TITLE: High rate of fatal overdose after release from prison in BC: a retrospective data linkage study

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ABSTRACT (250/250 words)

Background: People recently released from prison are at increased risk of preventable death. However, the impact of the current overdose epidemic on overdose deaths in this population is unknown. We aimed to document the incidence and identify risk factors for fatal overdose after release from provincial prisons in BC.

Methods: Within a random 20% sample of the BC population, we linked provincial health and correctional records 2010-2017 for individuals aged 18 or older on January 1 2010, who were released from provincial prisons at least once from 2015-2017. Exposures were ascertained during the period 2010-2017; deaths were identified during the period 2015-2017. We calculated the piecewise incidence of overdose-related and all-cause death after release from prison, excluding any time spent back in custody. We used multivariable, mixed-effects Cox regression to identify predictors of all-cause and overdose death.

Results: Among 6,106 adults released from prison 2015-2017 and followed in the commuity for a median of 1.6 (IQR 0.9-2.3) years, 77 (1.3%) died, 48 (0.8%) due to overdose. The incidence of overdose death was 11.2 (95%CI 9.2-13.5) per 1000 person years, but 38.8 (95%CI 3.2-22.6) in the first two weeks post-release. After adjusting for covariates, the hazard of overdose death was four times higher among those who had been dispensed opioids for pain.

Intepretation: People released from prison in BC are at markedly increased risk of fatal overdose. Overdose prevention efforts must go beyond provision of OAT and naloxone on release, to consider physical and mental health comorbidities, and psychosocial disadvantage.

KEYWORDS: drug overdose; opioid-related disorders; prisons; cause of death; British Columbia

INTRODUCTION

Overdose continues to be a significant public health issue in British Columbia (BC) that has lowered life expectancy in the province.[1] Since the declaration of a public health emergency in 2016 over 5,000 persons have died due to overdose in BC, and non-fatal overdose events continue to rise. Irrespective of population overdose trends, people recently released from prison are at increased risk of death due to overdose.[2] A key causal mechanism is thought to be reduced drug tolerance, such that most (although not all[3, 4]) studies observe a spike in the rate of death immediately after release.[2, 5, 6] To date only one study has examined deaths after release from prison in Canada: Kouyoumdjian and colleagues used data linkage to follow a cohort of 48,166 adults who were incarcerated in Ontario in 2000, for up to 12 years. The rate of overdose death in the first two weeks after release from prison was 56 times higher than in the age- and sex-matched general population; falling to 29 times higher in weeks 3-4 post-release.[7] The impact of the current overdose epidemic on mortality after release from prison is unknown.

Evidence that people released from prison are at increased risk of overdose is insufficient to inform targeted prevention. Internationally, few studies of this phenomenon have been able to identify risk and protective factors, largely due to the limitations of available administrative data.[6] The World Health Organization (WHO) recommends that authorities provide opioid agonist treatment (OAT) in prison, and make both OAT and naloxone available on release, as cornerstones of prevention.[5] However, these measures alone may be inadequate. Physical and mental health comorbidities may also contribute to fatal OD risk,[8-10] and there is growing evidence that persons released from prison with co-occurring substance use disorder (SUD) and mental illness – so-called 'dual diagnosis' – are particularly at risk of poor health outcomes.[11] More evidence on risk and protective factors is needed to inform targeted, evidence-based prevention. The aims of this study were to (a) measure risk of overdose-related and all-cause death in different time periods after release from incarceration; and (b) identify individual and socio-environmental characteristics associated with overdose-related and all-cause death after release from incarceration.

METHODS

This is a retrospective, open cohort study constructed from a random 20% sample of the BC population, linked with provincial health and correctional records. Exposures were measured during an accrual period from January 1 2010 until December 31 2017. Outcomes were measured during an observation period from January 1 2015 to December 31 2017.

Sampling frame

The 20% random sample was taken from the client roster of health insurance in BC, which is mandatory and therefore provides almost complete coverage of BC residents. Within this random sample we selected all individuals who (a) were aged 18 years or older on January 1 2010, and (b) had at least one record of release from a BC prison (remand or sentenced) between January 1 2015 and December 31 2017.

