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Causes of death among U.S. Veterans with a prior nonfatal opioid overdose

Sara Warfield[a,b,c,*], **Elizabeth Karras**[a,c,d], **Christa Lilly**[e], **Michael Brumage**[c,f], **Robert M. Bossarte**[a,b,c,g]

[a]Center of Excellence for Suicide Prevention, Department of Veterans Affairs, 400 Fort Hill Avenue, Canandaigua, NY, 14424, USA

[b]Department of Epidemiology, School of Public Health, West Virginia University, 64 Medical Center Drive, P.O. Box 9190, Morgantown, WV, 26506, USA

[c]Injury Control Research Center, West Virginia University, 3606 Collins Ferry Rd, Suites 201 & 202, Morgantown, WV 26505, USA

[d]Department of Psychiatry, University of Rochester, 601 Elmwood Avenue, Rochester, NY, 14642, USA

[e]Department of Biostatistics, West Virginia University, 64 Medical Center Drive, P.O. Box 9190, Morgantown, WV, 26506, USA

[f]Department of Occupational Medicine, West Virginia University, 64 Medical Center Drive, P.O. Box 9190, Morgantown, WV, 26506, USA

[g]Department of Behavioral Medicine and Psychiatry, West Virginia University, 64 Medical Center Drive, P.O. Box 9190, Morgantown, WV, 26506, USA

Abstract

Background: For over a decade, there has been a surge in opioid-related morbidity and mortality among Veterans. To better understand the impact of the growing epidemic, it is important to identify the cause-specific mortality rates among Veterans with a prior nonfatal opioid overdose.

Methods: We followed 8370 Veterans who received medical care for a nonfatal opioid overdose between 2011 through 2015.Mortality records were linked to clinical records from the Veterans Health Administration (VHA). We compared the mortality rates among those with a nonfatal opioid overdose to a 5 % stratified random sample of patients accessing services during the same time period. SMRs were calculated using age-adjusted cause-specific mortality rates for the l U.S.

[*]Corresponding author at: Research Ridge Office Suites, 3606 Collins Ferry Rd, Suites 201 & 202, Morgantown, WV, 26505, USA. scwarfield@hsc.wvu.edu (S. Warfield).

Contributors

Sara Warfield conceived the idea for the report, performed the analysis and contributed to writing the manuscript. Elizabeth Karras-Pilato provided feedback to the manuscript and helped provide access to the data. Christa Lilly provided input on interpreting data analysis and feedback to the manuscript. Michael Brumage provided feedback and edits to the manuscript. Robert Bossarte served as the senior scientist and worked with Sara on obtaining data, interpreting data analysis, and provided critical revision of the articles. All authors have read and approved the final manuscript.

Declaration of Competing Interest

All authors declare they have no conflict of interest. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Department of Veterans Affairs.

population obtained from the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER).

Results: The crude mortality for Veterans with a history of a nonfatal overdose was 370.6 per 10,000 person years. Those with a prior nonfatal overdose had a higher risk of substance-related mortality (aHR [adjusted Hazard Ratio] 5.0), including a higher risk of death from drugs (aHR 6.9) and alcohol (aHR 2.7). Similarly, cause-specific mortalities assessed between Veterans and the U.S. population, SMRs were also highest for deaths associated with substances (114.0).

Conclusion: Veterans with a prior nonfatal overdose experienced substantially higher mortality rates compared to other Veterans or the general U.S. population. Causes of death related to substance use and mental health were significantly higher than other causes of death, highlighting the importance of integrated treatment and substance use services.

Keywords

Opioid overdose; Drug mortality; Veterans; Overdose

1. Introduction

Overdoses have surged in the past decade and are now the leading cause of accidental death in the United States. More than 60 % of overdose deaths across the nation can be attributed to opioids (Hedegaard et al., 2017; Rudd et al., 2016a, b; Scholl et al., 2019; Seth et al., 2018). Between 2007 and 2017 the opioid overdose death rate more than doubled, from 6.1 per 100,000 to 14.9 per 100,000 (Centers for Disease Control and Prevention, 2018). Around the same time, nonfatal opioid overdoses resulting in inpatient and emergency department visits substantially increased, by more than 60 % and 99 % respectively (Weiss et al., 2017). The rise in opioid overdoses across the United States has been estimated to cost more than $740 million annually (Hsu et al., 2017). Despite the recent surge of nonfatal overdoses and associated mortality associated with opioid abuse/misuse, little is known regarding the patterns of mortality following a nonfatal opioid overdose.

