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Mortality among older adults with opioid use disorders in the Veteran's Health Administration, 2000–2011*

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Abstract

Background—The population of people with opioid use disorders (OUD) is aging. There has been little research on the effects of aging on mortality rates and causes of death in this group. We aimed to compare mortality in older (≥50 years of age) adults with OUD to that in younger (<50 years) adults with OUD and older adults with no history of OUD. We also examined risk factors for specific causes of death in older adults with OUD.

Methods—Using data from the Veteran's Health Administration National Patient Care Database (2000–2011), we compared all-cause and cause-specific mortality rates in older adults with OUD to those in younger adults with OUD and older adults without OUD. We then generated a Cox regression model with specific causes of death treated as competing risks.

Results—Older adults with OUD were more likely to die from any cause than younger adults with OUD. The drug-related mortality rate did not decline with age. HIV-related and liver-related deaths were higher among older OUD compared to same-age peers without OUD. There were very few clinically important predictors of specific causes of death.

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Contributors

SL and ASBB defined the research questions. DG conducted the statistical analyses. SL drafted the manuscript. ASMM, MAI, MH, FCB and LD reviewed and commented on manuscript drafts.

Conclusion—Considerable drug-related mortality in people with OUD suggests a need for greater access to overdose prevention and opioid substitution therapy across the lifespan. Elevated risk of liver-related death in older adults may be addressed through antiviral therapy for hepatitis C virus infection. There is an urgent need to explore models of care that address the complex health needs of older adults with OUD.

Keywords

opioid dependence; mortality; aging; veterans

1. INTRODUCTION

Opioid use disorders (OUD) are associated with significant mortality. Regular and dependent opioid users die at nearly 15 times the rate of their age- and sex-matched peers, with a crude mortality rate of 2% per year (Degenhardt et al., 2011). Common causes of death include drug overdose, suicide, trauma, and AIDS-related illnesses. The relative contribution of specific causes of death to overall mortality varies with factors such as geography, background HIV prevalence and access to opioid substitution treatment (Degenhardt et al., 2011).

One factor plausibly affecting mortality in OUD that has received little research attention is aging. Observational cohort studies of people with OUD have demonstrated that, among those who survive into their fifties and sixties, ongoing opioid use (whether regular or occasional) is more common than long-term abstinence (Hser et al., 2007, 2001). In recent years, concomitant with the aging of the general population, there have been substantial increases in the numbers of older drug users. In the United States, an increasing proportion of first-time entrants to drug treatment programs are aged over 55, and the proportion of these reporting heroin as a problem drug is also increasing (Arndt et al., 2011). Projected continued increases in the number of older people with substance use disorders (Han et al., 2009) suggest a need to better understand the health of this group, including mortality rates and causes of death as indicators of areas for intervention.

Although a small number of studies have reported that all-cause mortality rates increase with age (Degenhardt et al., 2009; Ødegård et al., 2007), there has been little analysis of how cause-specific mortality in older people with OUD may differ from that seen in younger cohorts. Deaths not directly related to drug use are more common among older people with OUD than their younger counterparts (Beynon et al., 2010; Ødegård et al., 2007); however, no studies on this issue have used a large enough sample to allow for further disaggregation of non-drug-related causes of death. As such, it is unclear what non-drug causes of death are most important as people with OUD age. It is also unclear if drug-related mortality among people with OUD decreases with age, and is replaced by non-drug deaths, or if non-drug deaths comprise an additional burden on people with OUD (Beynon et al., 2010; Ødegård et al., 2007).

A related question is how mortality in older people with OUD may be similar to, or differ from, mortality in same-age peers without OUD. It may be that aging-related increases in certain causes of death affect people with and without OUD similarly, and for these causes,

mortality rates in older people with OUD may simply be as they are in older people generally. In one opioid-dependent cohort, cancer mortality was elevated compared to the general population in those aged 35–54, but at age 55 and over, there was no significant difference between opioid dependent persons and the general population (Randall et al., 2011). This may not be the case, however, for causes of death that are directly drug-related, such as overdose, or indirectly drug-related, such as HIV or liver disease subsequent to hepatitis C infection.

