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Opioid substitution therapy as a strategy to reduce deaths in prison: Retrospective cohort study

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Abstract

Objectives: To describe deaths in prison among opioid-dependent people, and examine associations between receipt of opioid substitution therapy and risk of death in prison

Design: Retrospective cohort study

Setting: Adult prisons in New South Wales (NSW), Australia

Participants: 16,715 opioid-dependent people who were received to prison between 2000 and 2012.

Interventions: Opioid substitution therapy

Primary outcome measures: Natural and unnatural (suicide, drug-induced, violent and other injury) deaths in prison

Results: Cohort members were in prison for 30,998 person-years (PY), during which time there were 51 deaths. The all-cause crude mortality rate (CMR) in prison was 1.6 per 1,000 PY (95% CI: 1.2, 2.2 per 1,000 PY), and the unnatural death CMR was 1.1 per 1,000 PY (95% CI: 0.8, 1.6 per 1,000 PY). Compared to time out of OST, the hazard of all-cause death was 74% lower while in OST (adjusted hazard ratio (AHR): 0.26; 95% CI: 0.13 to 0.50), and the hazard of unnatural death was 87% lower while in OST (AHR: 0.13; 95% CI: 0.05 to 0.35). The all-cause and unnatural death CMRs during the first four weeks of incarceration were 6.6 per 1,000 PY (95% CI: 3.8, 10.6 per 1,000 PY) and 5.5 per 1,000 PY (95% CI: 2.9, 9.4 per 1,000 PY), respectively. Compared to periods not in OST, the hazard of all-cause death during the first four weeks of incarceration was 94% lower while in OST (AHR: 0.06; 95% CI: 0.01 to 0.48), and the hazard of unnatural death was 93% lower while in OST (AHR: 0.07; 95% CI: 0.01 to 0.53).

Conclusions: Mortality of opioid-dependent prisoners was significantly lower while in receipt of OST.

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Article summary

Article focus

- Deaths in prison are a significant concern, and correctional authorities have a responsibility to ensure that such deaths are kept to a minimum
- Opioid dependent people commonly experience imprisonment, and may be at particular risk of death in prison
- Opioid substitution treatment (OST) reduces mortality among opioid-dependent people residing in the community, but it is unclear if this is also the case in prison

Key messages

- Opioid-dependent prisoners receiving OST have a substantially lower risk of unnatural death than their untreated peers
- In addition to other known benefits of OST in prison (e.g. reduced opioid use and injecting drug use), to-scale provision of OST in prisons will dramatically reduce unnatural deaths among opioid-dependent prisoners

Strengths and limitations of this study

- This study is based on a large, statewide cohort with mortality outcomes determined via population-based registries
- Cohort members were not randomly allocated to treatment
- Data regarding onset of opioid dependence and current opioid dependence were not available

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Deaths in prison are a serious public health issue, raising questions as to the quality of care and supervision provided by correctional authorities. Reflecting such concerns, deaths in prison usually result in extensive post-mortem inquiries, and may also lead to litigation against correctional authorities and health care providers.[1]

Unnatural deaths in prison are of particular concern due to their preventable nature. Unnatural deaths include suicides, violent or drug-induced deaths, and other injury-related deaths. Studies in developed countries have found that unnatural deaths comprise 48-59% of all deaths in prison, with suicide the most common cause of unnatural death.[2-5] These figures suggest considerable opportunities to reduce unnatural deaths in prison.

Opioid-dependent people commonly experience imprisonment,[6] and there are several reasons to believe that opioid-dependent prisoners may be at particular risk of unnatural death in prison. Drug withdrawal has been implicated as a possible trigger for suicide in the first days of incarceration.[7 8] Additionally, use of illicitly obtained opioids while in prison[9] carries with it the risk of overdose. To our knowledge, deaths in prison specifically among opioid-dependent people have not previously been described. Furthermore, no studies have considered whether treatment for opioid dependence during incarceration reduces mortality risk, as it does among opioid-dependent people residing in the community.[10] In this study, we describe deaths in prison in a cohort of opioid-dependent people, and examine whether receiving opioid substitution therapy (OST) reduces the risk of death in prison.

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Methods

Ethical review

This study was approved by the research ethics committees of the University of New South Wales (NSW) (HC12019), the NSW Ministry of Health (2011/11/360), the Australian Institute of Health and Welfare (EC2011/2/13), the Alfred Hospital (165/11), Corrective Services NSW (11/82607), Justice Health (NSW) (G219/11), the NSW Aboriginal Health and Medical Research Council (AHMRC) (793/11) and Justice Health (Victoria) (CF/13/3440C).

Setting

NSW is the most populous state in Australia and houses around one-third of the country's prisoners, or 9,645 people at 31 June 2012.[11] There is a well-established OST program in NSW prisons.[12] People who enter prison while in OST can continue with treatment while incarcerated, or OST can be commenced during incarceration if indicated.[12] Most prisoners receiving OST are prescribed methadone due to the longer dosing procedure associated with buprenorphine, and concerns about diversion of buprenorphine. In 2012, 16% of NSW prisoners were prescribed OST.[11 12] Coverage of OST (the proportion of opioid-dependent prisoners receiving treatment) has been estimated at 43%.[13]

Data sources and linkage

Data for this retrospective cohort study were extracted from administrative datasets used to record OST programs, offending and incarceration, and mortality. The Pharmaceutical Drugs of Addiction System (PHDAS) is a database of all methadone and buprenorphine recipients in NSW since 1985. The PHDAS records each patient's full name, date of birth, sex and clinical variables including dates of OST entry and exit. Identifying variables in this dataset are considered to be of high accuracy as proof of identity must

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be shown to the prescribing doctor before a prescription can be issued. Data used for linkage were for the calendar years 1985-2010.

Offending and incarceration data were sourced from the NSW Bureau of Crime Statistics and Research (BOCSAR) Re-offending Database (ROD). This database includes dates and types of offences in criminal cases heard by Local, District and Supreme Courts of NSW, and dates of receptions to and discharges from the custody of Corrective Services NSW. All available data were provided for linkage; this included offending data for the period December 1 1993-December 31 2011, and incarceration data for the period January 1 2000-March 31 2012.

The National Death Index (NDI) is a database held by the Australian Institute of Health and Welfare (AIHW), containing mortality data collected from all the Registry of Births, Deaths and Marriages in each Australian State and Territory. Causes of death are recorded in the NDI by expert clinical coders on the basis of information contained in death certificates and, where available, coronial files, using the International Statistical Classification of Diseases and Related Health Problems 10th Edition (ICD-10). Dates of death were available for the entire period for which incarceration data were available (January 1 2000-March 31 2012); however, for administrative reasons, causes of death were available only for deaths occurring up to December 31 2010.

Linkage between the OST and offending/incarceration data was performed by BOCSAR staff, and linkage between the OST and mortality data was undertaken by AIHW staff. Linkage was completed using probabilistic linkage software. Variables used for matching purposes included full name, date of birth, sex, and date and state of last known contact where available. These linked datasets were forwarded to the investigators with identifiers removed.

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Cohort and data definitions

From the linked datasets, we identified a cohort of opioid-dependent people (people who were recorded in the PHDAS as having received OST at some point during 1986-2010) who had been incarcerated at least once (as recorded in the ROD). In defining receipt of OST, we excluded temporary treatment programs (usually interstate visitors) and treatment episodes that were part of a buprenorphine clinical trial (during which the individual may have been allocated to placebo). Periods in the custody of Corrective Services NSW were determined using reception and discharge dates in the ROD. We used the first recorded OST episode as a proxy for the onset of opioid dependence, and excluded prison episodes that occurred prior to the first OST episode; all subsequent prison episodes for an individual were included. If an individual's first OST episode commenced while incarcerated, that prison episode was included. Given the chronic and relapsing nature of opioid dependence,[14 15] we assumed that all cohort members remained opioid-dependent from their first episode of OST until death or the end of follow-up.

Deaths in prison were defined as deaths that occurred while the individual was recorded as being in the custody of Corrective Services NSW. This definition does not stipulate that a deceased individual was physically in prison at the time of death. Some decedents may have been receiving care in hospital at the time of death, while still in the custody of Corrective Services NSW. Deaths with known causes (i.e. all deaths occurring in the calendar years 2000-2010) were categorised as natural (i.e. disease-related) or unnatural deaths. We used the Corrective Services NSW definition of "unnatural deaths", which includes suicides, drug-induced deaths, violent deaths and deaths due to accidental injuries or injuries in which no intent (i.e. suicidal or violent) could be determined.[3] ICD-10 codes for unnatural deaths are provided in the Supplementary Materials.

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Periods of OST while in prison, and treatment status (in OST/out of OST) at the time of death, were determined used treatment entry and exit dates from the PHDAS. New treatment episodes were defined when an individual commenced treatment seven or more days after discharge from a previous treatment episode. A change in medicine (methadone to buprenorphine, or vice versa) was considered a continuous episode if there were less than seven days between ceasing one medicine and commencing the other.

Data analysis

Statistical analyses were undertaken in SAS 9.3. We used descriptive statistics to examine demographic characteristics and incarceration. Participants with any record of receiving OST in prison were compared to those who did not receive OST in prison using chi-square tests for categorical variables and the Wilcoxon rank-sum test for continuous variables. We constructed a frequency histogram to illustrate time from entry to prison until death. For dates for which comparable data were available (financial years 2000-01 to 2009-10), we compared the total number of unnatural deaths among prisoners in NSW[3] to the number of unnatural deaths in the opioid-dependent cohort.

We calculated all-cause and cause-specific crude mortality rates (CMR) with Poisson 95% confidence intervals (CI) for all time in prison, and the first four weeks in prison. Rates were also calculated by treatment status (in/out of OST). Person-years (PY) used in the calculation of CMRs accrued whenever participants were in the custody of Corrective Services NSW. Prison episodes where the participant was received and released on the same day were counted as one day. PY ceased accruing at death or 31st March 2012 for all-cause mortality rates, or 31st December 2010 for cause-specific mortality rates. Crude mortality rate ratios with 95% CI were calculated to assess unadjusted risk of death in treatment compared to that out of treatment. The rate ratio was not calculated if there were zero deaths in either the in-treatment or out-of-treatment condition.

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We used Cox regression to examine the adjusted association between OST exposure and two in-prison mortality outcomes: deaths from all causes, and unnatural deaths. Two models were developed for each outcome, the first considering mortality risk across all time in prison, and the second examining mortality risk during the first four weeks of incarceration. All prison episodes were included, with days in prison counted as discontinuous intervals at risk. Although participants could have multiple observations within the dataset, the internal computations of a Cox model are such that when there is only one event of interest per person (in this case, death), there is no need for adjustments for multiple observations.[16] OST exposure while in prison was coded as a time-dependent variable, with periods out of treatment coded as 0 and periods in treatment coded as 1. Demographic variables included in the models were sex, Indigenous (i.e. Aboriginal or Torres Strait Islander) status, and age at entry to prison; this latter variable increased as necessary with subsequent incarcerations within an individual. We also included variables that described prior experiences of incarceration during our observation periods, namely, number and duration (days) of prior incarcerations. These variables increased with each incarceration per person. We also included dichotomous variables that recorded if a participant had been charged with a drug, property or violent offence prior to incarceration. These were included because of possible associations between death in prison (particularly suicide) and prior offending (particularly violent offending).[17 18] The offending history variables could change from no to yes with subsequent incarcerations. Observations with missing covariate data were excluded from analyses. We tested each variable for its bivariate association with mortality, and entered all variables into a multivariate model. We tested the proportional hazards assumption for each static predictor variable in the multivariate model by including an interaction between it and log(time) in the model. All variables in both models were found to satisfy the proportional hazards assumption.

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Results

The cohort comprised 16,715 opioid-dependent people who had been incarcerated at least once between January 2000 and March 2012 (Table 1). The majority (79.0%; n=13,199) of the cohort was male, and 30.0% (n=5,011) identified as Indigenous. The median age at first entry to prison during our observation period was 30 years (ranging from 16-64 years).

Cohort members were received to prison a median of two times (ranging between 1-34). Duration of incarceration ranged from 1 day to the entire length of follow-up (12 years and 3 months), with a median duration of 71 days. Most participants (76.9%; n=12,852) received OST at some point while incarcerated. Compared to participants who received OST in prison, participants who did not receive OST in prison were significantly older, less likely to be Indigenous and had fewer incarcerations of shorter duration (Table 1).

Deaths in prison

Fifty-one cohort members died in prison (Table 2). Most were male (90%; n=46) and non-Indigenous (73%; n=37). The median age at death was 34 years (ranging between 20-54). Only 22% (n=11) of decedents were receiving OST at the time of death. Cause of death was available for 43 deaths in prison. Of these, nearly three-quarters (74%; n=32) were unnatural deaths: 19 suicides, six drug-related deaths, two violent deaths and five deaths due to other injuries. Between the financial years 2000-01 and 2009-10, unnatural deaths in this cohort accounted for 35% of all unnatural deaths in NSW prisons[3] (see Supplementary Materials for further details).

One-third of all deaths in prison (n=17) occurred during the first four weeks of incarceration (Figure 1). Of these, three-quarters (13/17; 76%) were unnatural deaths: 10 suicides, two other injury-related deaths, and one drug-related death.