Outcome

We identified deaths from 2015-2017 using linked administrative health data available in the BC Provincial Overdose Cohort. A detailed description of the Cohort is available elsewhere.[12] Overdose deaths were defined as (a) deaths identified by BC Vital Statistics as being due to opioid overdose (ICD-10: T40.0, T40.1, T40.2, T40.3, T40.4, T40.6) (b) unintentional illicit drug toxicity deaths identified by the BC Coroners Service, and/or (c) deaths due to any cause that occurred within 24 hours of an overdose event identified from linked ambulance, emergency department, and/or hospital data (for details, see Supplementary Materials).

Exposures

Exposures were identified from linked administrative data covering the period January 1 2010 to December 31 2017. Further information about exposure definition is provided in the Supplementary Materials.

From BC provincial correctional records we identified the number of times participants had been released from prison 2010-2014, and obtained all dates of incarceration and release from prison 2015-2017.

From hospital records we used ICD-9 and ICD-10 codes to identify persons with evidence of SUD and/or mental illness. Persons were defined as having SUD and/or mental illness if they had two or more outpatient visits within one year, and/or one hospitalisation record during the accrual period 2010-2017. Persons determined to have both SUD and mental illness during the accrual period were considered to have a dual diagnosis.

We coded hospital records for chronic disease comorbidity, using an adapted version of the Elixhauser Comorbidity Index.[13] For each of 31 chronic disease groups, if a disease was identified, the index for this group was set as "1"; otherwise, the index was set as "0". The sum of the indexes for the 31 groups forms the comorbidity index. For the analyses presented here, we removed four disease groups reflecting substance use and mental illness, to avoid collinearity with the dual diagnosis variable describe above. The adapted Index score was dichotomised (0, ≥1).

Dispensation of opioids for pain, and dispensation of benzodiazepines, during the accrual period were identified using provincial pharmaceutical data (PharmaNet), which contain all records of dispensed prescription medications in community pharmacies in the province. We excluded opioids used for treatment of opioid use disorders.

Statistical Analyses

The observation period commenced on the date of first release from custody 2015-2017 and was censored at death, or on December 31 2017, whichever came first. For the calculation of rates, any periods of reincarceration during follow-up (and any deaths in custody) were removed. We calculated the rate of all-cause and overdose-related death per 1000 person-years, excluding time in custody, expressed as the number of deaths in the community divided by person-years at risk, multiplied by 1000. Mortality rates were calculated for the full sample, and according to characteristics at the time of each release. The 95% confidence interval (95%CI) for mortality rates was calculated using the exact method (POIS.EXACT in R) under the assumption of a Poisson distribution.

We calculated the piecewise incidence rate of overdose-related and all-cause death during each two-week period in the first eight weeks post-release, and for all community follow-up, using all releases during follow-up.

To identify characteristics associated with overdose-related and all-cause death, we constructed mixed-effects Cox models (COXME in R), adjusting for the correlation among multiple releases within a person, to calculate unadjusted and adjusted hazard ratios (HRs) with corresponding 95%CI. This approach to data analysis permitted the value of all covariates (except for sex) to differ for each release. All analyses were conducted using the R statistical computing environment (version 3.5.2).

Ethics approval

Ethics approval for this project was not required as it was conducted as part of BCCDC's overdose surveillience and advanced analytics mandate.

RESULTS

The sample incuded 6,106 persons released from a BC prison at least once 2015-2017, of whom 77 (1.3%) died from any cause and 48 (0.8%) died from overdose-related causes, during 9632.8 person-years of community follow-up. The median (IQR) duration of community follow-up per person was 1.6 (IQR 0.9-2.3) years, and the median (IQR) duration of follow-up per episode of follow-up was 0.3 (IQR 0.1-1.0) years.

Table 1 compares the baseline characteristics of those who did and did not die from overdose-related causes, and from any cause, during community follow-up. Compared with those who did not die from overdose-related causes, those who died from overdose-related causes were significantly more likely to have a history of mental illness or dual diagnosis, to have a history of physical comorbidities, and to have been dispensed benzodiazepines or dispensed opioids for pain. The pattern was similar for all-cause death, except that age and number of previous incarcerations were also associated with death during follow-up.