There are few data sources that permit direct comparisons of mortality between people with and without OUD, or that contain detailed information about comorbidities that may affect mortality. One possible avenue for examining these relationships with sufficient sample size are electronic health records (EHR) linked to cause-specific mortality record. One such source of data is the Veterans Health Administration (VHA). The VHA is the largest integrated health system in the United States and has long used EHR nationally to record demographic and diagnostic information for all treatment contacts of patients seen anywhere in the national WHA system. Recent efforts have led to the linkage of VHA EHR data with cause-specific mortality data from the Centers for Disease Control and Prevention's National Death Index. Veterans who receive care from the VHA are a particular population of interest for the study of OUD and mortality among older adults. Although many Veterans who receive care from VHA are from recent conflicts, the majority of VHA patients are older adults. Opioid prescribing is common in VHA (Bohnert et al., 2014), and VHA patients have a high rate of drug-related mortality (Bohnert et al., 2011a).

In light of the aging of the OUD population and the lack of knowledge of how aging may impact cause-specific mortality in this group, this paper aimed to (a) describe mortality in a cohort of older (≥50 years) adults with a history of OUD; (b) compare mortality in this cohort to that in younger (<50 years) adults with a history of OUD, and older (≥50 years) adults with no record of OUD and (c) determine risk factors for cause-specific mortality in older adults with a history of OUD.

2. METHODS

This study was approved by the Institutional Review Boards of the Ann Arbor Veterans Health Administration (VA) and University of Michigan.

2.1 Data sources and linkage

Clinical data were obtained from the VA's National Patient Care Database (NPCD). The NPCD contains records of all clinical visits nationally in the VA system. The study cohort was defined as people with a lifetime diagnosis of an OUD in a 5% random sample of patients in the NPCD who were aged 50 years or over during FY2000–2011 (older OUD group). Individuals with an OUD diagnosis who reached 50 years during this time period entered the cohort on the date of their 50th birthday.

Two comparison cohorts were also defined. The first consisted of people with a lifetime diagnosis of OUD in a 5% random sample of patients in the NPCD who were aged under 50 years (younger OUD group). The second was an age- and sex-matched sample of VA

patients aged 50 years or over during FY2000–2011, with no record of an OUD in the NPCD (older non-OUD group). In light of low rates of remission from opioid dependence, in each OUD group, we assumed ongoing OUD from the time of diagnosis to the end of follow-up (Calabria et al., 2010; Darke, 2011; Grella and Lovinger, 2012; Hser et al., 2001). This may bias mortality rates downwards, as drug-related mortality risk would decrease with cessation of opioid use.

In addition to patient demographics (sex, date of birth, race and ethnicity), data extracted from the NPCD for each participant were used to measure the Charlson Comorbidity Index (Quan et al., 2005) in the year prior to cohort entry (dichotomised as 0 or ≥1) and diagnoses recorded any time prior to or on the date of cohort entry. Included diagnoses were hepatitis C virus, HIV, chronic pain, headache, neuropathy, alcohol use disorder, non-opioid drug use disorder, mood disorder, post-traumatic stress disorder, other anxiety disorder and schizophrenia.

The NPCD data were linked to mortality data from the Centers for Disease Control and Prevention National Death Index (NDI) Plus database. Variables from the NPCD submitted for linkage with the NDI were Social Security Number, last name, first name, middle initial, date of birth, race/ethnicity, sex and state of residence. Previous linkages between the NPCD and NDI have found that 99% of deaths are matched on complete Social Security Number (Bohnert et al., 2011b). Data returned from the NDI were date and cause of death. Deaths were categorised by cause, using a framework adapted from Randall et al. (2009). ICD-10 codes used to categorise causes of death are provided in the supplementary materials[1].

2.2 Data analysis

Demographic and diagnosis differences between the older OUD group and each comparison group were assessed using the χ^2 test. All-cause and cause-specific crude mortality rates (CMRs) were calculated, along with 95% confidence intervals, for each group. The older OUD CMRs were divided by the younger OUD CMRs to produce rate ratios and associated confidence intervals. Mortality in the older OUD group was compared to that in the older non-OUD group to obtain all-cause and cause-specific standardised mortality ratios and 95% confidence intervals.

The final analysis included only the older OUD group. A competing risks Cox regression model (Lunn and McNeil, 1995) was generated, comparing the hazard of death from accidental drug-related causes, suicide, accidental injury (together, the three most common external causes of death in the cohort), liver-related causes, cardiovascular disease, cancer (together, the three most common disease-related causes of death) and all other causes of death. In order to create mutually exclusive categories, liver cancer deaths were excluded from the cancer category and included in the liver-related category. Hazard ratios are reported for the three most common external causes of death, and the three most common disease-related causes of death.