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Crude mortality rates

The all-cause CMR in prison was 1.6 per 1,000 PY (95% CI: 1.2, 2.2 per 1,000 PY) (Table 3). The all-cause CMR was significantly lower while in OST (CMR: 0.7 per 1,000 PY; 95% CI: 0.3, 1.2 per 1,000 PY), compared to time out of OST (CMR: 2.7 per 1,000 PY; 95% CI: 2.0, 3.7 per 1,000 PY) (rate ratio (RR): 0.24; 95% CI: 0.12, 0.47).

Deaths from natural causes occurred at similar rates whether in (0.3 per 1,000 PY; 95% CI: 0.1, 0.8 per 1,000 PY) or out (0.5 per 1,000 PY; 95% CI: 0.2, 1.0 per 1,000 PY) of OST (RR: 0.68 (95% CI: 0.21, 2.21). There was, however, a marked effect of OST on rates of unnatural death. The in-treatment CMR for unnatural deaths was 0.3 per 1,000 PY (95% CI: 0.1, 0.8 per 1,000 PY), compared to 2.2 per 1,000 PY (95% CI: 1.4, 3.2 per 1,000 PY) while out of OST (RR: 0.15; 95% CI: 0.06, 0.39). Of the specific unnatural causes of death, suicides were significantly less frequent while in OST (CMR: 0.2 per 1,000 PY; 95% CI: 0.04, 0.6 per 1,000 PY) than while in OST (CMR: 0.2 per 1,000 PY; 95% CI: 0.04, 0.6 per 1,000 PY) (RR: 0.15; 95% CI: 0.04, 0.52). Of the six observed drug-induced deaths and five other injury deaths, none occurred during OST, but both violent deaths occurred while in OST.

During the first four weeks of incarceration, the all-cause CMR was 6.6 per 1,000 PY (95% CI: 3.8, 10.6 per 1,000 PY). Of the 17 cohort members who died during the first four weeks of incarceration, only one was receiving OST at the time of death. The in-treatment all-cause CMR in the first four weeks of incarceration was 0.8 deaths per 1,000 PY (95% CI: 0.02, 4.3 per 1,000 PY), significantly lower than the CMR of 12.7 per 1,000 PY (95% CI: 7.2, 20.6 per 1,000 PY) observed among out-of-treatment cohort members (RR: 0.06; 95% CI: 0.01, 0.45). As across all time in prison, during the first four weeks of incarceration, the natural mortality rate did not differ by OST status, but the in-treatment CMR for unnatural deaths (0.8 per 1,000 PY; 95% CI: 0.02, 4.4 per 1,000 PY) was significantly lower than the out-of-treatment CMR for unnatural deaths (11.0 per 1,000 PY; 95% CI: 5.7, 19.2 per 1,000 PY) (RR: 0.07;

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95% CI: 0.01, 0.55). The same pattern was observed in relation to suicide deaths (in-OST CMR: 0.8 per 1,000 PY; 95% CI: 0.02, 4.4 per 1,000 PY; out-of-OST CMR: 8.2 per 1,000 PY; 95% CI: 3.8, 15.6 per 1,000 PY; RR: 0.10; 95% CI: 0.01, 0.75).

Adjusted effect of OST on deaths in custody

In the first four weeks of a prison episode, the all-cause mortality hazard was 94% lower while in OST, compared to being out of OST (adjusted HR: 0.06; 95% CI: 0.01, 0.48), regardless of sex, Indigenous status, age, incarceration history or offending history (Table 4). A similar finding was observed in relation to unnatural deaths; during the first four weeks of a prison episode, while in OST, the hazard of unnatural death was 93% lower than while not in OST (adjusted HR 0.07; 95% CI: 0.01, 0.59).

Across all time in prison, the all-cause mortality hazard during periods of OST was reduced by three-quarters compared to periods not in OST (adjusted HR: 0.26; 95% CI: 0.13, 0.50), regardless of sex, Indigenous status, age, incarceration history or offending history. Across all time in prison, compared to periods not in OST, the hazard of unnatural death was 87% lower while in OST (adjusted HR: 0.13; 95% CI: 0.05, 0.35).

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Discussion

We have demonstrated a very strong association between receipt of OST and lowered mortality among opioid-dependent prisoners. After adjusting for demographic and criminal history factors, compared to time not in OST, being in OST was associated with a 74% lower hazard of dying in prison. The association between mortality risk and OST was driven by the reduction in unnatural deaths, with periods in OST associated with an 87% decrease in mortality hazard compared to time not in OST. One-third of deaths in prison in this cohort occurred during the first four weeks of incarceration; in these initial weeks in prison, compared to time not in OST, being in OST was associated with a 94% lower all-cause mortality hazard, and a 93% lower hazard of unnatural death. Although the confidence intervals around the hazard ratios were wide, even the uppermost limits of the intervals suggested substantial reductions in mortality while in OST. For example, across all time in prison, there was at least a 65% reduction in unnatural mortality hazard while in OST compared to time not in OST.

The cohort included in this study was drawn from a large, statewide administrative dataset of people receiving treatment for opioid dependence. As an observational study, cohort members were not randomly allocated to treatment. Although there were some differences between prisoners who did and did not receive OST, these variables did not affect the association between OST and mortality. We did not have clinical indicators of current opioid dependence, and it is possible that some members of our cohort may have ceased all opioid use, thereby reducing their baseline mortality risk. However, given the chronic and relapsing nature of opioid dependence,[14 15] this is unlikely to have been the case for any substantial proportion of the cohort. Inclusion of opioid-abstinent individuals would, at any rate, result in conservative mortality estimates. Finally, we used the first episode of OST as a proxy for the onset of opioid dependence. It is possible that some cohort members had previous incarcerations during which they were opioid dependent, but had not yet entered OST.

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To our knowledge, this is the first study of its kind. Prior studies have reported on all-cause or cause-specific mortality in prison among total prisoner populations.[4 19 20] We have extended on these studies by analysing mortality in opioid-dependent prisoners – a group with known mortality risk factors. Highlighting the vulnerability of this population, 74% of deaths in prison were due to unnatural causes, compared to 48-59% of deaths in studies of total prisoner populations.[2-5] The great majority of deaths occurred while prisoners were not receiving OST. Although this protective effect of OST against mortality is known,[10] this is the first time this association has been observed in a prison setting. Receipt of OST in prison also reduces illicit opioid use and injecting drug use, [21 22] and is associated with reduced institutional drug charges.[23] Opioid-dependent prisoners who receive OST are more likely than their untreated peers to enroll in OST following release,[24] and continuation of OST on release is associated with reduced re-incarceration[25] and reduced post-release mortality.[26]

Although we have demonstrated a very strong protective effect of OST against death in prison for opioid-dependent prisoners, several questions remain to be answered. This study was undertaken in a jurisdiction with relatively high OST coverage.[13] Our understanding of the relationship between OST and deaths in prison could benefit from further observational or simulation studies that assess the impact of varying levels of OST coverage on deaths. Further, this study was not able to determine why it is that OST should be associated with reduced unnatural deaths. Given that drug withdrawal symptoms have been implicated as a trigger for suicide in the first week of prison,[7 8] the association may, in part at least, be due to alleviation or prevention of opioid withdrawal. If it is the case that averting withdrawal symptoms is sufficient to prevent some prison suicides, there are important implications for the clinical management of withdrawal symptoms of prisoners dependent on non-opioid drugs. Research examining why there are fewer suicides among opioid-dependent prisoners in OST is needed, as is research examining whether management of withdrawal from non-opioid drugs has a similar impact on suicides in prison.

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The implication of these findings for correctional authorities and prison medical providers is clear: ensuring a high coverage of OST in correctional settings will help to minimise unnatural deaths among opioid-dependent prisoners. Given the particularly high mortality risk observed during the first four weeks of incarceration, it is critical that opioid-dependent prisoners can access OST in a timely manner. Opioid dependence and enrollment in OST immediately prior to entry to prison should be assessed during intake medical examinations. Prisoners enrolled in OST prior to prison entry should be able to continue this treatment with minimal interruption, and other opioid-dependent prisoners should be assessed for OST and offered treatment if clinically indicated. Although there are challenges to the implementation of OST programs in prisons and other correctional settings, these can be managed through strong executive leadership, ongoing training and education for health and custodial staff, and careful attention to issues of safety and security.[27]

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Data sharing

Data sharing is not available.

Contributorship

SL completed the analysis and led the writing, and is responsible for the overall content as guarantor. TD provided statistical advice and contributed to the writing. NG, MF, LB, AG and JK contributed to the writing. LD oversaw the larger project for which these data were obtained, and contributed to the writing. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests

LD has received untied educational grants from Reckitt Benckiser to conduct post-marketing surveillance of the diversion and injection of opioids. MF has participated in workshops in the Asia-Pacific region on the development of treatment services and on research with opioid users; these were supported by Reckitt Benckiser through an unrestricted educational grant, paid to the University of Adelaide. No other authors report relationships or activities that could appear to have influenced the submitted work.

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Table 1: Demographic characteristics of opioid-dependent persons received to prison, New South Wales, Australia, 2000-2012 (n=16,715)

Characteristic	Total (n=16,715)	Ever received OST in prison (n=12,852)	No OST in prison (n=3,863)	*P*
Male sex, n (%)	13,199 (79.0)	10,109 (78.7)	3,090 (80.0)	0.07
Age (years) at first observed entry to prison, median (min-max)	30 (16-64)	29 (16-63)	32 (17-64)	<.0001
Indigenous,* n (%)	5,011 (30.0)	4,208 (32.8)	803 (20.8)	<.0001
Number of prison episodes, median (min-max)	2 (1-34)	3 (1-34)	1 (1-23)	<.0001
Duration (days) of prison episodes, median (min-max)	71 (1-4,473)	77 (1-4,473)	46 (1-4,473)	<.0001
Any receipt of OST in prison	12,852 (76.9)	-	-	-

*Indigenous status missing for 10 individuals. *P*-values refer to comparison between participants who did or did not receive OST in prison (chi-square test for categorical variables; Wilcoxon rank-sum test for continuous variables).

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Table 2: Demographic characteristics and causes of death of opioid-dependent persons who died in prison, New South Wales, Australia, 2000-2012 (n=51)

Characteristic	N (%)
Male sex	46 (90)
Age (years) at death, median (min-max)	34 (20-54)
Indigenous	14 (27)
In OST at time of death	11 (22)
Deaths from natural causes*	11 (26)
Unnatural deaths*	32 (74)
Suicide	*19 (44)*
Drug-related	*6 (14)*
Violent	*2 (5)*
Other injury-related	*5 (12)*

*Cause of death unknown for 8 decedents. Percentage is based on n=43.

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Figure 1: Deaths from natural, unnatural and unknown causes, by time in prison prior to death among opioid-dependent people who died in prison, New South Wales, Australia, 2000-2012 (n=51)

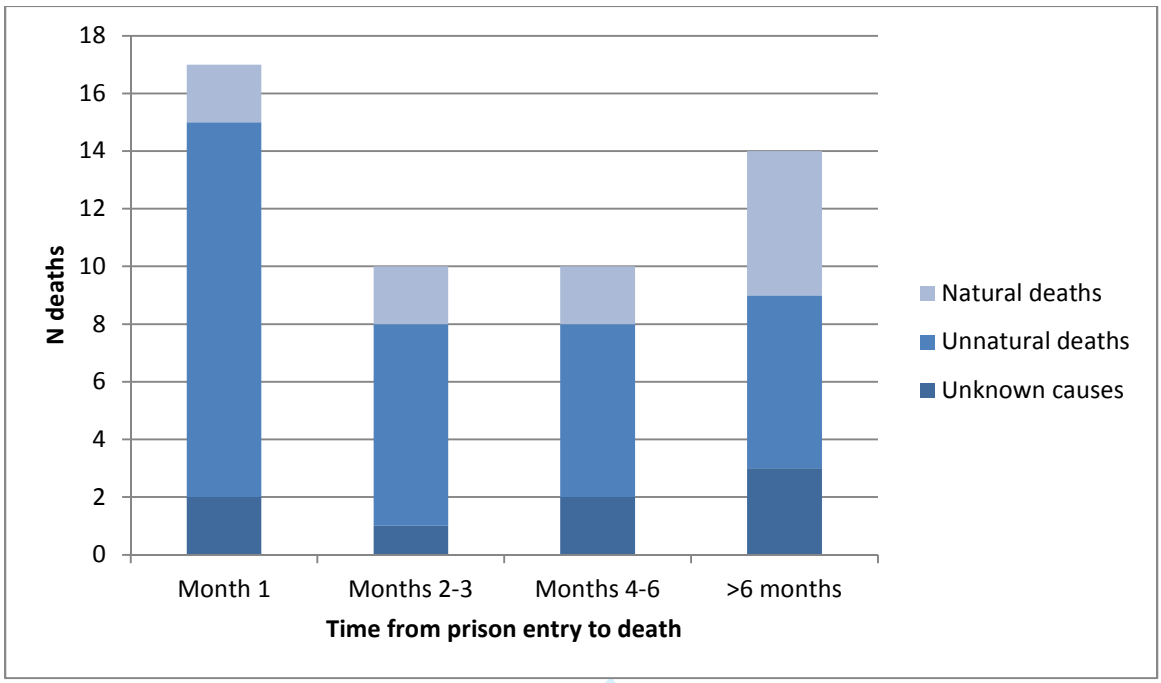

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Table 3: All-cause and cause-specific crude mortality rates per 1,000 person-years in prison among opioid-dependent people in New South Wales, Australia, 2000-2012 (n=16,715)

