1.02 (0.60–1.73)			
Heroin injecting in past week[a]						0.579		
None	455 (37.63%)	32 (42.11%)	2677.85	11.95 (8.45–16.90)	1			
Less than weekly	377 (21.18%)	29 (38.16%)	2484.01	11.67 (8.11–16.80)	0.98 (0.59–1.63)			
Weekly or more	377 (31.18%)	15 (19.74%)	1751.30	8.57 (5.16–14.21)	0.74 (0.40–1.37)			

(Continues)

TABLE 2 (Continued)

Characteristics	Overall *n* = 1209	Deaths *n* = 76 (6.3%)	PYs	CMR per 1000	Unadjusted HR	*P*-value	Adjusted HR (< 0.05)	
AUDIT-C score[a]						0.170		
Abstinent	551 (45.57%)	32 (42.11%)	2825.76	11.3 (8.01–16.01)	1			
Less than 8	413 (34.16%)	21 (27.63%)	2518.03	8.34 (5.44–12.79)	0.74 (0.42–1.28)			
8 or above	245 (20.26%)	23 (30.26%)	1569.38	14.66 (9.74–22.05)	1.29 (0.76–2.21)			
Currently on OAT[a]						0.491		
No	719 (59.47%)	44 (57.89%)	3771.27	11.67 (8.68–15.68)	1			
Yes	490 (40.53%)	32 42.11%)	3141.89	10.18 (7.20–14.40)	0.85 (0.54–1.36)			
Attended emergency department in past month[a]						0.004		0.933
No	1076 (89.00%)	60 (78.95%)	6168.05	9.72 (7.55–12.53)	1		1	
Yes	133 (11.00%)	16 (21.05%)	745.11	21.47 (13.16–35.05)	2.23 (1.28–3.88)		0.91 (0.43–1.92)	
Utilization of ambulance services in past month[a]						< 0.001		0.001
No	1106 (91.48%)	60 (78.95%)	6472.04	9.27 (7.20–11.94)	1		1	
Yes	103 (8.52%)	16 (21.05%)	441.13	3.63 (22.22–59.20)	3.98 (2.29–6.92)		3.77 (1.78–7.97)	
Attended GP services in past month[a]						0.698		
No	455 (37.63%)	27 (35.53%)	2585.82	10.44 (7.16–15.23)	1			
Yes	754 (62.37%)	49 (64.47%)	4327.35	11.32 (8.56–14.98)	1.10 (0.69–1.76)			
Attended a mental health professional in past month[a]						0.050		0.196
No	966 (79.90%)	58 (76.32%)	5841.76	9.93 (7.68–12.84)	1		1	
Yes	243 (20.10%)	18 (23.68%)	1071.40	16.80 (10.59–26.67)	1.70 (1.00–2.89)		1.44 (0.84–2.46)	
Life-time incarceration(s)[a]						0.002		0.001
None	666 (55.09%)	24 (31.58%)	3186.76	7.53 (5.05–11.24)	1		1	
1–3 times	394 (32.59%)	30 (39.47%)	2774.93	10.8 (7.56–15.46)	1.43 (0.83–2.46)		1.26 (0.74–2.20)	
≥ 4 times	149 (12.32%)	22 (28.95%)	951.48	23.12 (15.22–35.12)	2.97 (1.66–5.32)		2.78 (1.55–4.99)	

AUDIT-C, alcohol use disorders identification test–consumption; CMR, crude death rate; GP, general practitioner; HR, hazard ratio; OAT, opioid agonist treatment; PY, person-years.
[a]Time-varying exposures.

incarcerations over time and all-cause mortality in the SuperMIX cohort. These findings have been used to indicate the need for overdose prevention (including provision of OAT) among people being released from prison with a history of injecting drug use. However, half the SuperMIX mortality cases were not accidental drug-induced deaths, meaning that interventions to prevent other mortality causes, including injury and other medical conditions, are also necessary.

Our study is limited by the use of self-reported behavioural data and short recall periods for health service utilization [33]. However, self-report is often utilized in injecting drug use research and there is evidence of its reliability [34]. There is currently no opportunity to link to administrative data on OAT use in Victoria, critical to further investigation of the impact of OAT on mortality risk in this population. Further work is also needed to disambiguate the causes of ambulance attendances, which will be further investigated in this cohort when approved access to ambulance system data is received. Left truncation may be present in this sample, highlighted by our finding of longer duration of injecting career resulting in a reduction in risk, as those at higher risk may not have joined the study, potentially as a result of premature death. Cause-specific analysis was not possible for this cohort due to low rates of overall mortality. Delays in assigning causes of death to mortality data in Australia meant that with 11% of deaths recorded did not yet have a cause of death specified at the time of linkage.