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Statistical analyses were completed in SAS v9.3 (SAS Institute, Cary, NC). Given the large sample size and potential for type 1 errors, care was taken in interpreting associations that were statistically significant, but potentially spurious. Only those risk ratios and hazard ratios of 2.0 or greater, or 0.5 or less, with 95% confidence intervals excluding 1.0, were interpreted as being potentially clinically important (Grimes and Schulz, 2012).

3. RESULTS

The older OUD cohort comprised 36,608 patients (97.3% male) with a median age of 55 years at cohort entry (Table 1). Compared to younger OUD, older OUD were more likely to be male and less likely to be Caucasian or 'other' race. By design, the older non-OUD patients were of the same age and sex as the older OUD patients; however, older OUD were more likely than older non-OUD to be African American.

Older OUD patients were significantly more likely than younger OUD patients to have a Charlson Comorbidity Index of greater than zero, and significantly more likely to have been diagnosed with hepatitis C, HIV, chronic pain, neuropathy, mood disorder and post-traumatic stress disorder. Younger OUD patients, however, were significantly more likely than older OUD patients to have been diagnosed with alcohol use disorder or non-opioid drug use disorder. Compared to older non-OUD patients, older OUD patients were significantly more likely to have a Charlson Comorbidity Index of greater than zero, and significantly more likely to have been diagnosed with all disorders included in the analysis.

There were 6,754 deaths in the older OUD patient group, giving an all-cause CMR of 36.2 per 1,000 person-years (Table 2). Overall, older OUD were twice as likely to die compared to younger OUD (RR=2.2; 95% CI: 2.2, 2.3) (Table 3). Older and younger OUD showed similar risks for drug-related and traumatic (suicide, violent, or accidental injury) deaths; in other words, mortality risks typically associated with younger OUD did not decline with age. As may be expected, older OUD were more likely than younger OUD to die from all assessed diseases, with the exception of HIV infection.

Older OUD patients had a statistically significant increase in mortality risk (RR1.6, 95% CI: 1.5, 1.6) compared tonon-OUD of the same age and sex, although this difference did not meet our criteria for clinical significance (Table 3). Among both older groups, the majority of deaths were accounted for by three causes: cardiovascular disease, cancer and liver-related causes. With the exception of HIV-related deaths (RR 2.7; 95% CI: 2.2, 3.2) and liver-related deaths (RR 3.0; 95% CI: 2.8, 3.1), there was insufficient evidence to suggest that older OUD died of disease-related causes at greater rates than their non-OUD peers. The greatest elevation in risk for older OUD compared to older non-OUD was for accidental drug-related deaths (RR 9.5; 95% CI: 8.7, 10.3), suggesting ongoing opioid and other drug use in older OUD. Older OUD also had clinically important elevations in suicide (RR 2.1; 95% CI: 1.7, 2.4) and violent (RR 2.0; 95% CI: 1.3, 2.7) deaths compared to non-OUD peers.

Although a number of associations between diagnoses and specific causes of death were statistically significant, there were very few clinically important indicators of cause-specific

mortality risk (Table 4). The small proportion of participants with unknown ethnicity showed elevated mortality for all six specific causes of death examined. None of the diagnoses examined were clinically important predictors of accidental drug-related, suicide, or accidental injury deaths. A Charlson Comorbidity Index of greater than 1 was associated with elevated cardiovascular (adjusted hazard ratio (HR): 2.18; 95% CI: 1.96, 2.43) and cancer (adjusted HR: 2.00; 95% CI: 1.79, 2.24) mortality risk, but no specific diagnoses predicted cardiovascular or cancer deaths. Male sex (adjusted HR 3.09; 95% CI: 1.38, 6.90) and hepatitis C virus infection (adjusted HR 3.58; 95% CI: 3.11, 4.12) were associated with increased risk of liver-related death.

4. DISCUSSION

In this study we found that, in contrast to younger people with an OUD, older people with an OUD are more likely to die from chronic illness than drug-related causes. This is consistent with studies in other settings (Beynon et al., 2010; Ødegård et al., 2007). Unlike some studies (Beynon et al., 2010), we did not observe a decrease in drug-related deaths with age. Our findings suggest that mortality risks traditionally associated with OUD – overdose, suicide and other unnatural deaths – may not decline with age, and are augmented by diseases associated with aging.