Cause of death	Total time in prison				First 4 weeks in prison			
	PY	Deaths	Crude mortality rate (95% CI)	Rate ratio (95% CI)	PY	Deaths	Crude mortality rate (95% CI)	Rate ratio (95% CI)
All cause	30,988	51	1.6 (1.2, 2.2)		2,571	17	6.6 (3.8, 10.6)	
Out of OST	14,548	40	2.7 (2.0, 3.7)		1,263	16	12.7 (7.2, 20.6)	
In OST	16,440	11	0.7 (0.3, 1.2)	0.24 (0.12, 0.47)	1,308	1	0.8 (0.02, 4.3)	0.06 (0.01, 0.45)
Unnatural causes[1]	27,839	32	1.1 (0.8, 1.6)		2,374	13	5.5 (2.9, 9.4)	
Out of OST	12,462	27	2.2 (1.4, 3.2)		1,094	12	11.0 (5.7, 19.2)	
In OST	15,377	5	0.3 (0.1, 0.8)	0.15 (0.06, 0.39)	1,279	1	0.8 (0.02, 4.4)	0.07 (0.01, 0.55)
Suicide	27,839	19	0.7 (0.4, 1.1)		2,374	10	4.2 (2.0, 7.7)	
Out of OST	12,462	16	1.3 (0.7, 2.1)		1,094	9	8.2 (3.8, 15.6)	
In OST	15,377	3	0.2 (0.04, 0.6)	0.15 (0.04, 0.52)	1,279	1	0.8 (0.02, 4.4)	0.10 (0.01, 0.75)
Drug-induced	27,839	6	0.2 (0.08, 0.5)		2,374	1	0.4 (0.01, 2.3)	
Out of OST	12,462	6	0.5 (0.2, 1.0)		1,094	1	1.0 (0.02, 5.1)	
In OST	15,377	0	-	-	1,279	0	-	-
Violence	27,839	2	0.07 (0.01, 0.3)		2,374	0	-	
Out of OST	12,462	0	-		1,094	0	-	
In OST	15,377	2	0.1 (0.02, 0.5)	-	1,279	0	-	-
Other injuries	27,839	5	0.2 (0.06, 0.4)		2,374	2	0.8 (0.1, 3.0)	
Out of OST	12,462	5	0.4 (0.1, 0.9)		1,094	2	1.8 (0.2, 6.6)	
In OST	15,377	0	-	-	1,279	0	-	-
Natural causes	27,839	11	0.4 (0.2, 0.7)		2,374	2	0.8 (0.1, 3.0)	
Out of OST	12,462	6	0.5 (0.2, 1.0)		1,094	2	1.8 (0.2, 6.6)	
In OST	15,377	5	0.3 (0.1, 0.8)	0.68 (0.21, 2.21)	1,279	0	-	-

Notes: Cause of death missing for 8 deaths. OST: opioid substitution treatment. PY: person-years. CI: confidence interval. [1]Includes suicide, drug-induced, violent and other injury deaths.

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Table 4: Cox proportional hazards models of predictors of death in prison among opioid-dependent prisoners in New South Wales, Australia, 2000-2012 (n=16,715)

	Total time in prison				First 4 weeks in prison			
	All-cause deaths		Unnatural deaths		All-cause deaths		Unnatural deaths	
Predictor	**HR (95% CI)**	**Adjusted HR (95% CI)**	**HR (95% CI)**	**Adjusted HR (95% CI)**	**HR (95% CI)**	**Adjusted HR (95% CI)**	**HR (95% CI)**	**Adjusted HR (95% CI)**
Receipt of OST*	0.25 (0.13, 0.48)	0.26 (0.13, 0.50)	0.15 (0.06, 0.39)	0.13 (0.05, 0.35)	0.07 (0.01, 0.54)	0.06 (0.01, 0.48)	0.08 (0.01, 0.59)	0.07 (0.01, 0.53)
Male sex	1.21 (0.48, 3.04)	0.94 (0.36, 2.41)	0.75 (0.29, 1.96)	0.57 (0.22, 1.54)	0.66 (0.22, 2.04)	0.54 (0.16, 1.76)	0.48 (0.15, 1.57)	0.34 (0.10, 1.18)
Indigenous	0.64 (0.34, 1.18)	0.84 (0.44, 1.59)	0.92 (0.44, 1.90)	1.02 (0.48, 2.21)	0.70 (0.24, 1.98)	0.71 (0.23, 2.13)	1.13 (0.37, 3.46)	0.98 (0.30, 3.18)
Age at prison reception	1.06 (1.03, 1.10)	1.05 (1.01, 1.09)	1.03 (0.98, 1.07)	1.02 (0.97, 1.07)	1.00 (0.93, 1.07)	0.98 (0.91, 1.06)	0.99 (0.91, 1.07)	0.99 (0.91, 1.07)
No. prior incarcerations	1.01 (0.91, 1.12)	1.09 (0.99, 1.21)	1.10 (0.97, 1.24)	1.13 (0.99, 1.28)	0.94 (0.79, 1.12)	0.96 (0.81, 1.14)	0.99 (0.78, 1.24)	1.01 (0.80, 1.27)
Duration of prior incarcerations#	0.98 (0.96, 1.00)	0.98 (0.96, 1.00)	1.01 (0.98, 1.04)	1.01 (0.98, 1.04)	0.98 (0.95, 1.01)	0.99 (0.95, 1.02)	1.02 (0.97, 1.06)	1.02 (0.97, 1.07)
Any prior drug offences	0.95 (0.53, 1.70)	0.97 (0.53, 1.76)	0.96 (0.46, 2.01)	0.92 (0.43, 1.95)	1.12 (0.36, 3.51)	1.21 (0.38, 3.82)	0.84 (0.25, 2.78)	0.91 (0.27, 3.07)
Any prior property offences	0.47 (0.25, 0.92)	0.76 (0.37, 1.57)	0.71 (0.29, 1.75)	0.81 (0.31, 2.14)	0.59 (0.13, 2.69)	0.70 (0.15, 3.36)	1.04 (0.13, 8.39)	1.15 (0.14, 9.67)
Any prior violent offences	0.53 (0.30, 0.94)	0.69 (0.37, 1.26)	0.65 (0.31, 1.34)	0.70 (0.32, 1.50)	0.49 (0.18, 1.33)	0.49 (0.18, 1.37)	0.64 (0.20, 1.98)	0.56 (0.17, 1.83)

*Time-dependent variable. HR: hazard ratio. CI: confidence interval. OST: opioid substitution treatment. #Hazard ratio refers to change in hazard associated with 28-day increase in duration of prior incarcerations.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9, Table 1
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	9-10, Tables 1 and 2

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Outcome data	15*	Report numbers of outcome events or summary measures over time	9, Table 2, Figure 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11, Tables 3 and 4
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Opioid substitution therapy as a strategy to reduce deaths in prison: Retrospective cohort study

Supplementary Materials

Sarah Larney, Natasa Gisev, Michael Farrell, Timothy Dobbins, Lucinda Burns, Amy Gibson, Jo Kimber, Louisa Degenhardt

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Supplementary Table 1: ICD-10 codes for defining unnatural deaths

Cause of death	ICD-10 codes
Drug-induced	F11-F16, F19, F55, X40-X44, X60-X64, X85, Y10-Y14
Suicide	X60-X84, Y87.0
Violence	X85-Y09, Y87.1
Other injuries*	V00-X39, X50-X59, Y10-Y39, Y85-Y86, Y88-Y89

*Includes accidental injuries and injuries for which no intent (i.e. suicidal or violent) could be inferred

Supplementary Table 2: BOCSAR codes for drug, violent and property crimes

Offence category	ANZSOC codes	Offence
Violent	011, 012, 013	Homicide
	021, 029	Assault
	0611, 0612	Robbery
	0311, 0312	Sexual assault and other sexual offences
Property	071	Break and enter
	081	Motor vehicle theft
	082	Theft
	091, 092	Fraud
Drug	101, 102	Import, deal or traffic illicit drugs
	103	Manufacture or cultivate illicit drugs
	104	Possession/use of illicit drugs
	109	Other illicit drug offences

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Additional data: Unnatural deaths in prison accounted for by the opioid-dependent cohort

Data on unnatural deaths in prison in NSW are released by Corrective Services NSW for each financial year (in Australia, 1 July to 30 June of the following year). We had data for the opioid dependent cohort that was comparable to the Corrective Services NSW data for the financial years 2000/01 to 2009/10. Between July 1 2000 and 30 June 2010, Corrective Services NSW reported 81 unnatural deaths. During the same time period, there were 28 unnatural deaths in the opioid dependent cohort, accounting for 35% of the total unnatural deaths in prison for that period (see Supplementary Table 3).

Supplementary Table 3: Unnatural deaths among all prisoners and opioid-dependent prisoners in New South Wales, Australia, by financial year.

Financial year	Unnatural deaths reported by CSNSW	Unnatural deaths in opioid dependent cohort	Deaths in opioid dependent cohort as a proportion of all unnatural deaths (%)
2000/01	12	1	8
2001/02	10	6	60
2002/03	11	3	27
2003/04	10	2	20
2004/05	10	4	40
2005/06	5	0	0
2006/07	8	3	38
2007/08	5	3	60
2008/09	5	5	100
2009/10	5	1	20
Total	81	28	35

CSNSW: Corrective Services New South Wales. Data on unnatural deaths reported by CSNSW are from: Corrective Services NSW. *Statistical Report 2011/12*. Sydney: Corrective Services NSW, 2012, p.30. Available from http://www.correctiveservices.nsw.gov.au/__data/assets/pdf_file/0011/379748/statistical-report-2010-2011.pdf.

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Opioid substitution therapy as a strategy to reduce deaths in prison: Retrospective cohort study

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Abstract

Objectives: To describe deaths in prison among opioid-dependent people, and examine associations between receipt of opioid substitution therapy and risk of death in prison

Design: Retrospective cohort study

Setting: Adult prisons in New South Wales (NSW), Australia

Participants: 16,715 opioid-dependent people who were received to prison between 2000 and 2012.

Interventions: Opioid substitution therapy

Primary outcome measures: Natural and unnatural (suicide, drug-induced, violent and other injury) deaths in prison

Results: Cohort members were in prison for 30,998 person-years (PY), during which time there were 51 deaths. The all-cause crude mortality rate (CMR) in prison was 1.6 per 1,000 PY (95% CI: 1.2, 2.2 per 1,000 PY), and the unnatural death CMR was 1.1 per 1,000 PY (95% CI: 0.8, 1.6 per 1,000 PY). Compared to time out of OST, the hazard of all-cause death was 74% lower while in OST (adjusted hazard ratio (AHR): 0.26; 95% CI: 0.13 to 0.50), and the hazard of unnatural death was 87% lower while in OST (AHR: 0.13; 95% CI: 0.05 to 0.35). The all-cause and unnatural death CMRs during the first four weeks of incarceration were 6.6 per 1,000 PY (95% CI: 3.8, 10.6 per 1,000 PY) and 5.5 per 1,000 PY (95% CI: 2.9, 9.4 per 1,000 PY), respectively. Compared to periods not in OST, the hazard of all-cause death during the first four weeks of incarceration was 94% lower while in OST (AHR: 0.06; 95% CI: 0.01 to 0.48), and the hazard of unnatural death was 93% lower while in OST (AHR: 0.07; 95% CI: 0.01 to 0.53).

Conclusions: Mortality of opioid-dependent prisoners was significantly lower while in receipt of OST.

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Article summary

Article focus

- Deaths in prison are a significant concern, and correctional authorities have a responsibility to ensure that such deaths are kept to a minimum
- Opioid dependent people commonly experience imprisonment, and may be at particular risk of death in prison
- Opioid substitution treatment (OST) reduces mortality among opioid-dependent people residing in the community, but it is unclear if this is also the case in prison

Key messages

- Opioid-dependent prisoners receiving OST have a substantially lower risk of unnatural death than their untreated peers
- In addition to other known benefits of OST in prison (e.g. reduced opioid use and injecting drug use), to-scale provision of OST in prisons will dramatically reduce unnatural deaths among opioid-dependent prisoners

Strengths and limitations of this study

- This study is based on a large, statewide cohort with mortality outcomes determined via population-based registries
- Cohort members were not randomly allocated to treatment
- Data regarding onset of opioid dependence and current opioid dependence were not available

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Deaths in prison are a serious public health issue, raising questions as to the quality of care and supervision provided by correctional authorities. Reflecting such concerns, deaths in prison usually result in extensive post-mortem inquiries, and may also lead to litigation against correctional authorities and health care providers.[1]

Unnatural deaths in prison are of particular concern due to their preventable nature. Unnatural deaths include suicides, violent or drug-induced deaths, and other injury-related deaths. Studies in developed countries have found that unnatural deaths comprise 48-59% of all deaths in prison, with suicide the most common cause of unnatural death.[2-5] These figures suggest considerable opportunities to reduce unnatural deaths in prison.

Opioid-dependent people commonly experience imprisonment,[6] and there are several reasons to believe that opioid-dependent prisoners may be at particular risk of unnatural death in prison. Drug withdrawal has been implicated as a possible trigger for suicide in the first days of incarceration.[7 8] Additionally, use of illicitly obtained opioids while in prison[9] carries with it the risk of overdose. To our knowledge, deaths in prison specifically among opioid-dependent people have not previously been described. Furthermore, no studies have considered whether treatment for opioid dependence during incarceration reduces mortality risk, as it does among opioid-dependent people residing in the community.[10] In this study, we describe deaths in prison in a cohort of opioid-dependent people, and examine whether receiving opioid substitution therapy (OST) reduces the risk of death in prison.