Our analysis provides recent mortality estimates in a cohort of community-recruited people who inject drugs in Australia, with findings comparable to previous Australian estimates. Our results highlight the need to prioritize all-cause mortality prevention programmes to people who inject drugs, especially those frequently using ambulance services and those who are or have been incarcerated.

ACKNOWLEDGEMENTS

The MIX/SuperMIX study is supported by The Colonial Foundation Trust and the National Health and Medical Research Council (545891 and 1126090). P.L.H. is the recipient of a NHMRC Postgraduate Scholarship and P.D., M.S. and L.M. are recipients of NHMRC Senior Research Fellowships. M.H. is NIHR Senior Investigator. The authors gratefully acknowledge the contribution to this work of the Victorian Operational Infrastructure Support Program's support of the Burnet Institute. The funding bodies played no role in the study design, data analysis or preparation of the manuscript for publication. M.H. acknowledges support from NIHR HPRU in Behavioural Science and Evaluation. The authors wish to thank the participants of the SuperMIX study, together with the staff of the community-based organizations who assisted in recruitment. Thank you to the members of the SuperMIX study team who assisted with participant recruitment, follow-up and interviewing. We would also like to acknowledge the support of the staff at the AIFS and AIHW who assisted with linked data access. Open access publishing facilitated by Monash University, as part of the Wiley - Monash University agreement via the Council of Australian University Librarians.

DECLARATION OF INTERESTS

P.D. has received an investigator-driven grant from Gilead Sciences for unrelated work on hepatitis C and an untied educational grant from Reckitt Benckiser for unrelated work on the introduction of buprenorphine–naloxone into Australia. M.S. has received investigator-initiated funding from Gilead Sciences, AbbVie and Bristol Myers Squibb for research unrelated to this work. M.H. has received in the last 3 years unrestricted honoraria/speaker fees from MSD and Gilead.

AUTHOR CONTRIBUTIONS

Penelope L. Hill: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration. **Mark Stoové:** Conceptualization; investigation; project administration; supervision. **Paul A. Agius:** Formal analysis; investigation; methodology; project administration. **Lisa Maher:** Investigation; project administration. **Matthew Hickman:** Investigation; project administration. **Slone Crawford:** Investigation; project administration. **Paul Dietze:** Conceptualization; data curation; funding acquisition; investigation; methodology; project administration; supervision.

ORCID

Penelope L. Hill https://orcid.org/0000-0003-0593-5887
Lisa Maher https://orcid.org/0000-0001-6020-6519
Matthew Hickman https://orcid.org/0000-0001-9864-459X

REFERENCES

1. Pierce M, Bird SM, Hickman M, Millar T. National record linkage study of mortality for a large cohort of opioid users ascertained by drug treatment or criminal justice sources in England, 2005–2009. Drug Alcohol Depend. 2015;146:17–23.
2. Degenhardt L, Bucello C, Mathers BM, Briegleb C, Ali H, Hickman M, et al. Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. Addiction. 2011;106:32–51.
3. Larney S, Tran LT, Leung J, Santo T Jr, Santomauro D, Hickman M, et al. All-cause and cause-specific mortality among people using Extramedical opioids: a systematic review and meta-analysis. JAMA Psychiatry. 2020;77:493–502.
4. Ayoo K, Mikhaeil J, Huang A, Wąsowicz M. The opioid crisis in North America: facts and future lessons for Europe. Anaesthesiol Intensive Ther. 2020;52:139–47.
5. Hall WD, Farrell M. Reducing the opioid overdose death toll in North America. PLOS Med. 2018;15:e1002626.
6. Evans JL, Tsui JI, Hahn JA, Davidson PJ, Lum PJ, Page K. Mortality among young injection drug users in San Francisco: a 10-year follow-up of the UFO study. Am J Epidemiol. 2012;175:302–8.
7. Stoove MA, Dietze PM, Aitken CK, Jolley D. Mortality among injecting drug users in Melbourne: a 16-year follow-up of the Victorian injecting cohort study (VICS). Drug Alcohol Depend. 2008;96:281–5.
8. Nambiar D, Agius PA, Stoové M, Hickman M, Dietze P. Mortality in the Melbourne injecting drug user cohort study (MIX). Harm Reduct J. 2015;12:55.
9. Merrall ELC, Kariminia A, Binswanger IA, Hobbs MS, Farrell M, Marsden J, et al. Meta-analysis of drug-related deaths soon after release from prison. Addiction. 2010;105:1545–54.