We have extended the existing research by examining specific causes of death in older people with OUD and comparing to mortality in same-age peers without OUD. The most common causes of death in older adults with OUD were similar to those for older people more generally; namely, cardiovascular disease and cancer. With the exception of HIV and liver-related causes, older OUD died from disease-related causes at similar or only slightly higher rates as their peers of the same age and sex without an OUD.

This study has also extended on previous research by attempting to identify predictors for some of the most common causes of death among older people with OUD. No diagnoses were found to be clinically important predictors of unnatural deaths. A Charlson Comorbidity Index of 1 or greater was predictive of cardiovascular and cancer mortality, but no specific diagnoses were identified that would suggest an elevated risk of cardiovascular or cancer death. Hepatitis C infection was predictive of liver-related death, suggesting opportunities to improve access to, and uptake of, hepatitis C antiviral therapies in this population.

These findings suggest that older adults with an OUD have complex health needs compared to both younger adults with OUDs, and older adults who do not have an OUD. Older adults with OUDs typically have high rates of mental illness and chronic diseases, as well as long histories of health risks such as cigarette smoking and poor nutrition (Hser et al., 2004; Rosen et al., 2011, 2008). In this sample of older adults with OUD, we observed high rates of comorbid, non-opioid substance use disorders. However, most of the older adults with OUD in this sample died from the same diseases that dominate deaths in older adults generally. Comprehensive health care for this group therefore needs to encompass interventions specific to OUD-related issues as well as standard geriatric care. Several authors have suggested the need for specialised training in addiction medicine for

geriatricians, and vice versa (Koechl et al., 2012; Rosen et al., 2008). Given our findings, we would add to this a recommendation for access to hepatitis C virus screening, treatment and care. Furthermore, given ongoing overdose mortality into older age, there is a need for overdose prevention interventions such as take-home naloxone across the lifespan, as well as greater access to opioid substitution therapy, which more than halves fatal overdose risk among opioid dependent persons (Degenhardt et al., 2011).

4.1 Limitations

This study used a large, national sample of opioid users and matched comparators, and to our knowledge is the only study to have compared mortality rates in older adults with OUD to older adults without OUD. Because this was an observational study with a large sample size, we took care not to place undue importance on small effect sizes that may have been a result of bias or unmeasured confounding (Grimes and Schulz, 2012). The study sample was limited to people who use VA health care services, which may affect the generalizability of findings. We identified people with OUD on the basis of lifetime diagnosis and assumed chronicity of disorder, but some people in each OUD group may have ceased opioid use. This would likely bias mortality rates downwards, as cessation of opioid use would lower drug-related mortality risk. However, opioid dependence is a chronic, relapsing disease with low remission rates (Calabria et al., 2010; Hser et al., 2007) and the similarity in drug-related mortality rates of older and younger OUD suggests that ongoing opioid use was a concern in this sample.

We utilized clinical data gathered during the provision of standard care, and it is possible that a more extensive diagnostic interview would have identified additional cases of OUDs or any of the other clinical conditions examined within the study. Inclusion of nicotine dependence in our analyses may have provided further insight into risk factors for specific causes of death. Furthermore, the sample contained few women, and as there are sex differences in the health of older adults who use opioids (Grella and Lovinger, 2012) and in mortality patterns in general, there are likely to be sex differences in mortality of older adults with OUD that we were not able to identify with these data.

4.2 Conclusions and future directions

The number of older adults with OUD is increasing, and will continue to do so for some time (Han et al., 2009). It is not clear that diagnostic information from electronic health records is useful for identifying people with OUD who are at higher risk of non-natural death, suggesting that interventions to address these causes of death may be best delivered universally to people with OUD. Although causes of death usually associated with OUD occurred in older adults with OUD at similar rates as in younger adults with OUD, the majority of older adults with OUD died of chronic diseases. There is an urgent need to explicate models of care that integrate OUD-related treatment and care with general medical care for older adults.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Role of the funding source

No funders had any role in the design of this study, the data analysis or interpretation, the writing of the manuscript, or the decision to submit for publication.

Conflict of interest

LD has received untied educational grants from Reckitt Benckiser for the post-marketing surveillance of opioid substitution therapy medications in Australia, the development of an opioid-related behavior scale, and a study of opioid substitution therapy uptake among chronic non-cancer pain patients. LD has also received untied educational grants from Mundipharma to conduct surveillance of the use of Oxycontin in Australia. All such studies' design, conduct and interpretation of findings are the work of the investigators; the funders had no role in those studies. Neither funder had any knowledge of this manuscript.