Table 1. Characteristics of the cohort at first release from custody 2015-2017

	Overdose-Related Death			All-Cause Death		
	No	**Yes**	**P value[a]**	**No**	**Yes**	**P value[a]**
Number of persons	6058	48		6029	77	
Age group (years)			0.998			0.027
18-34	3163 (52.2)	25 (52.1)		3156 (52.3)	32 (41.6)	
35-44	1528 (25.2)	12 (25.0)		1522 (25.2)	18 (23.4)	
≥ 45	1367 (22.6)	11 (22.9)		1351 (22.4)	27 (35.1)	
Sex			0.690			0.793
Male	5291 (87.3)	41 (85.4)		5264 (87.3)	68 (88.3)	
Female	767 (12.7)	7 (14.6)		765 (12.7)	9 (11.7)	
Days of stay during most recent incarceration			0.134			0.272
≤ 3 days	1611 (26.6)	20 (41.7)		1603 (26.6)	28 (36.4)	
4-15 days	1683 (27.8)	10 (20.8)		1676 (27.8)	17 (22.1)	
16-60 days	1264 (20.9)	8 (16.7)		1257 (20.8)	15 (19.5)	
> 60 days	1500 (24.8)	10 (20.8)		1493 (24.8)	17 (22.1)	
Number of previous incarcerations			0.067			0.007
1	3447 (56.9)	21 (43.8)		3438 (57.0)	30 (39.0)	
2-3	1233 (20.4)	15 (31.2)		1227 (20.4)	21 (27.3)	
4-7	970 (16.0)	11 (22.9)		960 (15.9)	21 (27.3)	
≥ 8	408 (6.7)	1 (2.1)		404 (6.7)	5 (6.5)	
SUD and mental illness			0.007			0.002
None	3234 (53.4)	16 (33.3)		3224 (53.5)	26 (33.8)	
SUD	706 (11.7)	5 (10.4)		701 (11.6)	10 (13.0)	
Mental illness	708 (11.7)	6 (12.5)		704 (11.7)	10 (13.0)	
SUD and mental illness	1410 (23.3)	21 (43.8)		1400 (23.2)	31 (40.3)	
Comorbidity index			0.001			< 0.001
None	5572 (92.0)	38 (79.2)		5551 (92.1)	59 (76.6)	
≥ 1	486 (8.0)	10 (20.8)		478 (7.9)	18 (23.4)	
Dispensed benzodiazepines			< 0.001			< 0.001
No	4551 (75.1)	26 (54.2)		4535 (75.2)	42 (54.5)	
Yes	1507 (24.9)	22 (45.8)		1494 (24.8)	35 (45.5)	
Dispensed opioids for pain			< 0.001			< 0.001
No	3140 (51.8)	10 (20.8)		3136 (52.0)	14 (18.2)	
Yes	2918 (48.2)	38 (79.2)		2893 (48.0)	63 (81.8)	

SUD = substance use disorder.
[a]p values derived from chi-square tests.

Tables 2 and 3 show the incidence of overdose-related and all-cause death in the cohort, and the unadjusted and adjusted hazard of death, according to characteristics at release. During community follow-up the incidence of overdose-related death was 11.2 (95%CI 9.2-13.5) per 1000 person years. The hazard of overdose-related death was higher among those who had been incarcerated four or more times; those with a history of SUD, mental illness, or dual diagnosis; those with a history of physical comorbidity; and those who had been dispensed benzodiazepines or dispensed opioids for pain. In the fully adjusted model, the

hazard of overdose-related death was four times higher among those who had been dispensed opioids for pain.

Table 2. Incidence and hazard of overdose-related death after release from prison, according to characteristics at release