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Methods

Ethical review

This study was approved by the research ethics committees of the University of New South Wales (NSW) (HC12019), the NSW Ministry of Health (2011/11/360), the Australian Institute of Health and Welfare (EC2011/2/13), the Alfred Hospital (165/11), Corrective Services NSW (11/82607), Justice Health (NSW) (G219/11), the NSW Aboriginal Health and Medical Research Council (AHMRC) (793/11) and Justice Health (Victoria) (CF/13/3440C).

Setting

NSW is the most populous state in Australia and houses around one-third of the country's prisoners, or 9,645 people at 31 June 2012.[11] Health services in NSW prisons are provided under the Ministry of Health, and there is a well-established prison OST program that operates as part of the state-wide opioid treatment program.[12 13] People who enter prison while in OST may continue treatment while incarcerated, and OST can be commenced during incarceration if clinically indicated.[12] Clinical indications for OST are the same as in community settings.[13] Most prisoners receiving OST are prescribed methadone due to the longer dosing procedure associated with buprenorphine, and concerns about diversion of buprenorphine. In 2012, 16% of NSW prisoners were prescribed OST.[11 12] Coverage of OST (the proportion of opioid-dependent prisoners receiving treatment) has been estimated at 43%.[14]

Data sources and linkage

Data for this retrospective cohort study were extracted from administrative datasets used to record OST programs, offending and incarceration, and mortality. The Pharmaceutical Drugs of Addiction System (PHDAS) is a database of all methadone and buprenorphine recipients in NSW since 1985. The PHDAS

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records each patient's full name, date of birth, gender and clinical variables including dates of OST entry and exit. Identifying variables in this dataset are considered to be of high accuracy as proof of identity must be shown to the prescribing doctor before a prescription can be issued. Data used for linkage were for the calendar years 1985-2010.

Offending and incarceration data were sourced from the NSW Bureau of Crime Statistics and Research (BOCSAR) Re-offending Database (ROD). This database includes dates and types of offences in criminal cases heard by Local, District and Supreme Courts of NSW, and dates of receptions to and discharges from the custody of Corrective Services NSW. All available data were provided for linkage; this included offending data for the period December 1 1993-December 31 2011, and incarceration data for the period January 1 2000-March 31 2012.

The National Death Index (NDI) is a database held by the Australian Institute of Health and Welfare (AIHW), containing mortality data collected from all the Registry of Births, Deaths and Marriages in each Australian State and Territory. Causes of death are recorded in the NDI by expert clinical coders on the basis of information contained in death certificates and, where available, coronial files, using the International Statistical Classification of Diseases and Related Health Problems 10th Edition (ICD-10). Dates of death were available for the entire period for which incarceration data were available (January 1 2000-March 31 2012); however, for administrative reasons, causes of death were available only for deaths occurring up to December 31 2010.

Linkage between the OST and offending/incarceration data was performed by BOCSAR staff, and linkage between the OST and mortality data was undertaken by AIHW staff. Linkage was completed using probabilistic linkage software. Variables used for matching purposes included full name, date of birth, gender, and date and state of last known contact where available. These linked datasets were forwarded to the investigators with identifiers removed.

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Cohort and data definitions

From the linked datasets, we identified a cohort of opioid-dependent people (people who were recorded in the PHDAS as having received OST at some point during 1986-2010) who had been incarcerated at least once (as recorded in the ROD). In defining receipt of OST, we excluded temporary treatment programs (usually interstate visitors) and treatment episodes that were part of a buprenorphine clinical trial (during which the individual may have been allocated to placebo). Periods in the custody of Corrective Services NSW were determined using reception and discharge dates in the ROD. We used the first recorded OST episode as a proxy for the onset of opioid dependence, and excluded prison episodes that occurred prior to the first OST episode; all subsequent prison episodes for an individual were included. If an individual's first OST episode commenced while incarcerated, that prison episode was included. Given the chronic and relapsing nature of opioid dependence,[15 16] we assumed that all cohort members remained opioid-dependent from their first episode of OST until death or the end of follow-up.

Deaths in prison were defined as deaths that occurred while the individual was recorded as being in the custody of Corrective Services NSW. This definition does not stipulate that a deceased individual was physically in prison at the time of death. Some decedents may have been receiving care in hospital at the time of death, while still in the custody of Corrective Services NSW. Deaths with known causes (i.e. all deaths occurring in the calendar years 2000-2010) were categorised as natural (i.e. disease-related) or unnatural deaths. We used the Corrective Services NSW definition of "unnatural deaths", which includes suicides, drug-induced deaths, violent deaths and deaths due to accidental injuries or injuries in which no intent (i.e. suicidal or violent) could be determined.[3] ICD-10 codes for unnatural deaths are provided in the Supplementary Materials.

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Periods of OST while in prison, and treatment status (in OST/out of OST) at the time of death, were determined using treatment entry and exit dates from the PHDAS. New treatment episodes were defined when an individual commenced treatment seven or more days after discharge from a previous treatment episode. A change in medicine (methadone to buprenorphine, or vice versa) was considered a continuous episode if there were less than seven days between ceasing one medicine and commencing the other.

Data analysis

Statistical analyses were undertaken in SAS 9.3. We used descriptive statistics to examine demographic characteristics and incarceration. Participants with any record of receiving OST in prison were compared to those who did not receive OST in prison using chi-square tests for categorical variables and the Wilcoxon rank-sum test for continuous variables. We constructed a frequency histogram to illustrate time from entry to prison until death. For dates for which comparable data were available (financial years 2000-01 to 2009-10), we compared the total number of unnatural deaths among prisoners in NSW[3] to the number of unnatural deaths in the opioid-dependent cohort.

We calculated all-cause and cause-specific crude mortality rates (CMR) with Poisson 95% confidence intervals (CI) for all time in prison, and the first four weeks in prison. Rates were also calculated by treatment status (in/out of OST). Person-years (PY) used in the calculation of CMRs accrued whenever participants were in the custody of Corrective Services NSW. Prison episodes where the participant was received and released on the same day were counted as one day. PY ceased accruing at death or 31st March 2012 for all-cause mortality rates, or 31st December 2010 for cause-specific mortality rates. Crude mortality rate ratios with 95% CI were calculated to assess unadjusted risk of death in treatment compared to that out of treatment. The rate ratio was not calculated if there were zero deaths in either the in-treatment or out-of-treatment condition.

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We used Cox regression to examine the adjusted association between OST exposure and two in-prison mortality outcomes: deaths from all causes, and unnatural deaths. Two models were developed for each outcome, the first considering mortality risk across all time in prison, and the second examining mortality risk during the first four weeks of incarceration. All prison episodes were included, with days in prison counted as discontinuous intervals at risk. Although participants could have multiple observations within the dataset, the internal computations of a Cox model are such that when there is only one event of interest per person (in this case, death), there is no need for adjustments for multiple observations.[17] OST exposure while in prison was coded as a time-dependent variable, with periods out of treatment coded as 0 and periods in treatment coded as 1. Demographic variables included in the models were gender, Indigenous (i.e. Aboriginal or Torres Strait Islander) status, and age at entry to prison; this latter variable increased as necessary with subsequent incarcerations within an individual. We also included variables that described prior experiences of incarceration during our observation periods, namely, number and duration (days) of prior incarcerations. These variables increased with each incarceration per person. We also included dichotomous variables that recorded if a participant had been charged with a drug, property or violent offence prior to incarceration. These were included because of possible associations between death in prison (particularly suicide) and prior offending (particularly violent offending).[18 19] The offending history variables could change from no to yes with subsequent incarcerations. Observations with missing covariate data were excluded from analyses. We tested each variable for its bivariate association with mortality, and entered all variables into a multivariate model. We tested the proportional hazards assumption for each static predictor variable in the multivariate model by including an interaction between it and log(time) in the model. All variables in both models were found to satisfy the proportional hazards assumption.

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Results

The cohort comprised 16,715 opioid-dependent people who had been incarcerated at least once between January 2000 and March 2012 (Table 1). The majority (79.0%; n=13,199) of the cohort was male, and 30.0% (n=5,011) identified as Indigenous. The median age at first entry to prison during our observation period was 30 years (ranging from 16-64 years).

Cohort members were received to prison a median of two times (ranging between 1-34). Duration of incarceration ranged from 1 day to the entire length of follow-up (12 years and 3 months), with a median duration of 71 days. Most participants (76.9%; n=12,852) received OST at some point while incarcerated. Compared to participants who received OST in prison, participants who did not receive OST in prison were significantly older, less likely to be Indigenous and had fewer incarcerations of shorter duration (Table 1).

Deaths in prison

Fifty-one cohort members died in prison (Table 2). Most were male (90%; n=46) and non-Indigenous (73%; n=37). The median age at death was 34 years (ranging between 20-54). Only 22% (n=11) of decedents were receiving OST at the time of death. Cause of death was available for 43 deaths in prison. Of these, nearly three-quarters (74%; n=32) were unnatural deaths: 19 suicides, six drug-related deaths, two violent deaths and five deaths due to other injuries. Between the financial years 2000-01 and 2009-10, unnatural deaths in this cohort accounted for 35% of all unnatural deaths in NSW prisons[3] (see Supplementary Materials for further details).

One-third of all deaths in prison (n=17) occurred during the first four weeks of incarceration (Figure 1). Of these, three-quarters (13/17; 76%) were unnatural deaths: 10 suicides, two other injury-related deaths, and one drug-related death.

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Crude mortality rates

The all-cause CMR in prison was 1.6 per 1,000 PY (95% CI: 1.2, 2.2 per 1,000 PY) (Table 3). The all-cause CMR was significantly lower while in OST (CMR: 0.7 per 1,000 PY; 95% CI: 0.3, 1.2 per 1,000 PY), compared to time out of OST (CMR: 2.7 per 1,000 PY; 95% CI: 2.0, 3.7 per 1,000 PY) (rate ratio (RR): 0.24; 95% CI: 0.12, 0.47).

Deaths from natural causes occurred at similar rates whether in (0.3 per 1,000 PY; 95% CI: 0.1, 0.8 per 1,000 PY) or out (0.5 per 1,000 PY; 95% CI: 0.2, 1.0 per 1,000 PY) of OST (RR: 0.68 (95% CI: 0.21, 2.21). There was, however, a marked effect of OST on rates of unnatural death. The in-treatment CMR for unnatural deaths was 0.3 per 1,000 PY (95% CI: 0.1, 0.8 per 1,000 PY), compared to 2.2 per 1,000 PY (95% CI: 1.4, 3.2 per 1,000 PY) while out of OST (RR: 0.15; 95% CI: 0.06, 0.39). Of the specific unnatural causes of death, suicides were significantly less frequent while in OST (CMR: 0.2 per 1,000 PY; 95% CI: 0.04, 0.6 per 1,000 PY) than while in OST (CMR: 0.2 per 1,000 PY; 95% CI: 0.04, 0.6 per 1,000 PY) (RR: 0.15; 95% CI: 0.04, 0.52). Of the six observed drug-induced deaths and five other injury deaths, none occurred during OST, but both violent deaths occurred while in OST.

During the first four weeks of incarceration, the all-cause CMR was 6.6 per 1,000 PY (95% CI: 3.8, 10.6 per 1,000 PY). Of the 17 cohort members who died during the first four weeks of incarceration, only one was receiving OST at the time of death. The in-treatment all-cause CMR in the first four weeks of incarceration was 0.8 deaths per 1,000 PY (95% CI: 0.02, 4.3 per 1,000 PY), significantly lower than the CMR of 12.7 per 1,000 PY (95% CI: 7.2, 20.6 per 1,000 PY) observed among out-of-treatment cohort members (RR: 0.06; 95% CI: 0.01, 0.45). As across all time in prison, during the first four weeks of incarceration, the natural mortality rate did not differ by OST status, but the in-treatment CMR for unnatural deaths (0.8 per 1,000 PY; 95% CI: 0.02, 4.4 per 1,000 PY) was significantly lower than the out-of-treatment CMR for unnatural deaths (11.0 per 1,000 PY; 95% CI: 5.7, 19.2 per 1,000 PY) (RR: 0.07;

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95% CI: 0.01, 0.55). The same pattern was observed in relation to suicide deaths (in-OST CMR: 0.8 per 1,000 PY; 95% CI: 0.02, 4.4 per 1,000 PY; out-of-OST CMR: 8.2 per 1,000 PY; 95% CI: 3.8, 15.6 per 1,000 PY; RR: 0.10; 95% CI: 0.01, 0.75).

Adjusted effect of OST on deaths in custody

In the first four weeks of a prison episode, the all-cause mortality hazard was 94% lower while in OST, compared to being out of OST (adjusted HR: 0.06; 95% CI: 0.01, 0.48), regardless of gender, Indigenous status, age, incarceration history or offending history (Table 4). A similar finding was observed in relation to unnatural deaths; during the first four weeks of a prison episode, while in OST, the hazard of unnatural death was 93% lower than while not in OST (adjusted HR 0.07; 95% CI: 0.01, 0.59).

Across all time in prison, the all-cause mortality hazard during periods of OST was reduced by three-quarters compared to periods not in OST (adjusted HR: 0.26; 95% CI: 0.13, 0.50), regardless of gender, Indigenous status, age, incarceration history or offending history. Across all time in prison, compared to periods not in OST, the hazard of unnatural death was 87% lower while in OST (adjusted HR: 0.13; 95% CI: 0.05, 0.35).