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Highlights

- We examined mortality in older (>50 years) adults with opioid use disorders
- Drug-related and traumatic mortality rates among older adults with OUD do not decline with age, and are augmented by chronic disease deaths
- Health care for this group requires interventions to address opioid-related mortality risk, as well as general geriatric care

Table 1

Demographic characteristics and diagnoses of older (≥50 years) opioid use disorder, younger (<50 years) opioid use disorder and older (≥50 years) no opioid use disorder VA patients, FY2000–2011

Characteristic	Older opioid use disorder (n=36,608) n (%)	Younger opioid use disorder (n=23,662) n (%)	Older no opioid use disorder (n=36,608) n (%)
Sex			
Male	35,617 (97.3)	21,548 (91.1)[b]	35,617 (97.3)
Female	991 (2.7)	2114 (8.9)	991 (2.7)
Median age in years at cohort entry (range)	55 (50–95)	44 (18–49)[b]	55 (50–96)
Race			
African American	12,925 (35.3)	7,331 (31.0)[b]	6,530 (17.8)[b]
Caucasian	21, 696 (59.3)	14,896 (63.0)	24,456 (66.8)
Other[a]	1,987 (5.4)	1,435 (6.1)	5,622 (15.4)
Ethnicity			
Hispanic	2,183 (6.0)	1,317 (5.6)	1,806 (4.9)[b]
Non-Hispanic	31,588 (86.3)	20,543 (86.8)	28,742 (78.5)
Unknown	2,837 (7.8)	1,802 (7.6)	6,060 (16.6)
Charlson comorbidity score			
0	17,738 (48.5)	17,369 (73.4)[b]	20,084 (54.9)[b]
≥1	18,870 (51.5)	6,293 (26.6)	16,524 (45.1)
Hepatitis C virus	8,982 (24.5)	2,843 (12.0)[b]	1,866 (5.1)[b]
HIV	1,020 (2.8)	592 (2.5)*	284 (0.8)[b]
Chronic pain	21,538 (58.8)	11,575 (48.9)[b]	17,566 (48.0)[b]
Headache	2,608 (7.1)	2,329 (9.8)[b]	1,708 (4.7)[b]
Neuropathy	1,702 (4.7)	455 (1.9)[b]	1,390 (3.8)[b]
Alcohol use disorder	10,724 (29.3)	7,485 (31.6)[b]	3,188 (8.7)[b]
Non-opioid drug use disorder	12,027 (32.9)	8,755 (37.0)[b]	1,731 (4.7)[b]
Mood disorder	15,922 (43.5)	9,942 (41.9)[b]	8,335 (22.8)[b]
Post-traumatic stress disorder	8,799 (24.0)	3,422 (14.5)[b]	4,454 (12.2)[b]
Other anxiety disorder	4,999 (13.7)	3,413 (14.4)[c]	2,752 (7.5)[b]
Schizophrenia	2,774 (7.6)	1,880 (8.0)	1,554 (4.2)[b]

[a] Includes Native American, Asian/Pacific Islander, multi-racial and unknown.

[b] Statistically significant difference between older OUD group and comparison group, χ^2 $p<.0001$.

[c] Statistically significant difference between older OUD group and comparison group, χ^2 $p<.05$.

Table 2

All-cause and cause-specific mortality rates in older (≥50 years) opioid use disorder, younger (<50 years) opioid use disorder and older (≥50 years) no opioid use disorder VA patients, FY2000–2011