`	Incidence per 1000 person years (95%CI)	Unadjusted HR (95%CI)	Adjusted HR[a] (95%CI)
Overall	11.2 (9.2 - 13.5)	--	--
Age group (years)			
18-34	11.2 (8.4 - 14.6)	Ref.	Ref.
35-44	11.7 (7.8 - 16.7)	1.06 (0.67 - 1.66)	0.85 (0.54 - 1.34)
≥45	10.8 (6.9 - 16.0)	1.04 (0.65 - 1.66)	0.83 (0.51 - 1.35)
Sex			
Male	10.9 (8.7 - 13.3)	Ref.	Ref.
Female	13.6 (7.9 - 21.8)	0.76 (0.45 - 1.28)	0.98 (0.57 - 1.68)
Days of stay during most recent incarceration			
≤ 3 days	12.1 (8.1 - 17.5)	Ref.	Ref.
4-15 days	8.4 (5.4 - 12.7)	0.67 (0.38 - 1.16)	0.60 (0.34 - 1.04)
16-60 days	14.0 (9.5 - 19.9)	1.03 (0.62 - 1.72)	0.80 (0.48 - 1.34)
> 60 days	10.9 (7.1 - 15.9)	0.83 (0.48 - 1.41)	0.74 (0.43 - 1.26)
Number of previous incarcerations			
1	5.8 (3.6 - 8.9)	Ref.	Ref.
2-3	10.1 (6.7 - 14.7)	1.71 (0.97 - 3.01)	1.28 (0.72 - 2.28)
4-7	15.7 (10.8 - 22.1)	2.48 (1.43 - 4.30)	1.59 (0.90 - 2.82)
≥ 8	21.4 (14.1 - 31.1)	3.00 (1.67 - 5.39)	1.59 (0.86 - 2.95)
SUD and mental illness			
None	4.8 (3.1 - 7.1)	Ref.	Ref.
SUD	13.5 (7.6 - 22.3)	2.74 (1.46 - 5.16)	1.26 (0.64 - 2.45)
Mental illness	10.8 (5.6 - 18.9)	2.19 (1.10 - 4.36)	1.34 (0.66 - 2.72)
SUD and mental illness	25.0 (18.9 - 32.5)	4.73 (2.94 - 7.62)	1.69 (0.97 - 2.97)
Comorbidity index			
None	9.5 (7.6 - 11.7)	Ref.	Ref.
≥ 1	31.1 (19.9 - 46.3)	3.10 (1.97 - 4.88)	1.61 (0.99 - 2.61)
Dispensed benzodiazepines			
No	6.8 (5.0 - 9.0)	Ref.	Ref.
Yes	24.5 (18.6 - 31.6)	3.31 (2.27 - 4.84)	1.41 (0.91 - 2.18)
Dispensed opioids for pain			
No	2.8 (1.5 - 4.7)	Ref.	Ref.
Yes	20.3 (16.4 - 24.8)	6.77 (3.86 - 11.89)	4.01 (2.14 - 7.52)

SUD = substance use disorder.
[a]Adjusted for all other variables in this table.

During community follow-up the incidence of all-cause death was 16.1 (95%CI 13.7-18.8) per 1000 person years (Table 3). The hazard of all-cause death was higher among those who were aged 45 years or older; those who had been incarcerated two or more times; those with a history of SUD, mental illness, or dual diagnosis; those with a history of physical comorbidities; and those who had been dispensed benzodiazepines or dispensed opioids for pain. In the fully adjusted model, the hazard of all-cause death was greater among those with a history of four or more prior incarcerations, those with physical comorbidities, and those who had been dispensed opioids for pain.

Table 3. Incidence and hazard of all-cause death after release from prison, according to characteristics at release

