Addiction
RESEARCH REPORT
doi:10.1111/add.12337

Causes of death in a cohort treated for opioid dependence between 1985 and 2005

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ABSTRACT

Aims To examine changes in causes of death in a cohort treated for opioid dependence, across time and age; quantify years of potential life lost (YPLL); and identify avoidable causes of death. **Design** People in New South Wales (NSW) who registered for opioid substitution therapy (OST), 1985–2005, were linked to a register of all deaths in Australia. **Setting** NSW, Australia. **Measurements** Crude mortality rates (CMRs), age–sex-standardized mortality rates (ASSRs) and standardized mortality ratios (SMRs) across time, sex and age. Years of potential life lost (YPLL) were calculated with reference to Australian life tables and by calculating years lost before the age of 65 years. **Findings** There were 43 789 people in the cohort, with 412 216 person-years of follow-up. The proportion of the cohort aged 40+ years increased from 1% in 1985 to 39% in 2005. Accidental opioid overdoses, suicides, transport accidents and violent deaths declined with age; deaths from cardiovascular disease, liver disease and cancer increased. Among men, 89% of deaths were potentially avoidable; among women, 86% of deaths were avoidable. There were an estimated 160 555 YPLL in the cohort, an average of 44 YPLL per decedent and an average of 29 YPLL before age 65 years. **Conclusions** Among a cohort of opioid-dependent people in New South Wales, 1985–2005, almost nine in 10 deaths in the cohort were avoidable. There is huge scope to improve mortality among opioid-dependent people.

Keywords Ageing, heroin, injecting drug use, mortality, opioid dependence.

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Submitted 28 November 2012; initial review completed 25 February 2013; final version accepted 13 August 2013

INTRODUCTION

Elevated mortality rates and excess mortality have been well described in opioid-dependent populations in developed countries. Dependent opioid users in these countries may be 15 times more likely to die than their non-opioid-using peers [1]. Drug overdose is the most common cause of death and chronic diseases, suicide and injury also contribute to excess mortality [1–3].

In recent decades changes have been observed in the contribution of different causes of death to premature mortality in opioid users. For example, AIDS-related deaths in Italy and Spain increased throughout the 1980s and 1990s, and then decreased after the introduction of highly active antiretroviral therapy [2,4–6]. Recent studies have reported an increased contribution of liver disease [7,8] and cancer [9] to mortality in Australian cohorts. Few studies, however, have described the full range of causes of death in this population and how they have varied over time and with age [1,10]. This is a particularly pertinent issue given the ageing of opioid-dependent populations in Australia and western Europe [11,12].

A second important public health consideration is to what extent deaths among opioid-dependent people are avoidable, given current knowledge about effective preventive and health care [13]. Analysis of 'avoidable mortality' and years of potential life lost may identify potential targets for intervention [10]. Avoidable mortality includes conditions in which current health care may reduce case fatality, as well as conditions for which there are effective preventive interventions [13].

We were able to examine causes of death and potentially avoidable mortality in a cohort of all opioid-dependent people who entered opioid substitution therapy (OST) in New South Wales (NSW), Australia, between 1985 and 2005. Our aims were to (i): describe changes in causes of death across time and age group (ii); quantify years of potential life lost; and (iii) identify potentially avoidable causes of death in an Australian population of opioid-dependent people seeking treatment.

METHODS

Data sources and linkage

Data for this study were derived from the Pharmaceutical Drugs of Addiction System (PHDAS) database and the National Death Index (NDI). The PHDAS contains records of all people in New South Wales (NSW) who register for opioid substitution treatment. Records for all people registering for OST during the calendar years 1985–2005 were linked probabilistically to the NDI, a statutory register of all deaths, including cause of death, in Australia. Linkage was performed by staff at the Australian Institute of Health and Welfare (the NDI data custodian) using an in-house probabilistic record linkage program called REMA (REcord MAtcher). The variables used for matching included full name, date of birth, sex and date and State of last known contact.

Measurements and coding

Causes of death were recorded in the NDI using the International Classification of Diseases (ICD) version 9 (for deaths occurring 1985–96) and version 10 (1997–2005). Using data coded using both ICD-9 and ICD-10 in Australia for 1997 and 1998, we found ICD-9 and ICD-10 groupings to be consistent [14].