	Older opioid use disorder (n=36,608; 186,750 py)		Younger opioid use disorder (n=23,662; 161,374 py)		Older no opioid use disorder (n=36,608; 192,999 py)	
Cause of death[a]	**N (%) deaths**	**CMR per 1,000 py (95% CI)**	**N (%) deaths**	**CMR per 1,000 py (95 % CI)**	**N (%) deaths**	**CMR per 1,000 py (95% CI)**
All cause	6,754 (100)	36.2 (35.3, 37.0)	2,632 (100)	16.3 (15.7, 16.9)	4,407 (100)	22.8 (22.2, 23.5)
Drug-related	659 (9.8)	3.5 (3.3, 3.8)	676 (25.7)	4.2 (3.9, 4.5)	79 (1.8)	0.4 (0.3, 0.5)
Accidental drug-related	562 (8.3)	3.0 (2.8, 3.3)	551 (20.9)	3.4 (3.1, 3.7)	61 (1.4)	0.3 (0.2, 0.4)
Suicide	149 (2.2)	0.8 (0.7, 0.9)	132 (5.0)	0.8 (0.7, 1.0)	75 (1.7)	0.4 (0.3, 0.5)
Violence	35 (0.5)	0.2 (0.1, 0.3)	49 (1.9)	0.3 (0.2, 0.4)	18 (0.4)	0.09 (0.06, 0.1)
Accidental injuries	193 (2.9)	1.0 (0.9, 1.2)	100 (3.8)	0.6 (0.5, 0.7)	113 (2.6)	0.6 (0.5, 0.7)
Cancer	1,518 (22.5)	8.1 (7.7, 8.5)	305 (11.6)	1.9 (1.7, 2.1)	1,240 (28.1)	6.4 (6.1, 6.8)
HIV	124 (1.8)	0.7 (0.6, 0.8)	92 (3.5)	0.6 (0.5, 0.7)	47 (1.1)	0.2 (0.2, 0.3)
Cardiovascular disease	1,711 (25.3)	9.2 (8.7, 9.6)	523 (19.9)	3.2 (3.0, 3.5)	1,367 (31.0)	7.1 (6.7, 7.5)
Liver-related	1000 (14.8)	5.4 (5.0, 5.7)	375 (14.2)	2.3 (2.1, 2.6)	349 (7.9)	1.8 (1.6, 2.0)
Chronic respiratory disease	411 (6.1)	2.2 (2.0, 2.4)	79 (3.0)	0.5 (0.4, 0.6)	254 (5.8)	1.3 (1.2, 1.5)
Respiratory infections	103 (1.5)	0.6 (0.5, 0.7)	26 (1.0)	0.2 (0.1, 0.2)	71 (1.6)	0.4 (0.3, 0.5)
Diabetes	181 (2.7)	1.0 (0.8, 1.1)	72 (2.7)	0.4 (0.3, 0.6)	199 (4.5)	1.0 (0.9, 1.2)

[a]Causes of death are neither mutually exclusive nor exhaustive.

CMR: crude mortality rate. py: person-years. CI: confidence interval. Sex-disaggregated data are provided in the Supplementary Materials2.

Table 3

Relative risk of death in older (≥50 years) adults with opioid use disorder, compared to younger (<50 years) adults with opioid use disorder and older (≥50 years) adults without opioid use disorder, VA patients, FY2000–2011

Cause of death	Relative risk (95% CI) of death in older adults with opioid use disorder (n=36,608), compared to:	
	Younger opioid use disorder (n=23,662)[a]	Older no opioid use disorder (n=36,608)[b]
All cause	2.2 (2.2, 2.3)	1.6 (1.5, 1.6)
Drug-related	0.8 (0.8, 0.9)	8.6 (8.0, 9.3)
Accidental drug-related	0.9 (0.8, 1.0)	9.5 (8.7, 10.3)
Suicide	1.0 (0.8, 1.1)	2.1 (1.7, 2.4)
Violence	0.6 (0.4, 0.8)	2.0 (1.3, 2.7)
Accidental injuries	1.7 (1.4, 1.9)	1.8 (1.5, 2.0)
Cancer	4.3 (4.1, 4.5)	1.3 (1.2, 1.3)
HIV	1.2 (1.0, 1.4)	2.7 (2.2, 3.2)
Cardiovascular disease	2.8 (2.7, 3.0)	1.3 (1.2, 1.4)
Liver-related	2.3 (2.2, 2.4)	3.0 (2.8, 3.1)
Chronic respiratory disease	4.5 (4.1, 4.9)	1.7 (1.5, 1.8)
Respiratory infections	3.4 (2.8, 4.1)	1.5 (1.2, 1.8)
Diabetes	2.2 (1.9, 2.5)	0.9 (0.8, 1.1)

CI=confidence interval.

[a] Older opioid use disorder CMR/younger opioid use disorder CMR.

[b] Older opioid use disorder CMR/Older, no opioid use disorder CMR. Sex-disaggregated data are provided in the Supplementary Materials3.