10. Pavarin RM, Berardi D, Gambini D. Emergency department presentation and mortality rate due to overdose: a retrospective cohort study on nonfatal overdoses. Subst Abuse. 2016;37:558–63.
11. 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;91:102–23.
12. Horyniak D, Higgs P, Jenkinson R, Degenhardt L, Stoove M, Kerr T, et al. Establishing the Melbourne injecting drug user cohort study (MIX): rationale, methods, and baseline and twelve-month follow-up results. Harm Reduct J. 2013;10. https://doi.org/10.1186/1477-7517-10-11
13. Dietze P, Jenkinson R, Aitken C, Stoove M, Jolley D, Hickman M, et al. The relationship between alcohol use and injecting drug use: impacts on health, crime and wellbeing. Drug Alcohol Depend. 2013;128:111–5.
14. Miller CL, Kerr T, Strathdee SA, Li K, Wood E. Factors associated with premature mortality among young injection drug users in Vancouver. Harm Reduct J. 2007;4:1.
15. Aitkin M. An Introduction to Medical Statistics, 3rd edn. Biometrics. 2001;57:329.
16. Harrell FE. Cox Proportional hazards regression Model. In: Harrell FE, editorRegression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis New York, NY: Springer New York; 2001:465–507.
17. Kimber J, Stoové M, Maher L. Mortality among people who inject drugs: ten-year follow-up of the hepatitis C virus cohort. Drug Alcohol Rev. 2019;38:270–3.
18. Degenhardt L, Randall D, Hall W, Law M, Butler T, Burns L. Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: risk factors and lives saved. Drug Alcohol Depend. 2009;105:9–15.
19. 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;115:190–5.
20. Darke S, Marel C, Mills KL, Ross J, Slade T, Tessson M. Years of potential life lost amongst heroin users in the Australian treatment outcome study cohort, 2001–2015. Drug Alcohol Depend. 2016;162:206–10.
21. Nambiar D, Stoove M, Dietze P. Frequent emergency department presentations among people who inject drugs: a record linkage study. Int J Drug Policy. 2017;44:115–20.
22. Lewer D, Freer J, King E, Larney S, Degenhardt L, Tweed EJ, et al. Frequency of health-care utilization by adults who use illicit drugs: a systematic review and meta-analysis. Addiction. 2020;115:1011–23.
23. Black E, Monds LA, Chan B, Brett J, Hutton JE, Acheson L, et al. Overdose and take-home naloxone in emergency settings: a pilot study examining feasibility of delivering brief interventions addressing overdose prevention with 'take-home naloxone' in emergency departments. Emerg Med Australas. 2022. https://doi.org/10.1111/1742-6723.13925
24. Booker MJ, Shaw ARG, Purdy S. Why do patients with 'primary care sensitive' problems access ambulance services? A systematic mapping review of the literature. BMJ Open. 2015;5:e007726.
25. Wang CL, Vlahov D, Galai N, Cole SR, Bareta J, Pollini R, et al. The effect of HIV infection on overdose mortality. Aids. 2005;19:935–42.
26. Walton GR, Hayashi K, Bach P, Dong H, Kerr T, Ahamad K, et al. The impact of benzodiazepine use on mortality among polysubstance users in Vancouver. Canada. Public Health Rep. 2016;131:491–9.
27. Sordo L, Barrio G, Bravo MJ, Indave BI, Degenhardt L, Wiessing L, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ. 2017;357:j1550.
28. Booker MJ, Purdy S, Shaw ARG. Seeking ambulance treatment for 'primary care' problems: a qualitative systematic review of patient, carer and professional perspectives. BMJ Open. 2017;7:e016832.
29. Nambiar D, Stoové M, Dietze P. A cross-sectional study describing factors associated with utilisation of GP services by a cohort of people who inject drugs. BMC Health Serv Res. 2014;14:308.
30. Richardson L, Wood E, Li K, Kerr T. Factors associated with employment among a cohort of injection drug users. Drug Alcohol Rev. 2010;29:293–300.
31. Binswanger IA, Blatchford PJ, Mueller SR, Stern MF. Mortality after prison release: opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009. Ann Intern Med. 2013;159:592–600.
32. Pizzicato LN, Drake R, Domer-Shank R, Johnson CC, Viner KM. Beyond the walls: risk factors for overdose mortality following release from the Philadelphia Department of Prisons. Drug Alcohol Depend. 2018;189:108–15.
33. Nambiar D, Agius PA, Stoove M, Hickman M, Dietze P. Cessation of injecting drug use: the effects of health service utilisation, drug use and demographic factors. Drug Alcohol Depend. 2015;154:208–13.
34. Darke S. Self-report among injecting drug users: a review. Drug Alcohol Depend. 1998;51:253–63.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Hill PL, Stoové M, Agius PA, Maher L, Hickman M, Crawford S, et al. Mortality in the SuperMIX cohort of people who inject drugs in Melbourne, Australia: a prospective observational study. Addiction. 2022. https://doi.org/10.1111/add.15975