The most common causes of death were classified according to the categories defined in Randall *et al.* [15]. This coding scheme is intentionally neither mutually exclusive nor exhaustive. Deaths were classified as drug-related (with subordinate categories of accidental opioid-related or accidental other drug-related), unintentional injuries (with subordinate category of motor vehicle accident), violence, suicide, liver-related (with subordinate categories of chronic liver disease and viral hepatitis), cardiovascular, cancer, HIV, alcohol-related, chronic respiratory disease and respiratory infections.

A set of mutually exclusive causes of death was also coded, with the most common causes of death given prominence. Mutually exclusive categories were: accidental opioid-related, accidental other drug-related, suicide, motor vehicle accidents, violence, liver-related, cardiovascular, cancer and HIV, with all other deaths coded as 'other'. ICD-9 and ICD-10 codes included in each category are available in the online appendix.

We followed Page *et al.* [13] in classifying conditions into the broad 'avoidable' category, that included 'amenable' causes—for which existing health-care interventions could reduce case fatality—and 'preventable' causes—mortality which could be avoided through prevention at the individual and/or population level through life-style and environmental modification or health policy. Their taxonomy of conditions was applied to the causes of death in our cohort (for details of all conditions see [13]). It is important to note that we have reported only the overarching category of 'avoidable' because of changes over the study period in availability of effective prevention and treatment interventions and access to these interventions. The intent with these analyses was to estimate the extent of avoidable mortality (regardless of whether or not it could be avoided through prevention or treatment). While there may have been some changes to causes of deaths considered 'avoidable' during the study period, Page *et al.* applied their taxonomy to Australian deaths between 1997 and 2001, and the bulk of the deaths in our data (82%) occurred after 1995.

Data analysis

All analyses were conducted in SAS version 9.3 [16]. Total and cause-specific crude mortality rates (CMRs) and Poisson 95% confidence intervals (CI) were calculated from the number of deaths and the number of person-years (PY) follow-up. PY were calculated by age, calendar year and sex, from the first treatment registration until death or 31 December 2005, whichever occurred first. Directly age–sex–standardized mortality rates (ASSRs, standardized to the average age and sex profile of the cohort) and Poisson 95% CI were calculated and year group (1985–89, 1990–94, 1995–99, 2000–05) was entered into a Poisson regression model adjusted for age group and sex to determine the significance of trends in standardized mortality over time. Standardized mortality ratios (SMRs) with Poisson 95% CI were calculated as the observed number of deaths divided by the expected number of deaths, with age-, sex- and year-specific mortality rates in the NSW population used to calculate the expected number of deaths.

We compared the percentage of avoidable deaths in the cohort by sex to the percentage of these causes of death in the general Australian population for 15–64-year-olds in order to achieve a reasonably comparable age group.

Years of potential life lost (YPLL) were calculated in two ways. First, we used Australian life tables available on the Australian Bureau of Statistics website (http://www.abs.gov.au). Life tables by year and sex were avail-

able from 1993 to 2005; for 1985 to 1992, the 1993 life tables were used. For each death, the number of years of potential life lost was determined by the difference between the average life expectancy for someone of the same age and sex in that calendar year, and the age at death of the cohort member. Secondly, we calculated the number of years of life lost before the age of 65. This is the YPLL method used by the Centers for Disease Control and Prevention [17].

Ethical approval

Approval for the study was obtained from the NSW Population and Health Services Research Ethics Committee and the University of New South Wales Human Research Ethics Committee.

RESULTS

The study cohort included 43 789 people; 28 939 men (66%) and 14 860 women. There was a total of 412 216 PY of follow-up, with a median follow-up duration of 8.7 years. The age profile of the cohort changed over time, with the proportion of the cohort aged 40 years or older increasing from 1% in 1985 to 39% in 2005 (Cochrane–Armitage trend test, $P < 0.001$) (Fig. 1). The sex profile of the cohort also changed, with the proportion of men in the cohort increasing from 57% in 1985 to 65% in 2005 (Cochrane–Armitage trend test, $P < 0.001$) (Fig. 1).