	Incidence per 1000 person years (95%CI)	Unadjusted HR (95%CI)	Adjusted HR[a] (95%CI)
Overall	16.1 (13.7 - 18.8)	--	--
Age group (years)			
18-34	14.4 (11.3 - 18.2)	Ref.	Ref.
35-44	15.3 (10.8 - 21.0)	1.10 (0.74 - 1.63)	0.89 (0.59 - 1.33)
≥45	20.6 (15.1 - 27.5)	1.60 (1.11 - 2.30)	1.23 (0.84 - 1.82)
Sex			
Male	16.0 (13.4 - 18.9)	Ref.	Ref.
Female	16.8 (10.4 - 25.7)	0.94 (0.59 - 1.49)	1.14 (0.70 - 1.86)
Days of stay during most recent incarceration			
≤ 3 days	16.9 (12.0 - 23.1)	Ref.	Ref.
4-15 days	12.9 (9.0 - 17.9)	0.74 (0.46 - 1.16)	0.64 (0.40 - 1.03)
16-60 days	19.9 (14.5 - 26.7)	1.13 (0.74 - 1.72)	0.85 (0.55 - 1.31)
> 60 days	15.5 (10.9 - 21.3)	0.87 (0.55 - 1.36)	0.74 (0.47 - 1.17)
Number of previous incarcerations			
1	8.3 (5.6 - 11.9)	Ref.	Ref.
2-3	15.0 (10.7 - 20.4)	1.86 (1.16 - 2.97)	1.43 (0.88 - 2.30)
4-7	21.9 (16.0 - 29.2)	2.55 (1.60 - 4.06)	1.68 (1.04 - 2.73)
≥ 8	30.9 (22.0 - 42.2)	3.32 (2.03 - 5.43)	1.83 (1.09 - 3.08)
SUD and mental illness			
None	7.5 (5.4 - 10.3)	Ref.	Ref.
SUD	20.8 (13.2 - 31.2)	2.66 (1.61 - 4.42)	1.20 (0.70 - 2.07)
Mental illness	16.3 (9.6 - 25.7)	2.01 (1.15 - 3.52)	1.21 (0.67 - 2.16)
SUD and mental illness	33.5 (26.3 - 42.0)	4.03 (2.73 - 5.94)	1.47 (0.93 - 2.35)
Comorbidity index			
None	12.9 (10.6 - 15.5)	Ref.	Ref.
≥ 1	53.2 (38.2 - 72.1)	3.87 (2.69 - 5.57)	2.03 (1.37 - 3.02)
Dispensed benzodiazepines			
No	10.4 (8.2 - 13.0)	Ref.	Ref.
Yes	33.2 (26.3 - 41.3)	3.00 (2.19 - 4.11)	1.26 (0.87 - 1.82)
Dispensed opioids for pain			
No	4.4 (2.8 - 6.7)	Ref.	Ref.
Yes	28.7 (24.0 - 34.0)	6.07 (3.89 - 9.48)	3.67 (2.22 - 6.07)

SUD = substance use disorder.
[a]Adjusted for all other variables in this table.

Figure 1 shows the piecewise incidence of overdose-related and non-overdose-related death after release from incarceration. The incidence of overdose-related death was markedly elevated in the first two weeks post-release (IR 38.8, 95%CI 23.7-59.9, per 1000 person-years). The incidence of non-overdose-related death was also elevated in the first two weeks post-release (IR 9.7, 95%CI 3.2-22.6), although not to the same extent.