People who inject drugs (PWID), people diagnosed with an opioid use disorder (OUD) and those taking more than 90 morphine milligram equivalent (MME) are at highest risk for experiencing an opioid overdose (Baumblatt et al., 2014; Hall et al., 2008; Paulozzi, 2012; Paulozzi et al., 2011). Further, the type of opioid used has a direct impact on overdose risk and subsequent mortality; heroin and synthetic opioids attributing to the most recent surges in opioid overdoses in the U.S. (Hedegaard et al., 2020; Olfson et al., 2018). Although overdoses are the leading cause of death among PWID, research has found that PWID more often die from infection-related causes such as human immunodeficiency virus (HIV), Hepatitis C (HCV), and other substance-related deaths (Degenhardt et al., 2014; Mathers et al., 2013; Tyndall et al., 2001). Similarly, research suggests that people with an OUD more often die from infectious disease and liver disease when compared to the general population (Degenhardt et al., 2014; Larney et al., 2015). Patients taking a high volume of MME are often suffering from terminal cancer or chronic diseases associated with severe pain (Baumblatt et al., 2014; Paulozzi, 2012; Paulozzi et al., 2012). Several public health interventions have been developed to encourage safer prescribing practices

and educate patients on opioid use, especially for those with high MME such as those with chronic non-cancer pain (Baumblatt et al., 2014; Brady et al., 2016). Although many of these programs have been found to reduce the supply of prescription opioids (Paulozzi et al., 2011), there is still little known regarding the complex nature of overdose and subsequent mortality. Research among Medicaid enrollees suggests that mortality following a nonfatal overdose are often associated with substances, suicide, cancer, and the circulatory system; however, cause-specific mortality among Veterans using VHA services has yet to be examined (Olfson et al., 2018). The objective of this study is to assess the cause specific mortality among Veterans with a documented nonfatal opioid overdose. In order to describe the mortality for specific causes of deaths among Veterans with a nonfatal overdose, we will examine the mortality following a nonfatal overdose to a comparison group comprised of a 5 % random sample of other veterans using VHA services. We will then compare the mortality among Veterans with a nonfatal opioid overdose to the general population.

Given previous research examining mortality among Veterans with an OUD, we expected substance-related deaths to be significantly higher among this population (Bohnert et al., 2012, 2016; Degenhardt et al., 2014; Larney et al., 2015; Olfson et al., 2018). We also expected suicide death rates to be substantially higher given that Veterans have almost double the suicide death rate than the general population and previous research suggest that people with a history of a nonfatal overdose had higher suicide death rates (Veterans Health Administration, 2019; Bohnert et al., 2017; Olfson et al., 2018). Similarly, we expected deaths attributed to hepatitis to be significantly higher among our Veteran cohort, given that prevalence of hepatitis is two-times higher than civilians and is higher among those with a history of drug use (Backus et al., 2013; Degenhardt et al., 2014; Dominitz et al., 2005; Larney et al., 2015; Mishra et al., 2003).

2. Methods

2.1. Sources of data

In order to determine mortality following a nonfatal overdose among Veterans, we examined causes of death by linking clinical and mortality files from the Veterans Health Administration (VHA), which is the largest integrated healthcare system in the United States. We extracted records on individuals with a documented opioid overdose between January 1, 2011 and September 30, 2015 and identified corresponding causes of death, if any, among this cohort.

The study cohort examined clinical and death records for 10,522,835 records to identify Veterans with a documented opioid overdose and Veterans with no documented overdose for the comparison group. Veterans were identified as having an opioid overdose using clinical records from the VHA Corporate Data Warehouse (CDW; (Murphy et al., 2002). CDW records were linked with the VA/DoD Mortality Data Repository (MDR), using Social Security Numbers (SSNs; (Bossarte and Schneiderman, 2017; Statistics, 2013). All-cause mortality data for the VA/DoD SDR was obtained from the National Death Index (NDI). Sex and age were extracted from the SDR and CDW. Age was fixed and determined at the start of the study period. Age-adjusted mortality rates for each cause of death of interest were pulled from the Centers for Disease Control and Prevention Wide-Ranging Online Data

for Epidemiologic Research (CDC WONDER) Detailed Compressed Mortality Files from 2011 through 2015 (2018). To more precisely compare age-adjusted mortality rates with the Veteran population we pulled age-adjusted rates among 15–84 year old U.S. residents using CDC WONDER.