Mortality over time

There were 3685 deaths in the cohort between 1985 and 2005 for a crude mortality rate of 894 per 100 000 PY (95% CI = 865, 923) (Table 1). The majority of deaths were drug-related ($n = 1932$; 52%), with most of these ($n = 1574$; 82% of all drug-related deaths) coded as accidental opioid deaths. The bulk of remaining deaths were due to unintentional injuries ($n = 975$; 26% of all deaths) and suicide ($n = 484$; 13% of all deaths).

There was a dramatic decrease in standardized drug-related mortality rates from 1999–2000 to 2001–02 (Table 1, Fig. 2). Furthermore, there were strong increases in accidental injury mortality rates across the follow-up period (Table 1). It is important to note that there may have been period and cohort effects in these mortality rates which it is difficult to disentangle.

The overall age-, sex- and year-standardized mortality ratio was 6.5 (95% CI = 6.3–6.7), indicating that our cohort had 6.5 times the rate of mortality than that expected in the population. Cause-specific excess mortality across time is shown in Table 2. The causes with the greatest excess mortality rates were viral hepatitis (SMR 46.3; 95% CI = 38.5–55.2) and drug-related deaths (SMR 39.9; 95% CI = 38.0–41.8).

Table 3 shows that women were significantly more likely than men to die of cardiovascular disease ($P = 0.03$), cancer ($P = 0.03$) or violence ($P = 0.002$), while men were significantly more likely than women to die of suicide ($P = 0.05$). There were clear trends in causes of death with increasing age. Accidental opioid overdoses ($P < 0.0001$), suicides ($P < 0.0001$), motor vehicle accidents ($P < 0.0001$) and violent deaths ($P = 0.003$) all declined with age, while deaths related to cardiovascular disease ($P < 0.0001$), liver disease ($P < 0.0001$) and cancer ($P < 0.0001$) increased with age.

Avoidable mortality

Eighty-eight per cent (3240 of 3685) of all cohort deaths were from potentially avoidable causes: 89% of deaths in men and 86% of deaths in women. To provide a comparison for illustrative purposes, 73% of deaths among the Australian population aged 15–64 years from 1997 to 2001 were considered avoidable [13].

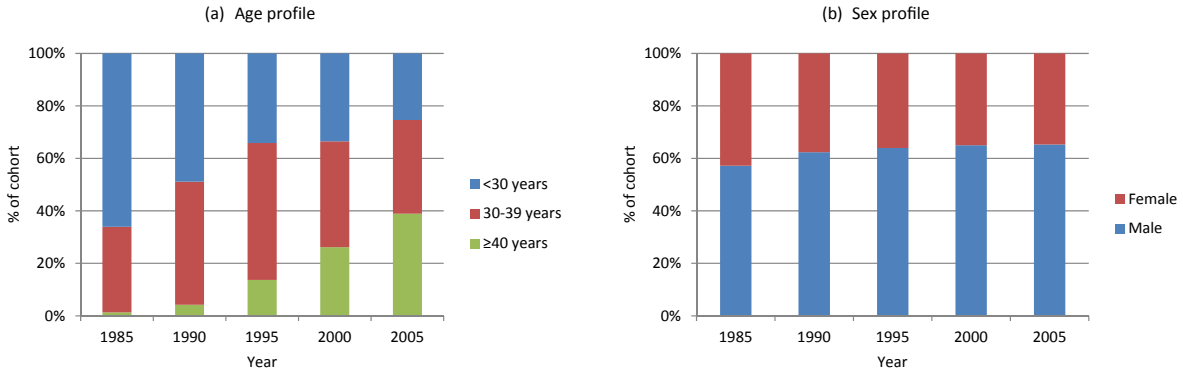

Figure 1 Change in age (left) and sex (right) profile of a cohort of people treated for opioid dependence in New South Wales between 1985 and 2005

Table 1 All-cause and cause-specific crude mortality rate per 100 000 person-years and age- and sex-standardized mortality rates per 100 000 person-years across time in a cohort of people treated for opioid dependence in NSW, 1985–2005.