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Discussion

We have demonstrated a very strong association between receipt of OST and lowered mortality among opioid-dependent prisoners. After adjusting for demographic and criminal history factors, compared to time not in OST, being in OST was associated with a 74% lower hazard of dying in prison. The association between mortality risk and OST was driven by the reduction in unnatural deaths, with periods in OST associated with an 87% decrease in mortality hazard compared to time not in OST. One-third of deaths in prison in this cohort occurred during the first four weeks of incarceration; in these initial weeks in prison, compared to time not in OST, being in OST was associated with a 94% lower all-cause mortality hazard, and a 93% lower hazard of unnatural death. Although the confidence intervals around the hazard ratios were wide, even the uppermost limits of the intervals suggested substantial reductions in mortality while in OST. For example, across all time in prison, there was at least a 65% reduction in unnatural mortality hazard while in OST compared to time not in OST.

The cohort included in this study was drawn from a large, statewide administrative dataset of people receiving treatment for opioid dependence. Although precise data are not available on the representativeness of this cohort, in sentinel surveillance studies of people who inject drugs in NSW (98% of whom have a history of illicit opioid use) almost 60% of participants are currently in OST, and more than 80% have a history of OST,[20] suggesting that the cohort is highly representative of the NSW opioid dependent population. The sub-set of this population that had been incarcerated was included in this study. As an observational study, cohort members were not randomly allocated to treatment. Although there were some differences between prisoners who did and did not receive OST, these variables did not affect the association between OST and mortality. We did not have clinical indicators of current opioid dependence, and it is possible that some members of our cohort may have ceased all opioid use, thereby reducing their baseline mortality risk. However, given the chronic and relapsing

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nature of opioid dependence,[15 16] this is unlikely to have been the case for any substantial proportion of the cohort. Inclusion of opioid-abstinent individuals would, at any rate, result in conservative mortality estimates. Finally, we used the first episode of OST as a proxy for the onset of opioid dependence. It is possible that some cohort members had previous incarcerations during which they were opioid dependent, but had not yet entered OST.

To our knowledge, this is the first study of its kind. Prior studies have reported on all-cause or cause-specific mortality in prison among total prisoner populations.[4 21 22] We have extended on these studies by analysing mortality in opioid-dependent prisoners – a group with known mortality risk factors. Compared to opioid-dependent populations at liberty, mortality rates were low in opioid-dependent prisoners.[10] This is likely a result of limited access to illicit opioids and low exposure to other common causes of death in this population, such as motor vehicle accidents.[23] Highlighting the vulnerability of this population, however, 74% of deaths in prison were due to unnatural causes, compared to 48-59% of deaths in studies of total prisoner populations.[2-5] The great majority of deaths occurred while prisoners were not receiving OST. Although this protective effect of OST against mortality is known,[10] this is the first time this association has been observed in a prison setting. Prior studies of OST in correctional settings, including a clinical trial[24] and prospective cohort studies,[25 26] have not reported any deaths during OST, but these were not powered to detect differences in mortality rates during periods in and out of treatment. Receipt of OST in prison also reduces illicit opioid use and injecting drug use, [24 27] and is associated with reduced institutional drug charges.[28] Opioid-dependent prisoners who receive OST are more likely than their untreated peers to enroll in OST following release,[29] and continuation of OST on release is associated with reduced re-incarceration[30] and reduced post-release mortality.[31]

Although we have demonstrated a very strong protective effect of OST against death in prison for opioid-dependent prisoners, several questions remain to be answered. This study was undertaken in a

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jurisdiction with relatively high OST coverage.[14] Our understanding of the relationship between OST and deaths in prison could benefit from further observational or simulation studies that assess the impact of varying levels of OST coverage on deaths. Further, this study was not able to determine why it is that OST should be associated with reduced unnatural deaths. Given that drug withdrawal symptoms have been implicated as a trigger for suicide in the first week of prison,[7 8] the association may, in part at least, be due to alleviation or prevention of opioid withdrawal. If it is the case that averting withdrawal symptoms is sufficient to prevent some prison suicides, there are important implications for the clinical management of withdrawal symptoms of prisoners dependent on non-opioid drugs. Research examining why there are fewer suicides among opioid-dependent prisoners in OST is needed, as is research examining whether management of withdrawal from non-opioid drugs has a similar impact on suicides in prison.

The implication of these findings for correctional authorities and prison medical providers is clear: ensuring a high coverage of OST in correctional settings will help to minimise unnatural deaths among opioid-dependent prisoners. Given the particularly high mortality risk observed during the first four weeks of incarceration, it is critical that opioid-dependent prisoners can access OST in a timely manner. Opioid dependence and enrollment in OST immediately prior to entry to prison should be assessed during intake medical examinations. Prisoners enrolled in OST prior to prison entry should be able to continue this treatment without interruption, and other opioid-dependent prisoners should be assessed for OST and offered treatment if clinically indicated. Although there are challenges to the implementation of OST programs in prisons and other correctional settings, these can be managed through strong executive leadership, ongoing training and education for health and custodial staff, and careful attention to issues of safety and security.[32]

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Data sharing

No additional data available.

Contributorship

SL completed the analysis and led the writing, and is responsible for the overall content as guarantor. TD provided statistical advice and contributed to the writing. NG, MF, LB, AG and JK contributed to the writing. LD oversaw the larger project for which these data were obtained, and contributed to the writing. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests

LD has received untied educational grants from Reckitt Benckiser to conduct post-marketing surveillance of the diversion and injection of opioids. MF has participated in workshops in the Asia-Pacific region on the development of treatment services and on research with opioid users; these were supported by Reckitt Benckiser through an unrestricted educational grant, paid to the University of Adelaide. No other authors report relationships or activities that could appear to have influenced the submitted work.

Figure legend

Figure 1: Deaths from natural, unnatural and unknown causes, by time in prison prior to death among opioid-dependent people who died in prison, New South Wales, Australia, 2000-2012 (n=51)

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Table 1: Demographic characteristics of opioid-dependent persons received to prison, New South Wales, Australia, 2000-2012 (n=16,715)

Characteristic	Total (n=16,715)	Ever received OST in prison (n=12,852)	No OST in prison (n=3,863)	*P*
Male, n (%)	13,199 (79.0)	10,109 (78.7)	3,090 (80.0)	0.07
Age (years) at first observed entry to prison, median (min-max)	30 (16-64)	29 (16-63)	32 (17-64)	<.0001
Indigenous,* n (%)	5,011 (30.0)	4,208 (32.8)	803 (20.8)	<.0001
Number of prison episodes, median (min-max)	2 (1-34)	3 (1-34)	1 (1-23)	<.0001
Duration (days) of prison episodes, median (min-max)	71 (1-4,473)	77 (1-4,473)	46 (1-4,473)	<.0001
Any receipt of OST in prison	12,852 (76.9)	-	-	-

*Indigenous status missing for 10 individuals. *P*-values refer to comparison between participants who did or did not receive OST in prison (chi-square test for categorical variables; Wilcoxon rank-sum test for continuous variables).

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Table 2: Demographic characteristics and causes of death of opioid-dependent persons who died in prison, New South Wales, Australia, 2000-2012 (n=51)

Characteristic	N (%)
Male	46 (90)
Age (years) at death, median (min-max)	34 (20-54)
Indigenous	14 (27)
In OST at time of death	11 (22)
Deaths from natural causes*	11 (26)
Unnatural deaths*	32 (74)
Suicide	*19 (44)*
Drug-related	*6 (14)*
Violent	*2 (5)*
Other injury-related	*5 (12)*

*Cause of death unknown for 8 decedents. Percentage is based on n=43.

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Table 3: All-cause and cause-specific crude mortality rates per 1,000 person-years in prison among opioid-dependent people in New South Wales, Australia, 2000-2012 (n=16,715)

Cause of death	Total time in prison				First 4 weeks in prison			
	PY	Deaths	Crude mortality rate (95% CI)	Rate ratio (95% CI)	PY	Deaths	Crude mortality rate (95% CI)	Rate ratio (95% CI)
All cause	30,988	51	1.6 (1.2, 2.2)		2,571	17	6.6 (3.8, 10.6)	
Out of OST	14,548	40	2.7 (2.0, 3.7)		1,263	16	12.7 (7.2, 20.6)	
In OST	16,440	11	0.7 (0.3, 1.2)	0.24 (0.12, 0.47)	1,308	1	0.8 (0.02, 4.3)	0.06 (0.01, 0.45)
Unnatural causes[1]	27,839	32	1.1 (0.8, 1.6)		2,374	13	5.5 (2.9, 9.4)	
Out of OST	12,462	27	2.2 (1.4, 3.2)		1,094	12	11.0 (5.7, 19.2)	
In OST	15,377	5	0.3 (0.1, 0.8)	0.15 (0.06, 0.39)	1,279	1	0.8 (0.02, 4.4)	0.07 (0.01, 0.55)
Suicide	27,839	19	0.7 (0.4, 1.1)		2,374	10	4.2 (2.0, 7.7)	
Out of OST	12,462	16	1.3 (0.7, 2.1)		1,094	9	8.2 (3.8, 15.6)	
In OST	15,377	3	0.2 (0.04, 0.6)	0.15 (0.04, 0.52)	1,279	1	0.8 (0.02, 4.4)	0.10 (0.01, 0.75)
Drug-induced	27,839	6	0.2 (0.08, 0.5)		2,374	1	0.4 (0.01, 2.3)	
Out of OST	12,462	6	0.5 (0.2, 1.0)		1,094	1	1.0 (0.02, 5.1)	
In OST	15,377	0	-	-	1,279	0	-	-
Violence	27,839	2	0.07 (0.01, 0.3)		2,374	0	-	
Out of OST	12,462	0	-		1,094	0	-	
In OST	15,377	2	0.1 (0.02, 0.5)	-	1,279	0	-	-
Other injuries	27,839	5	0.2 (0.06, 0.4)		2,374	2	0.8 (0.1, 3.0)	
Out of OST	12,462	5	0.4 (0.1, 0.9)		1,094	2	1.8 (0.2, 6.6)	
In OST	15,377	0	-	-	1,279	0	-	-
Natural causes	27,839	11	0.4 (0.2, 0.7)		2,374	2	0.8 (0.1, 3.0)	
Out of OST	12,462	6	0.5 (0.2, 1.0)		1,094	2	1.8 (0.2, 6.6)	
In OST	15,377	5	0.3 (0.1, 0.8)	0.68 (0.21, 2.21)	1,279	0	-	-

Notes: Cause of death missing for 8 deaths. OST: opioid substitution treatment. PY: person-years. CI: confidence interval. [1]Includes suicide, drug-induced, violent and other injury deaths.

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Table 4: Cox proportional hazards models of predictors of death in prison among opioid-dependent prisoners in New South Wales, Australia, 2000-2012 (n=16,715)

	Total time in prison				First 4 weeks in prison			
	All-cause deaths		Unnatural deaths		All-cause deaths		Unnatural deaths	
Predictor	HR (95% CI)	Adjusted HR (95% CI)	HR (95% CI)	Adjusted HR (95% CI)	HR (95% CI)	Adjusted HR (95% CI)	HR (95% CI)	Adjusted HR (95% CI)
Receipt of OST*	0.25 (0.13, 0.48)	0.26 (0.13, 0.50)	0.15 (0.06, 0.39)	0.13 (0.05, 0.35)	0.07 (0.01, 0.54)	0.06 (0.01, 0.48)	0.08 (0.01, 0.59)	0.07 (0.01, 0.53)
Male	1.21 (0.48, 3.04)	0.94 (0.36, 2.41)	0.75 (0.29, 1.96)	0.57 (0.22, 1.54)	0.66 (0.22, 2.04)	0.54 (0.16, 1.76)	0.48 (0.15, 1.57)	0.34 (0.10, 1.18)
Indigenous	0.64 (0.34, 1.18)	0.84 (0.44, 1.59)	0.92 (0.44, 1.90)	1.02 (0.48, 2.21)	0.70 (0.24, 1.98)	0.71 (0.23, 2.13)	1.13 (0.37, 3.46)	0.98 (0.30, 3.18)
Age at prison reception	1.06 (1.03, 1.10)	1.05 (1.01, 1.09)	1.03 (0.98, 1.07)	1.02 (0.97, 1.07)	1.00 (0.93, 1.07)	0.98 (0.91, 1.06)	0.99 (0.91, 1.07)	0.99 (0.91, 1.07)
No. prior incarcerations	1.01 (0.91, 1.12)	1.09 (0.99, 1.21)	1.10 (0.97, 1.24)	1.13 (0.99, 1.28)	0.94 (0.79, 1.12)	0.96 (0.81, 1.14)	0.99 (0.78, 1.24)	1.01 (0.80, 1.27)
Duration of prior incarcerations#	0.98 (0.96, 1.00)	0.98 (0.96, 1.00)	1.01 (0.98, 1.04)	1.01 (0.98, 1.04)	0.98 (0.95, 1.01)	0.99 (0.95, 1.02)	1.02 (0.97, 1.06)	1.02 (0.97, 1.07)
Any prior drug offences	0.95 (0.53, 1.70)	0.97 (0.53, 1.76)	0.96 (0.46, 2.01)	0.92 (0.43, 1.95)	1.12 (0.36, 3.51)	1.21 (0.38, 3.82)	0.84 (0.25, 2.78)	0.91 (0.27, 3.07)
Any prior property offences	0.47 (0.25, 0.92)	0.76 (0.37, 1.57)	0.71 (0.29, 1.75)	0.81 (0.31, 2.14)	0.59 (0.13, 2.69)	0.70 (0.15, 3.36)	1.04 (0.13, 8.39)	1.15 (0.14, 9.67)
Any prior violent offences	0.53 (0.30, 0.94)	0.69 (0.37, 1.26)	0.65 (0.31, 1.34)	0.70 (0.32, 1.50)	0.49 (0.18, 1.33)	0.49 (0.18, 1.37)	0.64 (0.20, 1.98)	0.56 (0.17, 1.83)

*Time-dependent variable. HR: hazard ratio. CI: confidence interval. OST: opioid substitution treatment. #Hazard ratio refers to change in hazard associated with 28-day increase in duration of prior incarcerations.