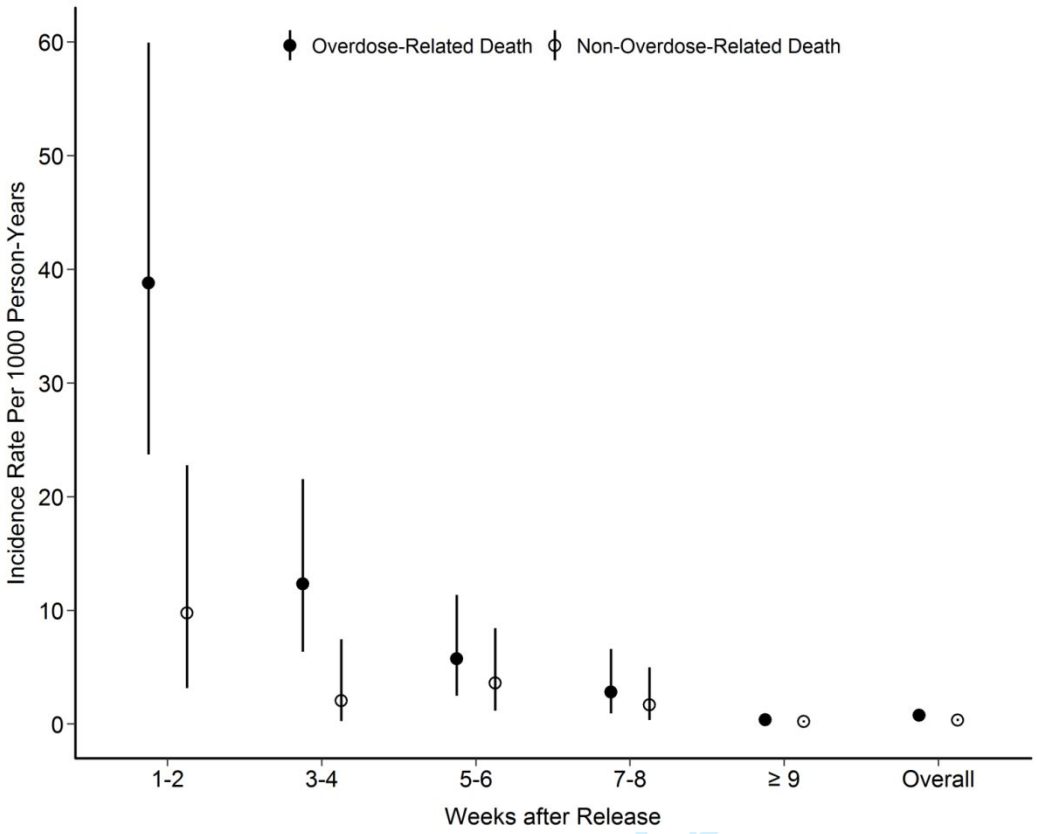

Figure 1. Piecewise incidence of overdose-related and non-overdose-related death according to time since release from prison

INTERPRETATION

In a large, representative sample of people released from prisons in BC, we found that almost two-thirds (62%) of observed deaths was overdose-related. In the context of an overdose epidemic that is disproportionately affecting people released from prison, there is a clear and pressing need to implement evidence-based overdose prevention efforts at scale. BC provides opioid agonist treatment (OAT) in all of its prisons and has more recently made naloxone widely available on release.[14] Although these efforts are commendable and in line with international evidence,[5] our findings indicate that they have not been sufficient to stem the tide of overdose deaths in this highly vulnerable segment of the population.

Complex morbidity and disadvantage are normative among people who experience incarceration.[15] In our study we found that these co-occurring health and social problems were associated with risk of overdose-related and all-cause death. In addition to OAT and naloxone, enhanced efforts to prevent untimely deaths after release from prison should consider targeting these co-occurring risk factors. Those with a history of multiple incarcerations were at increased risk of both overdose and all-cause death. Although this association was attenuated after adjustment for covariates, it remained a significant predictor of all-cause death, suggesting that efforts to minimise the use of incarceration, through prevention and diversion, may both be cost-effective and help prevent untimely deaths.

Even after adjusting for covariates, we found that individuals who had been prescribed opioids for pain were at markedly increased risk of overdose-related and all-cause death. There is a high prevalence of non-cancer chronic pain among both people in prison[16] and those receiving OAT,[17] and opioid analgesics may be an appropriate treatment for these individuals. However, given our unsurprising finding that dispensing of

opioids for pain was independently associated with a more than four-fold increase in risk of overdose-related death after release from prison, it appears that enhanced clinical supervision and harm reduction measures are warranted to ensure that medications intended to treat chronic pain do not result in preventable deaths in these medically complex individuals.

We found that co-occurring physical and mental health comorbidities increased the risk of both overdose-related and all-cause death. Again, after adjustment for covariates this association attenuated to the null for overdose death, but physical comorbidity remained a significant predictor of all-cause death. Whereas the burden of infectious diseases such as HIV, hepatitis and tuberculosis in prisons is now well recognised,[18] less attention has been paid to the high rates of non-communicable disease (NCD) in these settings.[19] In addition to their direct contribution to mortality in people released from prison, certain NCDs including those that result in hepatic or lung dysfunction may increase the risk of overdose.[20] As prison populations in Canada and elsewhere age,[21] the importance of providing coordinated and continuous treatment for NCDs in people who experience incarceration will only increase.

Consistent with evidence that people with a dual diagnosis are at increased risk of injury after release from prison,[11] we found that these individuals were more than four times more likely than those with neither disorder to die due to overdose or any cause. These associations attenuated to the null in adjusted models, however we cannot rule out the possibility that their effect was mediated by covariates. Future studies using prospective data linkage may have greater capacity to tease out the causal pathways between physical and mental health comorbidity, and death after release from prison.

Consistent with previous studies,[2] we observed a spike in the incidence of overdose-related death in the first two weeks after release from prison, highlighting the importance of effective prevention in this high-risk period. However, in our study the vast majority of overdose deaths occurred more than two weeks post-release, underscoring the importance of maintaining preventive efforts after this acute period. We also observed a modest spike in non-overdose related deaths in the two weeks after release from prison, suggesting that efforts to prevent untimely deaths after release from prison should not be restricted to overdose prevention.