	Total		*1985–89*		*1990–94*		*1995–99*		*2000–05*		
	n (%)	*CMR (95% CI)*	*n (%)*	*Standardized mortality rate (95% CI)*	*n (%)*	*Standardized mortality rate (95% CI)*	*n (%)*	*Standardized mortality rate (95% CI)*	*n (%)*	*Standardized mortality rate (95% CI)*	*Poisson test for time trend P*
Total mortality	3685 (100)	894 (865–923)	132 (100)	780 (445, 1160)	527 (100)	941 (837, 1052)	1295 (100)	1163 (1098, 1231)	1731 (100)	770 (733, 808)	0.009
All drug-related	1932 (52)	469 (448–490)	77 (58)	331 (179, 510)	310 (59)	518 (445, 597)	805 (62)	703 (655, 755)	740 (43)	354 (328, 381)	<0.0001
Accidental drug-related	1738 (47)	421 (402–442)	71 (54)	315 (164, 495)	268 (51)	449 (380, 523)	727 (56)	634 (587, 682)	672 (39)	322 (298, 348)	0.0003
Accidental opioid-related	1574 (43)	382 (363–401)	65 (49)	294 (144, 473)	251 (48)	418 (354, 489)	681 (53)	593 (548, 640)	577 (33)	277 (254, 301)	<0.0001
Accidental other drug-related	164 (4)	40 (34–46)	6 (1)	22 (7, 49)	17 (3)	31 (10, 62)	46 (4)	41 (30, 54)	95 (5)	45 (36, 55)	0.04
Unintentional injuries	975 (26)	236 (222–252)	29 (22)	115 (73, 170)	93 (18)	142 (106, 184)	296 (23)	262 (232, 295)	557 (32)	266 (244, 289)	<0.0001
Motor vehicle accidents	180 (5)	44 (38–51)	17 (13)	72 (39, 121)	29 (6)	39 (26, 55)	64 (5)	57 (44, 73)	70 (4)	34 (26, 43)	0.02
Violence	85 (2)	21 (16–25)	3 (1)	12 (1, 39)	17 (3)	22 (13, 35)	31 (2)	28 (18, 40)	34 (2)	17 (12, 24)	0.3
Suicide	484 (13)	117 (107–128)	20 (15)	83 (29, 157)	80 (15)	131 (99, 168)	154 (12)	137 (115, 161)	230 (13)	111 (96, 126)	0.6
All liver-related	254 (7)	62 (54–70)	5 (1)	23 (6, 56)	24 (5)	53 (30, 84)	57 (4)	57 (42, 75)	168 (10)	61 (52, 71)	0.5
Chronic liver disease	98 (3)	24 (19–29)	3 (1)	17 (3, 51)	11 (2)	23 (10, 43)	22 (2)	21 (12, 32)	62 (4)	22 (17, 29)	0.8
Viral hepatitis	124 (3)	30 (25–36)	2 (1)	6 (1, 21)	13 (2)	30 (12, 57)	31 (2)	31 (21, 45)	78 (5)	29 (23, 36)	0.9
Cardiovascular	206 (6)	50 (43–57)	4 (1)	209 (0, 678)	20 (4)	68 (33, 116)	49 (4)	51 (36, 68)	133 (8)	51 (43, 61)	0.4
Cancer	212 (6)	51 (45–59)	1 (1)	7 (0, 38)	13 (2)	39 (15, 75)	61 (5)	64 (48, 84)	137 (8)	49 (41, 58)	0.25
HIV/AIDS	91 (2)	22 (18–27)	0 (0)	0	30 (6)	60 (32, 97)	30 (2)	27 (18, 39)	31 (2)	14 (9, 20)	<0.0001
Alcohol-related	96 (3)	23 (19–28)	3 (1)	17 (3, 51)	11 (2)	20 (9, 37)	21 (2)	20 (12, 31)	61 (4)	22 (17, 29)	0.8
Chronic respiratory disease	32 (1)	8 (5–11)	2 (1)	30 (0, 132)	2 (1)	3 (0, 9)	6 (1)	6 (2, 14)	22 (1)	8 (5, 12)	0.9
Respiratory infections	24 (1)	6 (4–9)	1 (1)	3 (0, 18)	1 (1)	1 (0, 6)	8 (1)	8 (3, 17)	14 (1)	5 (3, 9)	0.9

CMR = crude mortality rate; CI = confidence interval. Cause of death categories are not mutually exclusive.