This study was reviewed and approved by the Institutional Review Board at the Syracuse VA Medical Center, New York.

2.2. Study sample

A nonfatal opioid overdose was identified using International Classification of Disease, Ninth Edition (ICD-9) codes: 965.00–965.02, 965.09, E850.0-E850.2 and ICD Tenth Edition (ICD-10) codes: X40-X44, X60-X64, X85, Y10-Y14 with secondary axis codes: T40.0-T40.4 and T40.6. The first opioid overdose documented in the clinical records was used as the index overdose. Those who died from a fatal index overdose were excluded from analyses. Among this nonfatal opioid overdose cohort roughly one third of the overdose cohort (n = 2659) experienced a nonfatal repeat opioid overdose.

A control group was constructed by extracting a 5 % random sample of Veterans, stratified by sex and age. Age was collapsed into three categories: ages 18–44, 45–64 and over 65 years old. Pulling a stratified random sample allowed the control group to be similar in composition to those with a nonfatal overdose (Gebregziabher et al., 2012). Given that VHA users are primarily older males, we intentionally stratified by sex and age to reduce potential bias that may influence observed mortality among the control group. The use of stratified random sample control populations has been used in previous research among the VHA patient population (Gradus et al., 2013; Park et al., 2015).

2.3. Exclusion criteria

The study cohort was restricted to Veterans between 18 and 90 years old. We excluded patients that had no follow-up visits within one year of the first overdose event or had a nonfatal overdose in the last three months of the study period (October 1, 2015–December 1, 2015). This mitigated potential bias among those with less than three months of risk for mortality. After applying this inclusion and exclusion criteria, 8370 Veterans were identified for the nonfatal overdose group and 325,073 Veterans with no documented overdose as the comparison group.

2.4. Mortality

We evaluated mortality from January 1, 2011 through December 31, 2015. Follow-up for the study ended the day the Veteran died or the end of the study period, whichever occurred first. In addition to all-cause mortality, cause-specific mortality was considered for the following: all external causes of death, suicide, homicide, accidents, substance-related deaths, drug-related deaths, alcohol-related deaths, infectious, viral hepatitis, human immunodeficiency virus (HIV), circulatory system, respiratory system, influenza, chronic respiratory disease, digestive system, cirrhosis and alcoholic liver disease and cancers. Specific types of cancers were categorized into the following groups using the International Classification of Diseases for Oncology (Fritz, 2013): lung and bronchus, liver and

intrahepatic bile duct, digestive system cancers, which included esophageal, stomach, small intestine, colon, rectal, anal, gallbladder and pancreatic cancers, lymphoma and leukemia and other cancers. (See Supplement Table A for the full list of cause-specific mortality and corresponding ICD-10 codes).

2.5. Analysis

We identified person-years of follow-up and mortality rates per 10,000 person-years for the entire cohort to compare mortality among Veterans with a history of nonfatal overdose to a comparison group of Veterans. Crude death rates were calculated and mortality rates were estimated using Cox proportional hazard models, adjusting for age and sex. Survival curves were relatively close, indicating the hazard ratio remained constant over time (Kleinbaum and Klein, 2010). Adjusted hazard ratios [aHR] and corresponding 95 % confidence interval [CI] were calculated for cause-specific mortality.

We calculated the standardized mortality rate ratios (SMRs) to compare the observed number of deaths among our overdose cohort to the number of expected number based on rates of mortality among members of the U.S. general population (Le and Eberly, 2016; Szklo and Nieto, 2014). The expected number of deaths was calculated using age-adjusted mortality rates from CDC WONDER and corresponding cohort size (Centers for Disease Controla and Prevention, 2018). (See Supplement Table B for the expected cause-specific mortality for the general population).

Alpha was set to 0.05 for all statistical tests. We analyzed data using SAS Enterprise Grid software (version 5.1, SAS Institute Inc.).