This is to our knowledge the first ever study to use linked health, correctional and mortality records to examine overdose death after release from prison. Key strengths include the population sampling frame, and use of linked health and correctional records to identify exposures. The study had six notable limitations. First, despite the large sample we had limited statistical power to identify associations. Future studies may benefit from longer accrual and follow-up periods, using full population samples rather than random samples from the population. Second, our study design excluded individuals aged <23 years at first release from prison and under-sampled those aged <25, among whom the elevation in risk of death after release from prison appears to be the greatest.[22] Third, administrative data may under-ascertain some exposures of interest, which would have attenuated observed associations. Fourth, our accrual period was left censored at 2010, such that exposures prior to this date (e.g., incarceration, mental disorder) would not have been detected. Again, this would attenuate associations. Fifth, although provincial health insurance (MSP) records cover >95% of the BC population, we cannot exclude the possibility of modest sampling bias. Sixth, we were unable to identify transfers to federal prison, and as such over-estimated time at risk in the community, thereby under-estimating the incidence of death in the community. Future studies, combining provincial and federal correctional records, would provide a more complete picture of the epidemiology of overdose among people who experience incarceration in Canada.

Conclusions

People recently released from prisons in BC are at markedly increased risk of preventable death, mainly due to overdose. As such, people transitioning from prison to the community should be a key target population for overdose prevention efforts. To be maximally effective, these efforts must go beyond provision of OAT

and naloxone on release, to consider physical and mental health comorbidities, and psychosocial disadvantage. The recent transition of prison healthcare in BC from the Ministry of Public Safety and Solicitor General to the Ministry of Health is consistent with WHO recommendations and may have facilitated better continuity of care, however this assumption requires evaluation.[23]

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SUPPLEMENTARY MATERIALS

Diagnosis of Opioid Overdose: Overdose cases were identified by linking various administrative health data and using the International Statistical Classification of Diseases 9th (ICD-9) and 10th Revisions (ICD-10) [12]. An overdose event was defined using the following criteria: (1) An unintentional illicit drug toxicity death identified by the BC Coroners Service; (2) An emergency department visit with a diagnosis of opioid overdose (ICD-10: T40.1 or T40.6); (3) An ambulance-attended event in which the patient was provided naloxone by paramedics; (4) A hospitalization record with a diagnosis of opioid overdose (ICD-10: T40.0, T40.1, T40.2, T40.3, T40.4, or T40.6 as major discharge diagnosis); (5) An outpatient visit with a diagnosis of opioid overdose (ICD-9: 965.0, 965.00, 965.01, 965.02, 965.09, or E850.0); (6) A phone call to the BC Drug and Poison Information Centre for an opioid overdose event; (7) A death registration record with an overdose-related diagnosis (ICD-10: T40.0, T40.1, T40.2, T40.3, T40.4, T40.6) in the Vital Statistics Death. If multiple overdose records were identified for the same person, and the time period for these records was within 24 hours, these records were treated as a single overdose event.

Substance Use Disorder and Mental Illness: Substance use disorder (SUD) and mental illness were determined using outpatient data and hospitalization data. Persons were identified as having SUD or mental illness if they had two outpatient visits within one year or one hospitalization record for a specific disease during the 5-year exposure period [24].

Substance Use Disorder: SUD was identified using ICD-9 codes [drug-induced mental disorders (292); drug dependence (304); nondependent abuse of drugs (305) excluding alcohol abuse (305.0)] and ICD-10 codes [mental and behavioural disorders due to use of opioids (F11), cannabinoids (F12), sedatives or hypnotics (F13), cocaine (F14), other stimulants including caffeine (F15), hallucinogens (F16), tobacco (F17), volatile solvents (F18), and multiple drugs and other psychoactive substances (F19)].

Mental Illness: Mental illness included depression (ICD-9: 300.4; 311; 50B. ICD-10: F32; F33; F34.1), anxiety disorder (ICD-9: 300 excluding 300.4; 50B. ICD-10: F40; F41), stress disorder (ICD-9: 308; 309. ICD-10: F43), bipolar disorder (ICD-9: 296. ICD-10: F30; F31; F34 excluding F34.1; F38; F39), and/or schizophrenia (ICD-9: 295; 297; 298. ICD-10: F20-F25; F28; F29).