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Opioid substitution therapy as a strategy to reduce deaths in prison: Retrospective cohort study

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Abstract

Objectives: To describe deaths in prison among opioid-dependent people, and examine associations between receipt of opioid substitution therapy and risk of death in prison

Design: Retrospective cohort study

Setting: Adult prisons in New South Wales (NSW), Australia

Participants: 16,715 opioid-dependent people who were received to prison between 2000 and 2012.

Interventions: Opioid substitution therapy

Primary outcome measures: Natural and unnatural (suicide, drug-induced, violent and other injury) deaths in prison

Results: Cohort members were in prison for 30,998 person-years (PY), during which time there were 51 deaths. The all-cause crude mortality rate (CMR) in prison was 1.6 per 1,000 PY (95% CI: 1.2, 2.2 per 1,000 PY), and the unnatural death CMR was 1.1 per 1,000 PY (95% CI: 0.8, 1.6 per 1,000 PY). Compared to time out of OST, the hazard of all-cause death was 74% lower while in OST (adjusted hazard ratio (AHR): 0.26; 95% CI: 0.13 to 0.50), and the hazard of unnatural death was 87% lower while in OST (AHR: 0.13; 95% CI: 0.05 to 0.35). The all-cause and unnatural death CMRs during the first four weeks of incarceration were 6.6 per 1,000 PY (95% CI: 3.8, 10.6 per 1,000 PY) and 5.5 per 1,000 PY (95% CI: 2.9, 9.4 per 1,000 PY), respectively. Compared to periods not in OST, the hazard of all-cause death during the first four weeks of incarceration was 94% lower while in OST (AHR: 0.06; 95% CI: 0.01 to 0.48), and the hazard of unnatural death was 93% lower while in OST (AHR: 0.07; 95% CI: 0.01 to 0.53).

Conclusions: Mortality of opioid-dependent prisoners was significantly lower while in receipt of OST.

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Article summary

Article focus

- Deaths in prison are a significant concern, and correctional authorities have a responsibility to ensure that such deaths are kept to a minimum
- Opioid dependent people commonly experience imprisonment, and may be at particular risk of death in prison
- Opioid substitution treatment (OST) reduces mortality among opioid-dependent people residing in the community, but it is unclear if this is also the case in prison

Key messages

- Opioid-dependent prisoners receiving OST have a substantially lower risk of unnatural death than their untreated peers
- In addition to other known benefits of OST in prison (e.g. reduced opioid use and injecting drug use), to-scale provision of OST in prisons will dramatically reduce unnatural deaths among opioid-dependent prisoners

Strengths and limitations of this study

- This study is based on a large, statewide cohort with mortality outcomes determined via population-based registries
- Cohort members were not randomly allocated to treatment
- Data regarding onset of opioid dependence and current opioid dependence were not available

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Deaths in prison are a serious public health issue, raising questions as to the quality of care and supervision provided by correctional authorities. Reflecting such concerns, deaths in prison usually result in extensive post-mortem inquiries, and may also lead to litigation against correctional authorities and health care providers.[1]

Unnatural deaths in prison are of particular concern due to their preventable nature. Unnatural deaths include suicides, violent or drug-induced deaths, and other injury-related deaths. Studies in developed countries have found that unnatural deaths comprise 48-59% of all deaths in prison, with suicide the most common cause of unnatural death.[2-5] These figures suggest considerable opportunities to reduce unnatural deaths in prison.

Opioid-dependent people commonly experience imprisonment,[6] and there are several reasons to believe that opioid-dependent prisoners may be at particular risk of unnatural death in prison. Drug withdrawal has been implicated as a possible trigger for suicide in the first days of incarceration.[7 8] Additionally, use of illicitly obtained opioids while in prison[9] carries with it the risk of overdose. To our knowledge, deaths in prison specifically among opioid-dependent people have not previously been described. Furthermore, no studies have considered whether treatment for opioid dependence during incarceration reduces mortality risk, as it does among opioid-dependent people residing in the community.[10] In this study, we describe deaths in prison in a cohort of opioid-dependent people, and examine whether receiving opioid substitution therapy (OST) reduces the risk of death in prison.

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Methods

Ethical review

This study was approved by the research ethics committees of the University of New South Wales (NSW) (HC12019), the NSW Ministry of Health (2011/11/360), the Australian Institute of Health and Welfare (EC2011/2/13), the Alfred Hospital (165/11), Corrective Services NSW (11/82607), Justice Health (NSW) (G219/11), the NSW Aboriginal Health and Medical Research Council (AHMRC) (793/11) and Justice Health (Victoria) (CF/13/3440C).

Setting

NSW is the most populous state in Australia and houses around one-third of the country's prisoners, or 9,645 people at 31 June 2012.[11] Health services in NSW prisons are provided under the Ministry of Health, and ~~T~~there is a well-established prison OST program ~~in NSW prisons~~that operates as part of the state-wide opioid treatment program.[12 13] People who enter prison while in OST ~~can~~ may continue ~~with~~ treatment while incarcerated, ~~or~~ and OST can be commenced during incarceration if clinically indicated.[12] Clinical indications for OST are the same as in community settings.[13] Most prisoners receiving OST are prescribed methadone due to the longer dosing procedure associated with buprenorphine, and concerns about diversion of buprenorphine. In 2012, 16% of NSW prisoners were prescribed OST.[11 12] Coverage of OST (the proportion of opioid-dependent prisoners receiving treatment) has been estimated at 43%.[14]

Data sources and linkage

Data for this retrospective cohort study were extracted from administrative datasets used to record OST programs, offending and incarceration, and mortality. The Pharmaceutical Drugs of Addiction System (PHDAS) is a database of all methadone and buprenorphine recipients in NSW since 1985. The PHDAS

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records each patient's full name, date of birth, ~~sex~~ gender and clinical variables including dates of OST entry and exit. Identifying variables in this dataset are considered to be of high accuracy as proof of identity must be shown to the prescribing doctor before a prescription can be issued. Data used for linkage were for the calendar years 1985-2010.

Offending and incarceration data were sourced from the NSW Bureau of Crime Statistics and Research (BOCSAR) Re-offending Database (ROD). This database includes dates and types of offences in criminal cases heard by Local, District and Supreme Courts of NSW, and dates of receptions to and discharges from the custody of Corrective Services NSW. All available data were provided for linkage; this included offending data for the period December 1 1993-December 31 2011, and incarceration data for the period January 1 2000-March 31 2012.

The National Death Index (NDI) is a database held by the Australian Institute of Health and Welfare (AIHW), containing mortality data collected from all the Registry of Births, Deaths and Marriages in each Australian State and Territory. Causes of death are recorded in the NDI by expert clinical coders on the basis of information contained in death certificates and, where available, coronial files, using the International Statistical Classification of Diseases and Related Health Problems 10th Edition (ICD-10). Dates of death were available for the entire period for which incarceration data were available (January 1 2000-March 31 2012); however, for administrative reasons, causes of death were available only for deaths occurring up to December 31 2010.

Linkage between the OST and offending/incarceration data was performed by BOCSAR staff, and linkage between the OST and mortality data was undertaken by AIHW staff. Linkage was completed using probabilistic linkage software. Variables used for matching purposes included full name, date of birth, ~~sex~~gender, and date and state of last known contact where available. These linked datasets were forwarded to the investigators with identifiers removed.

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Cohort and data definitions

From the linked datasets, we identified a cohort of opioid-dependent people (people who were recorded in the PHDAS as having received OST at some point during 1986-2010) who had been incarcerated at least once (as recorded in the ROD). In defining receipt of OST, we excluded temporary treatment programs (usually interstate visitors) and treatment episodes that were part of a buprenorphine clinical trial (during which the individual may have been allocated to placebo). Periods in the custody of Corrective Services NSW were determined using reception and discharge dates in the ROD. We used the first recorded OST episode as a proxy for the onset of opioid dependence, and excluded prison episodes that occurred prior to the first OST episode; all subsequent prison episodes for an individual were included. If an individual's first OST episode commenced while incarcerated, that prison episode was included. Given the chronic and relapsing nature of opioid dependence,[15 16] we assumed that all cohort members remained opioid-dependent from their first episode of OST until death or the end of follow-up.

Deaths in prison were defined as deaths that occurred while the individual was recorded as being in the custody of Corrective Services NSW. This definition does not stipulate that a deceased individual was physically in prison at the time of death. Some decedents may have been receiving care in hospital at the time of death, while still in the custody of Corrective Services NSW. Deaths with known causes (i.e. all deaths occurring in the calendar years 2000-2010) were categorised as natural (i.e. disease-related) or unnatural deaths. We used the Corrective Services NSW definition of "unnatural deaths", which includes suicides, drug-induced deaths, violent deaths and deaths due to accidental injuries or injuries in which no intent (i.e. suicidal or violent) could be determined.[3] ICD-10 codes for unnatural deaths are provided in the Supplementary Materials.

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Periods of OST while in prison, and treatment status (in OST/out of OST) at the time of death, were determined usinged treatment entry and exit dates from the PHDAS. New treatment episodes were defined when an individual commenced treatment seven or more days after discharge from a previous treatment episode. A change in medicine (methadone to buprenorphine, or vice versa) was considered a continuous episode if there were less than seven days between ceasing one medicine and commencing the other.

Data analysis

Statistical analyses were undertaken in SAS 9.3. We used descriptive statistics to examine demographic characteristics and incarceration. Participants with any record of receiving OST in prison were compared to those who did not receive OST in prison using chi-square tests for categorical variables and the Wilcoxon rank-sum test for continuous variables. We constructed a frequency histogram to illustrate time from entry to prison until death. For dates for which comparable data were available (financial years 2000-01 to 2009-10), we compared the total number of unnatural deaths among prisoners in NSW[3] to the number of unnatural deaths in the opioid-dependent cohort.

We calculated all-cause and cause-specific crude mortality rates (CMR) with Poisson 95% confidence intervals (CI) for all time in prison, and the first four weeks in prison. Rates were also calculated by treatment status (in/out of OST). Person-years (PY) used in the calculation of CMRs accrued whenever participants were in the custody of Corrective Services NSW. Prison episodes where the participant was received and released on the same day were counted as one day. PY ceased accruing at death or 31st March 2012 for all-cause mortality rates, or 31st December 2010 for cause-specific mortality rates. Crude mortality rate ratios with 95% CI were calculated to assess unadjusted risk of death in treatment compared to that out of treatment. The rate ratio was not calculated if there were zero deaths in either the in-treatment or out-of-treatment condition.

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We used Cox regression to examine the adjusted association between OST exposure and two in-prison mortality outcomes: deaths from all causes, and unnatural deaths. Two models were developed for each outcome, the first considering mortality risk across all time in prison, and the second examining mortality risk during the first four weeks of incarceration. All prison episodes were included, with days in prison counted as discontinuous intervals at risk. Although participants could have multiple observations within the dataset, the internal computations of a Cox model are such that when there is only one event of interest per person (in this case, death), there is no need for adjustments for multiple observations.[17] OST exposure while in prison was coded as a time-dependent variable, with periods out of treatment coded as 0 and periods in treatment coded as 1. Demographic variables included in the models were ~~sex~~gender, Indigenous (i.e. Aboriginal or Torres Strait Islander) status, and age at entry to prison; this latter variable increased as necessary with subsequent incarcerations within an individual. We also included variables that described prior experiences of incarceration during our observation periods, namely, number and duration (days) of prior incarcerations. These variables increased with each incarceration per person. We also included dichotomous variables that recorded if a participant had been charged with a drug, property or violent offence prior to incarceration. These were included because of possible associations between death in prison (particularly suicide) and prior offending (particularly violent offending).[18 19] The offending history variables could change from no to yes with subsequent incarcerations. Observations with missing covariate data were excluded from analyses. We tested each variable for its bivariate association with mortality, and entered all variables into a multivariate model. We tested the proportional hazards assumption for each static predictor variable in the multivariate model by including an interaction between it and log(time) in the model. All variables in both models were found to satisfy the proportional hazards assumption.

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Results

The cohort comprised 16,715 opioid-dependent people who had been incarcerated at least once between January 2000 and March 2012 (Table 1). The majority (79.0%; n=13,199) of the cohort was male, and 30.0% (n=5,011) identified as Indigenous. The median age at first entry to prison during our observation period was 30 years (ranging from 16-64 years).

Cohort members were received to prison a median of two times (ranging between 1-34). Duration of incarceration ranged from 1 day to the entire length of follow-up (12 years and 3 months), with a median duration of 71 days. Most participants (76.9%; n=12,852) received OST at some point while incarcerated. Compared to participants who received OST in prison, participants who did not receive OST in prison were significantly older, less likely to be Indigenous and had fewer incarcerations of shorter duration (Table 1).