Table 4

Competing risks Cox regression model of common causes of death among older (≥50 years) VA patients with opioid use disorders, FY2000–2011

	Adjusted hazard ratio (95% CI)					
	Accidental drug-related	**Suicide**	**Accidental injury**	**Liver-related**	**Cardiovascular**	**Cancer[a]**
Age at cohort entry	0.95 (0.93, 0.96)	1.01 (0.99, 1.04)	1.02 (1.00, 1.04)	1.00 (0.98, 1.01)	1.05 (1.05, 1.06)	1.05 (1.05, 1.06)
Male sex	0.86 (0.53, 1.37)	1.23 (0.45, 3.34)	2.20 (0.54, 8.98)	3.09 (1.38, 6.90)	1.80 (1.18, 2.74)	1.34 (0.88, 2.05)
Race						
Caucasian	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
African American	0.67 (0.54, 0.81)	0.13 (0.06, 0.26)	0.53 (0.37, 0.76)	0.68 (0.58, 0.78)	0.84 (0.75, 0.94)	1.04 (0.93, 1.17)
Other	0.52 (0.34, 0.80)	0.99 (0.56, 1.75)	0.30 (0.13, 0.68)	0.78 (0.59, 1.04)	0.65 (0.52, 0.81)	0.65 (0.50, 0.84)
Ethnicity						
Non-Hispanic	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Hispanic	1.31 (0.96, 1.80)	0.28 (0.09, 0.89)	0.70 (0.34, 1.41)	1.80 (1.47, 2.19)	0.89 (0.71, 1.11)	0.95 (0.76, 1.20)
Unknown	3.63 (2.90, 4.55)	2.70 (1.75, 4.18)	4.04 (2.83, 5.78)	2.72 (2.26, 3.27)	2.94 (2.58, 3.34)	2.34 (2.02, 2.71)
Charlson index ≥1	1.24 (1.03, 1.49)	0.80 (0.56, 1.13)	1.37 (1.01, 1.87)	1.89 (1.63, 2.19)	2.18 (1.96, 2.43)	2.00 (1.79, 2.24)
HIV infection	1.12 (0.71, 1.77)	0.56 (0.08, 4.05)	0.60 (0.19, 1.91)	0.86 (0.63, 1.20)	0.77 (0.55, 1.07)	0.97 (0.78, 1.29)
Hepatitis C infection	1.59 (1.31, 1.92)	0.94 (0.60, 1.48)	1.32 (0.93, 1.87)	3.58 (3.11, 4.12)	0.88 (0.78, 1.00)	1.44 (1.27, 1.63)
Chronic pain	1.07 (0.89, 1.27)	1.34 (0.93, 1.91)	0.85 (0.63, 1.15)	0.71 (0.63, 0.81)	1.00 (0.90, 1.11)	0.87 (0.78, 0.97)
Alcohol use disorder	0.80 (0.65, 0.99)	0.81 (0.53, 1.23)	1.49 (1.06, 2.09)	1.69 (1.46, 1.96)	0.97 (0.86, 1.09)	1.10 (0.97, 1.25)
Non-opioid drug use disorder	1.45 (1.19, 1.76)	1.39 (0.93, 2.09)	1.06 (0.74, 1.51)	0.85 (0.73, 0.99)	1.12 (0.99, 1.26)	1.06 (0.93, 1.20)
Mood disorder	1.15 (0.95, 1.38)	1.62 (1.13, 2.32)	1.10 (0.80, 1.52)	0.80 (0.69, 0.92)	1.10 (0.99, 1.23)	0.94 (0.84, 1.05)
Post-traumatic stress disorder	0.97 (0.80, 1.18)	0.87 (0.59, 1.28)	1.20 (0.86, 1.66)	0.78 (0.67, 0.91)	0.86 (0.76, 0.97)	0.88 (0.77, 1.00)
Other anxiety disorder	1.44 (1.16, 1.79)	1.10 (0.72, 1.69)	0.83 (0.53, 1.29)	0.89 (0.73, 1.09)	1.22 (1.06, 1.40)	0.90 (0.76, 1.06)
Schizophrenia	0.96 (0.71, 1.30)	0.84 (0.41, 1.72)	0.71 (0.39, 1.32)	0.83 (0.66, 1.06)	1.18 (0.99, 1.40)	1.15 (0.96, 1.38)

Causes of death are mutually exclusive.

[a]Not including liver cancer deaths, which are counted under liver-related deaths.