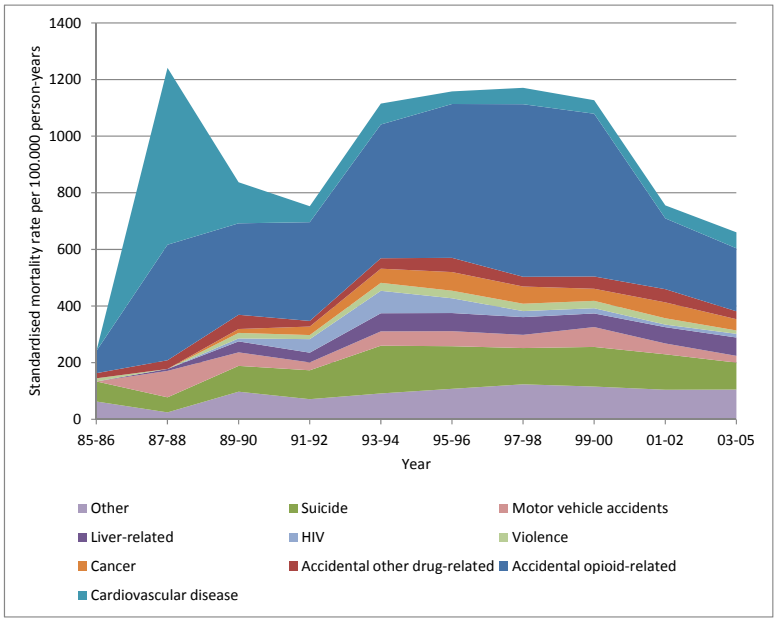

Figure 2 Age-standardized mortality rate in a cohort of people treated for opioid dependence in New South Wales, by 2-year groups, 1985–2005. Cause of death categories are mutually exclusive

Table 2 Standardized mortality ratios (SMR) for most common causes of death in a cohort of people treated for opioid dependence in New South Wales, 1985–2005, in total and by 5-year groups.

	SMR (95% CI)				
	Total	*1985–1989*	*1990–1994*	*1995–1999*	*2000–2005*
Total mortality	6.5 (6.3–6.7)	5.2 (4.3–6.1)	6.9 (6.4–7.6)	8.7 (8.2–9.2)	6.5 (6.2–6.8)
All drug-related	35.0 (33.4–36.6)	25.2 (19.9–31.5)	34.2 (30.5–38.3)	35.4 (33.0–38.0)	33.0 (30.6–35.4)
Accidental drug-related	39.9 (38.0–41.8)	30.0 (23.4–37.8)	39.8 (35.2–44.9)	38.2 (35.4–41.0)	36.5 (33.8–39.4)
Accidental opioid-related	42.8 (40.7–45.0)	33.4 (25.8–42.5)	43.0 (37.8–48.6)	39.4 (36.5–42.5)	40.2 (37.0–43.7)
Accidental other drug-related	24.1 (20.6–28.1)	14.3 (5.3–31.2)	19.1 (11.1–30.5)	26.1 (19.1–34.8)	23.4 (19.0–28.7)
Unintentional injuries	9.6 (9.0–10.2)	3.8 (2.5–5.4)	6.2 (5.0–7.6)	10.6 (9.4–11.8)	12.2 (11.2–13.3)
Motor vehicle accidents	3.2 (2.7–3.7)	3.1 (1.8–5.0)	3.3 (2.2–4.7)	4.7 (3.6–6.0)	3.4 (2.6–4.3)
Violence	7.6 (6.1–9.5)	4.6 (0.9–13.4)	9.3 (5.4–14.9)	8.7 (5.9–12.4)	7.4 (5.1–10.3)
Suicide	6.2 (5.6–6.7)	4.9 (3.0–7.6)	6.5 (5.2–8.1)	5.9 (5.0–6.9)	6.4 (5.6–7.3)
All liver-related	11.4 (10.1–12.9)	8.3 (2.7–19.5)	10.0 (6.4–14.9)	10.6 (8.0–13.7)	12.4 (10.6–14.4)
Chronic liver disease	6.5 (5.3–8.0)	6.2 (1.3–18.2)	6.4 (3.2–11.4)	6.7 (4.2–10.1)	8.4 (6.4–10.8)
Viral hepatitis	46.3 (38.5–55.2)	42.4 (5.1–153.1)	40.7 (21.7–69.6)	36.2 (24.6–51.3)	35.4 (28.0–44.1)
Cardiovascular	2.1 (1.9–2.5)	1.5 (0.4–4.0)	2.3 (1.4–3.6)	2.4 (1.8–3.2)	2.8 (2.4–3.4)
Cancer	1.7 (1.4–1.9)	0.3 (0.0–1.5)	1.0 (0.5–1.6)	2.2 (1.7–2.8)	2.0 (1.7–2.4)
HIV/AIDS	4.4 (3.5–5.3)	0.0 (0.0–5.0)	4.7 (3.2–6.8)	4.3 (2.9–6.2)	8.3 (5.6–11.8)
Alcohol-related	5.4 (4.4–6.6)	5.6 (1.2–16.3)	5.1 (2.5–9.0)	5.0 (3.1–7.7)	6.6 (5.1–8.5)
Chronic respiratory disease	3.9 (2.7–5.5)	4.3 (0.5–15.6)	2.2 (0.3–7.8)	4.3 (1.6–9.3)	6.6 (4.1–10.0)
Respiratory infections	7.9 (5.1–11.8)	8.4 (0.2–47.1)	2.7 (0.1–15.0)	15.3 (6.6–30.1)	7.5 (4.1–12.6)