Deaths in prison

Fifty-one cohort members died in prison (Table 2). Most were male (90%; n=46) and non-Indigenous (73%; n=37). The median age at death was 34 years (ranging between 20-54). Only 22% (n=11) of decedents were receiving OST at the time of death. Cause of death was available for 43 deaths in prison. Of these, nearly three-quarters (74%; n=32) were unnatural deaths: 19 suicides, six drug-related deaths, two violent deaths and five deaths due to other injuries. Between the financial years 2000-01 and 2009-10, unnatural deaths in this cohort accounted for 35% of all unnatural deaths in NSW prisons[3] (see Supplementary Materials for further details).

One-third of all deaths in prison (n=17) occurred during the first four weeks of incarceration (Figure 1). Of these, three-quarters (13/17; 76%) were unnatural deaths: 10 suicides, two other injury-related deaths, and one drug-related death.

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Crude mortality rates

The all-cause CMR in prison was 1.6 per 1,000 PY (95% CI: 1.2, 2.2 per 1,000 PY) (Table 3). The all-cause CMR was significantly lower while in OST (CMR: 0.7 per 1,000 PY; 95% CI: 0.3, 1.2 per 1,000 PY), compared to time out of OST (CMR: 2.7 per 1,000 PY; 95% CI: 2.0, 3.7 per 1,000 PY) (rate ratio (RR): 0.24; 95% CI: 0.12, 0.47).

Deaths from natural causes occurred at similar rates whether in (0.3 per 1,000 PY; 95% CI: 0.1, 0.8 per 1,000 PY) or out (0.5 per 1,000 PY; 95% CI: 0.2, 1.0 per 1,000 PY) of OST (RR: 0.68 (95% CI: 0.21, 2.21). There was, however, a marked effect of OST on rates of unnatural death. The in-treatment CMR for unnatural deaths was 0.3 per 1,000 PY (95% CI: 0.1, 0.8 per 1,000 PY), compared to 2.2 per 1,000 PY (95% CI: 1.4, 3.2 per 1,000 PY) while out of OST (RR: 0.15; 95% CI: 0.06, 0.39). Of the specific unnatural causes of death, suicides were significantly less frequent while in OST (CMR: 0.2 per 1,000 PY; 95% CI: 0.04, 0.6 per 1,000 PY) than while in OST (CMR: 0.2 per 1,000 PY; 95% CI: 0.04, 0.6 per 1,000 PY) (RR: 0.15; 95% CI: 0.04, 0.52). Of the six observed drug-induced deaths and five other injury deaths, none occurred during OST, but both violent deaths occurred while in OST.

During the first four weeks of incarceration, the all-cause CMR was 6.6 per 1,000 PY (95% CI: 3.8, 10.6 per 1,000 PY). Of the 17 cohort members who died during the first four weeks of incarceration, only one was receiving OST at the time of death. The in-treatment all-cause CMR in the first four weeks of incarceration was 0.8 deaths per 1,000 PY (95% CI: 0.02, 4.3 per 1,000 PY), significantly lower than the CMR of 12.7 per 1,000 PY (95% CI: 7.2, 20.6 per 1,000 PY) observed among out-of-treatment cohort members (RR: 0.06; 95% CI: 0.01, 0.45). As across all time in prison, during the first four weeks of incarceration, the natural mortality rate did not differ by OST status, but the in-treatment CMR for unnatural deaths (0.8 per 1,000 PY; 95% CI: 0.02, 4.4 per 1,000 PY) was significantly lower than the out-of-treatment CMR for unnatural deaths (11.0 per 1,000 PY; 95% CI: 5.7, 19.2 per 1,000 PY) (RR: 0.07;

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95% CI: 0.01, 0.55). The same pattern was observed in relation to suicide deaths (in-OST CMR: 0.8 per 1,000 PY; 95% CI: 0.02, 4.4 per 1,000 PY; out-of-OST CMR: 8.2 per 1,000 PY; 95% CI: 3.8, 15.6 per 1,000 PY; RR: 0.10; 95% CI: 0.01, 0.75).

Adjusted effect of OST on deaths in custody

In the first four weeks of a prison episode, the all-cause mortality hazard was 94% lower while in OST, compared to being out of OST (adjusted HR: 0.06; 95% CI: 0.01, 0.48), regardless of ~~sex~~gender, Indigenous status, age, incarceration history or offending history (Table 4). A similar finding was observed in relation to unnatural deaths; during the first four weeks of a prison episode, while in OST, the hazard of unnatural death was 93% lower than while not in OST (adjusted HR 0.07; 95% CI: 0.01, 0.59).

Across all time in prison, the all-cause mortality hazard during periods of OST was reduced by three-quarters compared to periods not in OST (adjusted HR: 0.26; 95% CI: 0.13, 0.50), regardless of ~~sex~~gender, Indigenous status, age, incarceration history or offending history. Across all time in prison, compared to periods not in OST, the hazard of unnatural death was 87% lower while in OST (adjusted HR: 0.13; 95% CI: 0.05, 0.35).

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Discussion

We have demonstrated a very strong association between receipt of OST and lowered mortality among opioid-dependent prisoners. After adjusting for demographic and criminal history factors, compared to time not in OST, being in OST was associated with a 74% lower hazard of dying in prison. The association between mortality risk and OST was driven by the reduction in unnatural deaths, with periods in OST associated with an 87% decrease in mortality hazard compared to time not in OST. One-third of deaths in prison in this cohort occurred during the first four weeks of incarceration; in these initial weeks in prison, compared to time not in OST, being in OST was associated with a 94% lower all-cause mortality hazard, and a 93% lower hazard of unnatural death. Although the confidence intervals around the hazard ratios were wide, even the uppermost limits of the intervals suggested substantial reductions in mortality while in OST. For example, across all time in prison, there was at least a 65% reduction in unnatural mortality hazard while in OST compared to time not in OST.

The cohort included in this study was drawn from a large, statewide administrative dataset of people receiving treatment for opioid dependence. Although precise data are not available on the representativeness of this cohort, in sentinel surveillance studies of people who inject drugs in NSW (98% of whom have a history of illicit opioid use) almost 60% of participants are currently in OST, and more than 80% have a history of OST,[20] suggesting that the cohort is highly representative of the NSW opioid dependent population. The sub-set of this population that had been incarcerated was included in this study. As an observational study, cohort members were not randomly allocated to treatment. Although there were some differences between prisoners who did and did not receive OST, these variables did not affect the association between OST and mortality. We did not have clinical indicators of current opioid dependence, and it is possible that some members of our cohort may have ceased all opioid use, thereby reducing their baseline mortality risk. However, given the chronic and relapsing

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nature of opioid dependence,[15 16] this is unlikely to have been the case for any substantial proportion of the cohort. Inclusion of opioid-abstinent individuals would, at any rate, result in conservative mortality estimates. Finally, we used the first episode of OST as a proxy for the onset of opioid dependence. It is possible that some cohort members had previous incarcerations during which they were opioid dependent, but had not yet entered OST.

To our knowledge, this is the first study of its kind. Prior studies have reported on all-cause or cause-specific mortality in prison among total prisoner populations.[4 21 22] We have extended on these studies by analysing mortality in opioid-dependent prisoners – a group with known mortality risk factors. Compared to opioid-dependent populations at liberty, mortality rates were low in opioid-dependent prisoners.[10] This is likely a result of limited access to illicit opioids and low exposure to other common causes of death in this population, such as motor vehicle accidents.[23] Highlighting the vulnerability of this population, however, 74% of deaths in prison were due to unnatural causes, compared to 48-59% of deaths in studies of total prisoner populations.[2-5] The great majority of deaths occurred while prisoners were not receiving OST. Although this protective effect of OST against mortality is known,[10] this is the first time this association has been observed in a prison setting. Prior studies of OST in correctional settings, including a clinical trial[24] and prospective cohort studies,[25 26] have not reported any deaths during OST, but these were not powered to detect differences in mortality rates during periods in and out of treatment. Receipt of OST in prison also reduces illicit opioid use and injecting drug use, [24 27] and is associated with reduced institutional drug charges.[28] Opioid-dependent prisoners who receive OST are more likely than their untreated peers to enroll in OST following release,[29] and continuation of OST on release is associated with reduced re-incarceration[30] and reduced post-release mortality.[31]

Although we have demonstrated a very strong protective effect of OST against death in prison for opioid-dependent prisoners, several questions remain to be answered. This study was undertaken in a

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jurisdiction with relatively high OST coverage.[14] Our understanding of the relationship between OST and deaths in prison could benefit from further observational or simulation studies that assess the impact of varying levels of OST coverage on deaths. Further, this study was not able to determine why it is that OST should be associated with reduced unnatural deaths. Given that drug withdrawal symptoms have been implicated as a trigger for suicide in the first week of prison,[7 8] the association may, in part at least, be due to alleviation or prevention of opioid withdrawal. If it is the case that averting withdrawal symptoms is sufficient to prevent some prison suicides, there are important implications for the clinical management of withdrawal symptoms of prisoners dependent on non-opioid drugs. Research examining why there are fewer suicides among opioid-dependent prisoners in OST is needed, as is research examining whether management of withdrawal from non-opioid drugs has a similar impact on suicides in prison.

The implication of these findings for correctional authorities and prison medical providers is clear: ensuring a high coverage of OST in correctional settings will help to minimise unnatural deaths among opioid-dependent prisoners. Given the particularly high mortality risk observed during the first four weeks of incarceration, it is critical that opioid-dependent prisoners can access OST in a timely manner. Opioid dependence and enrollment in OST immediately prior to entry to prison should be assessed during intake medical examinations. Prisoners enrolled in OST prior to prison entry should be able to continue this treatment without ~~minimal~~ interruption, and other opioid-dependent prisoners should be assessed for OST and offered treatment if clinically indicated. Although there are challenges to the implementation of OST programs in prisons and other correctional settings, these can be managed through strong executive leadership, ongoing training and education for health and custodial staff, and careful attention to issues of safety and security.[32]

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Data sharing

Data sharing is not available.

Contributorship

SL completed the analysis and led the writing, and is responsible for the overall content as guarantor. TD provided statistical advice and contributed to the writing. NG, MF, LB, AG and JK contributed to the writing. LD oversaw the larger project for which these data were obtained, and contributed to the writing. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Acknowledgements

We wish to acknowledge all data custodians for providing access to the datasets used in this study: the NSW Ministry of Health (PHDAS dataset), the Bureau of Crime Statistics and Research (ROD dataset) and the Australian Institute of Health and Welfare (NDI dataset). Thank you to Judy Trevena for her work on the initial preparation and cleaning of datasets, Pia Salmelainen (NSW Health) for expert advice about the PHDAS dataset, and Jacqui Fitzgerald (BOCSAR) for advice regarding the ROD. We also wish to thank the members of our Indigenous Reference Group: Michael Doyle, Anton Clifford, Megan Williams and Luke Bell.

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Competing interests

LD has received untied educational grants from Reckitt Benckiser to conduct post-marketing surveillance of the diversion and injection of opioids. MF has participated in workshops in the Asia-Pacific region on the development of treatment services and on research with opioid users; these were supported by Reckitt Benckiser through an unrestricted educational grant, paid to the University of Adelaide. No other authors report relationships or activities that could appear to have influenced the submitted work.

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Table 1: Demographic characteristics of opioid-dependent persons received to prison, New South Wales, Australia, 2000-2012 (n=16,715)

Characteristic	Total (n=16,715)	Ever received OST in prison (n=12,852)	No OST in prison (n=3,863)	*P*
Male ~~sex~~, n (%)	13,199 (79.0)	10,109 (78.7)	3,090 (80.0)	0.07
Age (years) at first observed entry to prison, median (min-max)	30 (16-64)	29 (16-63)	32 (17-64)	<.0001
Indigenous,* n (%)	5,011 (30.0)	4,208 (32.8)	803 (20.8)	<.0001
Number of prison episodes, median (min-max)	2 (1-34)	3 (1-34)	1 (1-23)	<.0001
Duration (days) of prison episodes, median (min-max)	71 (1-4,473)	77 (1-4,473)	46 (1-4,473)	<.0001
Any receipt of OST in prison	12,852 (76.9)	-	-	-

*Indigenous status missing for 10 individuals. *P*-values refer to comparison between participants who did or did not receive OST in prison (chi-square test for categorical variables; Wilcoxon rank-sum test for continuous variables).

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Table 2: Demographic characteristics and causes of death of opioid-dependent persons who died in prison, New South Wales, Australia, 2000-2012 (n=51)

Characteristic	N (%)
Male ~~sex~~	46 (90)
Age (years) at death, median (min-max)	34 (20-54)
Indigenous	14 (27)
In OST at time of death	11 (22)
Deaths from natural causes*	11 (26)
Unnatural deaths*	32 (74)
Suicide	*19 (44)*
Drug-related	*6 (14)*
Violent	*2 (5)*
Other injury-related	*5 (12)*

*Cause of death unknown for 8 decedents. Percentage is based on n=43.

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Figure 1: Deaths from natural, unnatural and unknown causes, by time in prison prior to death among opioid-dependent people who died in prison, New South Wales, Australia, 2000-2012 (n=51)

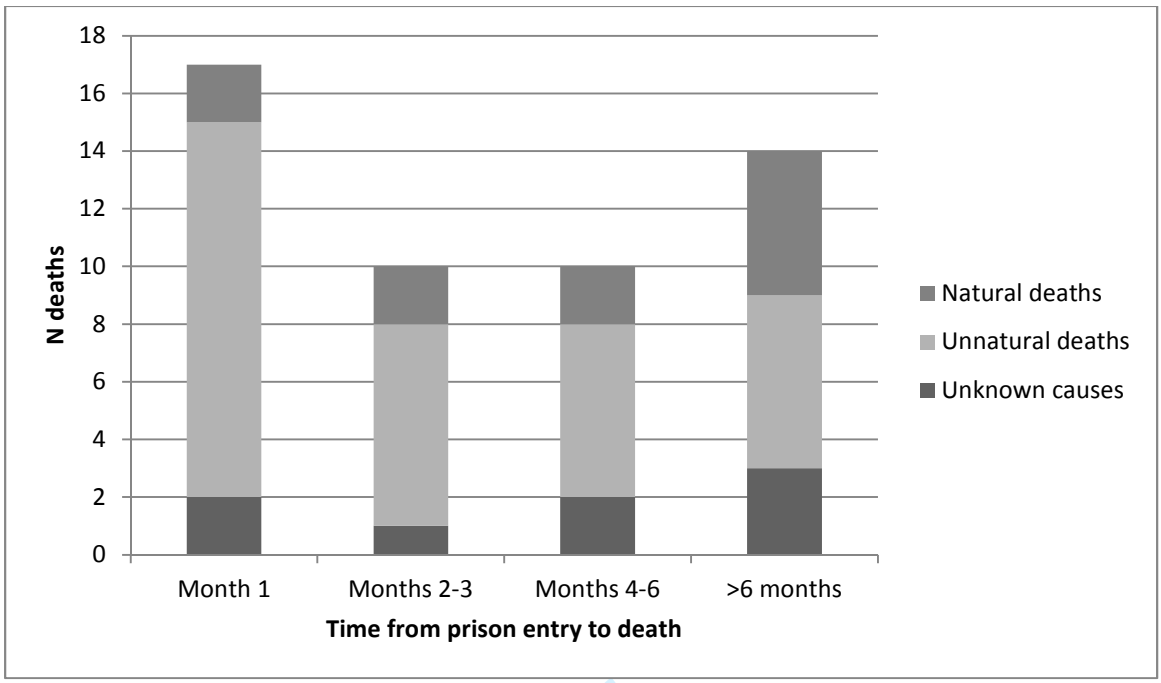

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Table 3: All-cause and cause-specific crude mortality rates per 1,000 person-years in prison among opioid-dependent people in New South Wales, Australia, 2000-2012 (n=16,715)

Cause of death	Total time in prison				First 4 weeks in prison			
	PY	Deaths	Crude mortality rate (95% CI)	Rate ratio (95% CI)	PY	Deaths	Crude mortality rate (95% CI)	Rate ratio (95% CI)
All cause	30,988	51	1.6 (1.2, 2.2)		2,571	17	6.6 (3.8, 10.6)	
Out of OST	14,548	40	2.7 (2.0, 3.7)		1,263	16	12.7 (7.2, 20.6)	
In OST	16,440	11	0.7 (0.3, 1.2)	0.24 (0.12, 0.47)	1,308	1	0.8 (0.02, 4.3)	0.06 (0.01, 0.45)
Unnatural causes[1]	27,839	32	1.1 (0.8, 1.6)		2,374	13	5.5 (2.9, 9.4)	
Out of OST	12,462	27	2.2 (1.4, 3.2)		1,094	12	11.0 (5.7, 19.2)	
In OST	15,377	5	0.3 (0.1, 0.8)	0.15 (0.06, 0.39)	1,279	1	0.8 (0.02, 4.4)	0.07 (0.01, 0.55)
Suicide	27,839	19	0.7 (0.4, 1.1)		2,374	10	4.2 (2.0, 7.7)	
Out of OST	12,462	16	1.3 (0.7, 2.1)		1,094	9	8.2 (3.8, 15.6)	
In OST	15,377	3	0.2 (0.04, 0.6)	0.15 (0.04, 0.52)	1,279	1	0.8 (0.02, 4.4)	0.10 (0.01, 0.75)
Drug-induced	27,839	6	0.2 (0.08, 0.5)		2,374	1	0.4 (0.01, 2.3)	
Out of OST	12,462	6	0.5 (0.2, 1.0)		1,094	1	1.0 (0.02, 5.1)	
In OST	15,377	0	-	-	1,279	0	-	-
Violence	27,839	2	0.07 (0.01, 0.3)		2,374	0	-	
Out of OST	12,462	0	-		1,094	0	-	
In OST	15,377	2	0.1 (0.02, 0.5)	-	1,279	0	-	-
Other injuries	27,839	5	0.2 (0.06, 0.4)		2,374	2	0.8 (0.1, 3.0)	
Out of OST	12,462	5	0.4 (0.1, 0.9)		1,094	2	1.8 (0.2, 6.6)	
In OST	15,377	0	-	-	1,279	0	-	-
Natural causes	27,839	11	0.4 (0.2, 0.7)		2,374	2	0.8 (0.1, 3.0)	
Out of OST	12,462	6	0.5 (0.2, 1.0)		1,094	2	1.8 (0.2, 6.6)	
In OST	15,377	5	0.3 (0.1, 0.8)	0.68 (0.21, 2.21)	1,279	0	-	-

Notes: Cause of death missing for 8 deaths. OST: opioid substitution treatment. PY: person-years. CI: confidence interval. [1]Includes suicide, drug-induced, violent and other injury deaths.

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Table 4: Cox proportional hazards models of predictors of death in prison among opioid-dependent prisoners in New South Wales, Australia, 2000-2012 (n=16,715)

	Total time in prison				First 4 weeks in prison			
	All-cause deaths		Unnatural deaths		All-cause deaths		Unnatural deaths	
Predictor	**HR (95% CI)**	**Adjusted HR (95% CI)**	**HR (95% CI)**	**Adjusted HR (95% CI)**	**HR (95% CI)**	**Adjusted HR (95% CI)**	**HR (95% CI)**	**Adjusted HR (95% CI)**
Receipt of OST*	0.25 (0.13, 0.48)	0.26 (0.13, 0.50)	0.15 (0.06, 0.39)	0.13 (0.05, 0.35)	0.07 (0.01, 0.54)	0.06 (0.01, 0.48)	0.08 (0.01, 0.59)	0.07 (0.01, 0.53)
Male ~~sex~~	1.21 (0.48, 3.04)	0.94 (0.36, 2.41)	0.75 (0.29, 1.96)	0.57 (0.22, 1.54)	0.66 (0.22, 2.04)	0.54 (0.16, 1.76)	0.48 (0.15, 1.57)	0.34 (0.10, 1.18)
Indigenous	0.64 (0.34, 1.18)	0.84 (0.44, 1.59)	0.92 (0.44, 1.90)	1.02 (0.48, 2.21)	0.70 (0.24, 1.98)	0.71 (0.23, 2.13)	1.13 (0.37, 3.46)	0.98 (0.30, 3.18)
Age at prison reception	1.06 (1.03, 1.10)	1.05 (1.01, 1.09)	1.03 (0.98, 1.07)	1.02 (0.97, 1.07)	1.00 (0.93, 1.07)	0.98 (0.91, 1.06)	0.99 (0.91, 1.07)	0.99 (0.91, 1.07)
No. prior incarcerations	1.01 (0.91, 1.12)	1.09 (0.99, 1.21)	1.10 (0.97, 1.24)	1.13 (0.99, 1.28)	0.94 (0.79, 1.12)	0.96 (0.81, 1.14)	0.99 (0.78, 1.24)	1.01 (0.80, 1.27)
Duration of prior incarcerations#	0.98 (0.96, 1.00)	0.98 (0.96, 1.00)	1.01 (0.98, 1.04)	1.01 (0.98, 1.04)	0.98 (0.95, 1.01)	0.99 (0.95, 1.02)	1.02 (0.97, 1.06)	1.02 (0.97, 1.07)
Any prior drug offences	0.95 (0.53, 1.70)	0.97 (0.53, 1.76)	0.96 (0.46, 2.01)	0.92 (0.43, 1.95)	1.12 (0.36, 3.51)	1.21 (0.38, 3.82)	0.84 (0.25, 2.78)	0.91 (0.27, 3.07)
Any prior property offences	0.47 (0.25, 0.92)	0.76 (0.37, 1.57)	0.71 (0.29, 1.75)	0.81 (0.31, 2.14)	0.59 (0.13, 2.69)	0.70 (0.15, 3.36)	1.04 (0.13, 8.39)	1.15 (0.14, 9.67)
Any prior violent offences	0.53 (0.30, 0.94)	0.69 (0.37, 1.26)	0.65 (0.31, 1.34)	0.70 (0.32, 1.50)	0.49 (0.18, 1.33)	0.49 (0.18, 1.37)	0.64 (0.20, 1.98)	0.56 (0.17, 1.83)

*Time-dependent variable. HR: hazard ratio. CI: confidence interval. OST: opioid substitution treatment. #Hazard ratio refers to change in hazard associated with 28-day increase in duration of prior incarcerations.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9, Table 1
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	9-10, Tables 1 and 2

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Outcome data	15*	Report numbers of outcome events or summary measures over time	9, Table 2, Figure 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11, Tables 3 and 4
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Supplementary Table 1: ICD-10 codes for defining unnatural deaths

Cause of death	ICD-10 codes
Drug-induced	F11-F16, F19, F55, X40-X44, X60-X64, X85, Y10-Y14
Suicide	X60-X84, Y87.0
Violence	X85-Y09, Y87.1
Other injuries*	V00-X39, X50-X59, Y10-Y39, Y85-Y86, Y88-Y89

*Includes accidental injuries and injuries for which no intent (i.e. suicidal or violent) could be inferred

Supplementary Table 2: BOCSAR codes for drug, violent and property crimes

Offence category	ANZSOC codes	Offence
Violent	011, 012, 013	Homicide
	021, 029	Assault
	0611, 0612	Robbery
	0311, 0312	Sexual assault and other sexual offences
Property	071	Break and enter
	081	Motor vehicle theft
	082	Theft
	091, 092	Fraud
Drug	101, 102	Import, deal or traffic illicit drugs
	103	Manufacture or cultivate illicit drugs
	104	Possession/use of illicit drugs
	109	Other illicit drug offences

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Additional data: Unnatural deaths in prison accounted for by the opioid-dependent cohort

Data on unnatural deaths in prison in NSW are released by Corrective Services NSW for each financial year (in Australia, 1 July to 30 June of the following year). We had data for the opioid dependent cohort that was comparable to the Corrective Services NSW data for the financial years 2000/01 to 2009/10. Between July 1 2000 and 30 June 2010, Corrective Services NSW reported 81 unnatural deaths. During the same time period, there were 28 unnatural deaths in the opioid dependent cohort, accounting for 35% of the total unnatural deaths in prison for that period (see Supplementary Table 3).

Supplementary Table 3: Unnatural deaths among all prisoners and opioid-dependent prisoners in New South Wales, Australia, by financial year.

Financial year	Unnatural deaths reported by CSNSW	Unnatural deaths in opioid dependent cohort	Deaths in opioid dependent cohort as a proportion of all unnatural deaths (%)
2000/01	12	1	8
2001/02	10	6	60
2002/03	11	3	27
2003/04	10	2	20
2004/05	10	4	40
2005/06	5	0	0
2006/07	8	3	38
2007/08	5	3	60
2008/09	5	5	100
2009/10	5	1	20
Total	81	28	35

CSNSW: Corrective Services New South Wales. Data on unnatural deaths reported by CSNSW are from: Corrective Services NSW. *Statistical Report 2011/12*. Sydney: Corrective Services NSW, 2012, p.30. Available from http://www.correctiveservices.nsw.gov.au/__data/assets/pdf_file/0011/379748/statistical-report-2010-2011.pdf.

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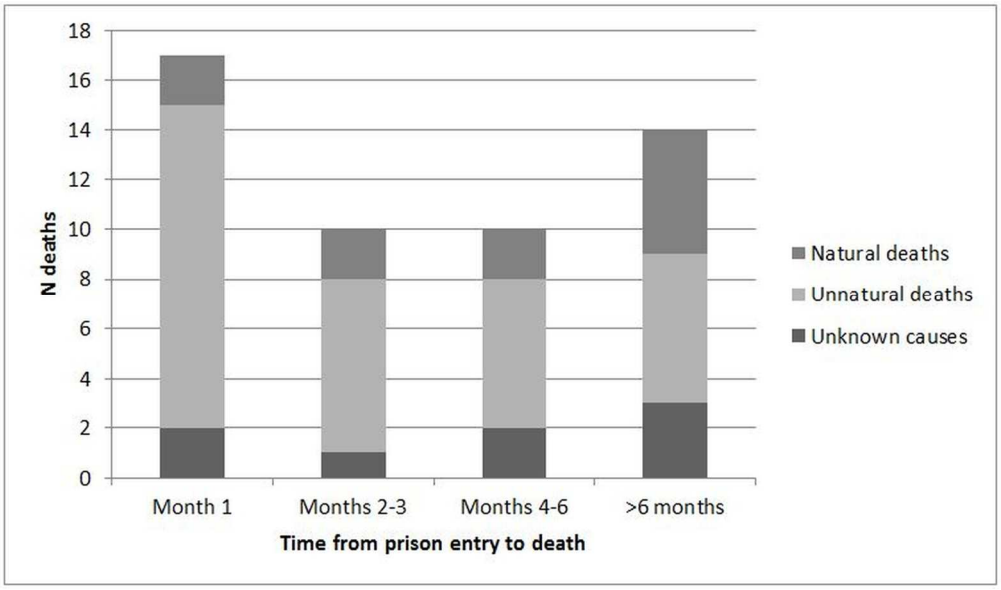

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