SMR = standardized mortality ratio; CI: confidence interval. Cause of death categories are not mutually exclusive.

Years of potential life lost (YPLL)

Using the Australian life tables approach, there was an estimated 160 055 YPLL in this cohort, an average of 44 YPLL per person who died, and 29 years of YPLL before age 65 (Table 4). Just under half (45%) of the YPLL were due to accidental opioid-related deaths (an average loss of 46 years of potential life, or 31 years prior to age 65). Motor vehicle accidents accounted for the highest average YPLL, 47 years, or 33 years before age 65.

DISCUSSION

We have reported mortality over 21 years in all people entering OST at some point between 1985 and 2005 in

Table 3 Most common causes of death in a cohort of people treated for opioid dependence in New South Wales, 1985–2006, by sex and age at death.

	Sex				*Age at death*[b]							
	Male[a]		*Female*		*<25 years*		*25–34 years*		*35–44 years*		*45 years +*	
Cause of death	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Accidental opioid-related	1186	43.4	388	41.8	209	59.5	699	50.9	542	40.9	124	20.3^
Accidental other drug-related	123	4.5	41	4.4	14	4.0	71	5.2	56	4.2	23	3.8
Suicide	379	13.9	105	11.3*	53	15.1	211	1543	167	12.6	53	8.7^^
Liver-related	201	7.4	53	5.7	1	0.3	23	1.7	124	9.4	106	17.3^^
Cardiovascular	140	5.1	66	7.1*	2	0.6	38	2.8	82	6.2	84	13.7^^
Cancer	129	4.7	61	6.6*	3	0.9	17	1.2	90	6.8	80	13.1^^
HIV	74	2.7	17	1.8	6	1.7	37	2.7	33	2.5	15	2.5
Motor vehicle accidents	137	5.0	43	4.6	26	7.4	96	7.0	42	3.2	16	2.6^^
Violence	51	1.9	34	3.7**	11	3.1	37	2.7	31	2.3	6	1.0^
Other	312	11.4	120	12.9	26	0.0	144	10.5	157	11.9	105	17.2^
Total	2732	100	928	100	351	100	1373	100	1324	100	612	100

Cause of death categories are mutually exclusive. [a]Missing cause of death data for 17 male participants and eight female participants. [b]Missing cause of death data for six participants aged 25–34 years at death, six participants aged 35–44 years at death and 13 participants aged 45 years or older at death. *χ^2 test $P < 0.05$; ** χ^2 test $P < 0.001$; ^Cochrane–Armitage trend test $P < 0.05$; ^^Cochran–Armitage trend test $P < 0.0001$.

Table 4 Years of potential life lost (YPLL) in a cohort of people treated for opioid dependence in New South Wales, 1985–2005, by most common causes of death.

Cause of death[a]	*No. of deaths*	*% of deaths*	*Total YPLL*	*% of total YPLL*	*Average YPLL*	*Average years before age 65*
Accidental opioid-related	1574	43.0	72 090	45.0	45.8	31.2
Accidental other-drug related	164	4.5	7 288	4.5	44.4	29.3
Suicide	484	13.2	21 792	13.6	45.0	30.3
Liver-related	254	6.9	9 405	5.9	37.0	21.4
Cardiovascular	206	5.6	7 936	5.0	38.5	22.5
Cancer	190	5.2	7 118	4.4	37.5	21.3
HIV	91	2.5	3 907	2.4	42.9	28.7
Motor vehicle accidents	180	4.9	8 480	5.3	47.1	32.6
Violence	85	2.3	3 942	2.5	46.4	31.0
Other	432	11.8	18 097	11.3	41.9	26.4
Total	3660	100	160 055	100	43.7	28.7

Cause of death categories are mutually exclusive. [a]Missing cause of death data for 25 participants.

NSW. This cohort is likely to represent the majority of opioid-dependent people in that State during this period, perhaps as high as 80% [18]. The proportion of males in the cohort increased marginally over time. The cohort aged significantly over the study period, reflecting a combination of the ageing of cohort members who enrolled early in the study period and lower rates of younger entrants in the latter part of the study period. This ageing effect has been noted in other Australian studies of people who inject drugs as well as opioid users. One potential reason for this trend could be the Australian 'heroin shortage' (discussed in more detail below) beginning in 2001. From 2001, there is good evidence that population-level drug injecting decreased [19] as did blood-borne virus (BBV) notifications among young people [20]. Younger injectors may have ceased injecting following the reduction in heroin supply and there were fewer new initiates to heroin use [21]. Since 2001, surveillance studies of needle and syringe programme attendees [22] and regular drug injectors sampled in the Illicit Drug Reporting System [18,23,24] have documented steady increases in the average age of injectors.

The substantial increase in accidental drug-induced deaths during the mid to late 1990s coincided with ready availability of heroin in major Australian drug markets [25]. This was followed by a substantial decrease in drug overdose mortality in 2001 that coincided with a decrease in heroin availability and an increase in its price in Australia [26] after the beginning of 2001 and was sustained for the remainder of the study period [27–29].

Further impacts of the Australian 'heroin shortage' have been discussed in detail elsewhere [27,30].

Liver disease, cardiovascular disease and cancer became increasingly important sources of mortality over time. It is likely that this trend will continue in the future, as the cohort ages. These findings agree with the results of similar analyses of mortality in the United Kingdom, where mortality from chronic diseases increasingly dominates mortality in opioid users over 40 years of age [31].

Our examination of mortality due to various causes in a population of Australian opioid users found different results from opioid-dependent cohorts in Spain [4]. The higher HIV-related mortality in Spain reflects the much lower levels of HIV infection among Australian users, thanks in part to the HIV prevention effects of the early introduction of OST and needle and syringe programmes (NSPs) in the mid-1980s [32,33].

The average of 44 years of potential life lost for each fatality in the cohort highlights the fact that deaths in opioid users often occur at a young age. This was particularly the case for avoidable causes of death such as drug overdose and injuries. The pattern of YPLL was broadly similar to previous analyses of a Californian male cohort ($n = 581$) in the United States, followed from 1962 to 1997 [10]. Both studies found that opioid overdoses were the largest contributor to YPLL, but suicides made a larger contribution to YPLL in our cohort, and homicide a larger contribution in the Californian cohort. An additional, striking difference was that the average YPLL prior to the age of 65 years per death was far higher in our cohort than in the US cohort (mean of 28.7 years versus 18.3 years, respectively).

The results suggest the need for different approaches to reducing mortality in younger and older opioid users. The highest mortality risk at younger ages is from overdose, which remains the most frequent cause of death in this population despite the sustained and substantial decrease in these deaths since 2001. Enrolment in OST decreases the risk of fatal overdose significantly [1], but poor retention [34] means that many clients are exposed to an elevated overdose risk after treatment cessation and on re-induction to methadone [34,35]. In previous analyses of treatment exposure in this cohort, we observed that at least half of follow-up time was spent out of treatment [35]. This means that there is clearly substantial room to improve retention rates in OST in this population and thereby decrease overdoses. There are additional elevated risks of drug-related mortality in particular following release from prison [36], which is a common experience for many opioid-dependent people. In other work with this cohort, four in 10 had had at least one prison episode between 2000 and 2012 [37].

Additional interventions are needed to reduce overdose deaths when opioid-dependent people are not enrolled in OST. These include making naloxone available for peer administration to reduce fatal overdose [38–40] and measures to reduce overdose mortality after release from prison [36], where evidence is needed urgently on effective preventive interventions. Safe injection facilities can probably reduce overdose events in those who use them, but their limited scale of operation in most of the countries that allow them suggests that these facilities will have limited impact on opioid overdose mortality at a population level [41].

In older opioid-dependent people there are higher rates of death due to chronic diseases, reflecting increased risks of chronic infection with BBV such as HCV [42], heavy and dependent alcohol use [43] and cigarette smoking [43]. Although HIV is not prevalent among opioid-dependent people in Australia [44], this is an additional risk for mortality in many populations of opioid users world-wide [1]. Targeted prevention and treatment strategies are clearly needed. These include HCV screening and treatment [45]; HBV vaccination [46]; HIV prevention and treatment [33]; screening for and treatment of hazardous alcohol use; and smoking cessation interventions.

Older OST clients are likely to have a broader range of physical and mental health problems for which they might seek treatment [47,48]. These could be delivered via OST clinics dealing with an ageing population with better retention in older users. It is also important to consider alternative platforms where this population may present or receive other health interventions and where preventive interventions may still be delivered, including general practice, hospital emergency departments and aged care services [49].

Limitations

This study has several limitations. First, it relied on administrative data sets that were not designed for research purposes. The two data sets were linked probabilistically, creating a potential for errors in linkage. We believe that the linkage accuracy is high, given the similarity in our overall mortality patterns to that in Australian cohort of illicit drug users, where more detailed individual information was used to link to causes of death [50]. Secondly, although our cohort is comprised of opioid users who sought treatment, sentinel surveillance studies of people who inject drugs (98% of whom have a history of heroin use) suggest that half the opioid-dependent population are in OST at any time, and more than 80% report at least one episode of OST [18,23,24]. Thus, we believe that our cohort is reasonably representative of dependent opioid users in NSW. Thirdly, although we identified a cohort of people who were opioid-dependent upon treatment entry, not all people

would have remained dependent for the entire period of follow-up. This means that we are not necessarily tracking mortality in actively dependent opioid users. Nevertheless, there is good reason to believe that many remained actively opioid-dependent. For example, among those who entered OST between 1985 and 1994 and who were still alive on 1 January 1995 ($n = 17\ 253$), 11 060 (64%) had an episode of treatment in the period 1995–2006. This suggests that the great majority of our cohort were opioid-dependent across the study period. In so far as a proportion of this cohort was not, then our study findings have underestimated mortality among opioid-dependent people. Additionally, there are some exposures that occur during periods of active opioid use (e.g. hepatitis/HIV infection) whose consequences (e.g. AIDS and viral hepatitis-related deaths) persist even if opioid use ceases, so mortality related to these causes does not necessarily lessen with abstinence.

CONCLUSIONS

This study documented elevated mortality among opioid-dependent people, and a large loss of years of life because of the early age at which many deaths occurred. Accidental drug overdose was the largest contributor to death, especially among younger users, and contributed most to YPLL. As this cohort has aged, the profile of deaths has changed. Strategies to reduce deaths vary with age. In younger users, it is desirable to increase retention in OST to reduce overdose deaths and provide naloxone to reduce deaths outside treatment. In older adults, strategies to reduce BBV infection and liver disease and cardiovascular and respiratory diseases need to be the focus.

Declaration of interests

Louisa Degenhardt has received untied educational grant funding from Reckitt Benckiser (RB) to conduct post-marketing surveillance of buprenorphine–naloxone in Australia. The design, conduct, reporting and interpretation of the results of that work were determined by the study investigators. RB had no knowledge of this paper.

Acknowledgements

Louisa Degenhardt, Wayne Hall and Sarah Larney are supported by National Health and Medical Research Council (NHMRC) Principal Research, Australia and Early Career Research Fellowships respectively. This research was also supported by NHMRC Project Grant funding (#455451, #1005668). The project was also supported by a grant from the Australian Institute of Criminology (AIC) through the Criminology Research Grants Program. The views expressed are the responsibility of the author and are not necessarily those of the AIC. The National Drug and Alcohol Research Centre at the University of NSW is supported by funding from the Australian Government under the Substance Misuse Prevention and Service Improvements Grants Fund.

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Supporting information

Additional Supporting information may be found in the online version of this article at the publisher's website:

Appendix S1 Codes for categorising causes of death.