3. Results

This study identified 8370 Veterans with a history of nonfatal opioid overdose and a total follow-up of 39,207 person-years. Among this cohort of Veterans with history of a nonfatal overdose, approximately 17.4 % (n = 1453) experienced death during the follow-up period. The proportion of Veterans who died following a nonfatal overdose was similar to the proportion of Veterans who died in the control group (17.6%, n = 57,099). Despite the similar proportion of deaths among each group, there were distinct differences in cause-specific mortality rates and corresponding SMRs. The overall crude mortality rate for Veterans with a prior overdose was 370.6 per 10,000 person-years and for the control group was 384.1 per 10,000 person-years. Compared to the control group, Veterans with a nonfatal opioid overdose had a higher risk of all-cause mortality after adjusting for age and gender (aHR 1.5; 95 % CI 1.4–1.5). (Table 1)

The most common causes of death among Veterans with a prior nonfatal overdose were disorders of the circulatory system (26.7 %), cancer (19.3 %), respiratory disorders (13.1 %), and drug-related deaths (11.6 %). The Veteran cohort with a prior nonfatal overdose was more than six times likely to die from substance-related diseases (aHR [Adjusted Hazard Ratio] 5.0, 95 % CI [Confidence Interval]: 4.4–5.8) and more than six times (aHR 6.9, 95 % CI 5.8–8.1) likely to die from drug-related diseases compared to their Veteran peers. These Veterans were more than three times as likely to die from hepatitis (aHR 3.2, 95 % CI:

2.1–4.9) and cirrhosis or alcoholic liver disease than their Veteran peers (aHR 3.1, 95 % CI: 2.4–3.9). Veterans with a prior overdose were also more than two times more likely to die from suicide than their Veteran peers (aHR 2.2, 95 % CI: 1.6–3.1). Further, these Veterans were twice as likely to die of diseases associated with the digestive system (aHR 2.3, 95 % CI: 1.9–2.8), chronic respiratory disease (aHR 2.2, 95 % CI: 1.6–3.1) and HIV (aHR 2.6, 95 % CI: 1.3–5.4).

Similarly, they had an elevated risk of death from viral hepatitis (aHR 3.2, 95 % CI 2.1–4.9) and cirrhosis and alcoholic liver disease (aHR 3.1, 95 % CI 2.4–3.9). These Veterans had a higher risk of death attributed to HIV (aHR 2.6, 95 % CI 1.3–5.4), cancer of the liver or intrahepatic bile duct (aHR 2.3, 95 % CI 1.7–3.2), or death associated with the digestive system (aHR 2.3, 95 % CI 2.3, 95 % CI 1.9–2.8). Of note, death from suicide was markedly higher among Veterans with a prior nonfatal overdose compared to the control group of Veterans (aHR 2.2, 95 % CI 1.6–3.1). Conversely, Veterans with history of an overdose were significantly less likely to die from lymphoma or leukemia (aHR 0.5, 95 % CI 0.2–0.9) compared to Veterans in the control group.

Among cause-specific mortalities assessed and compared to the US population, SMRs were more than eight times higher among Veterans with a prior overdose. SMRs were highest for deaths associated with substances (114.0, 95 % CI: 98.8–128.7); including drugs (139.3, 95 % CI: 118.6–160.7) and alcohol (72.7, 95 % CI: 53.5–92.4). SMRs for viral hepatitis (107.4, 95 % CI: 65.5–152.7) and liver cancers (68.2, 95 % CI: 47.9–88.7) were substantially higher among Veterans with history of a nonfatal opioid overdose. Other cause-specific disease that were elevated in this population include HIV (34.9, 95 % CI: 10.7–58.9), suicide (29.0, 95 % CI: 20.0–38.2), and deaths related to the digestive system (45.2, 95 % CI: 36.7–53.7). (Table 2)

4. Discussion

4.1. Mortality comparison

Veterans with a documented nonfatal opioid overdose died at 26 times the rate of the general U.S. population aged 15–84 years. Moreover, mortality was markedly higher among Veterans with a prior nonfatal overdose when compared to a comparison population of Veterans who use VHA services or the general U.S. population (aHR 1.46, 95 % CI: 1.39–1.54). These findings suggest that excess mortality among Veterans with a prior nonfatal overdose may be associated with patterns and consequences of substance use. Mortality associated with substance use for Veterans with a prior nonfatal overdose was significantly elevated among those with a prior nonfatal overdose. The rate of alcohol-related deaths was 72 times higher than the rate of alcohol-related deaths in the general population. These findings underscore the need for further understanding on the trajectory of substance use, patterns of co-occurring substance use disorders and complex treatment needs among this Veteran cohort.

Similarly, Veterans with a prior nonfatal overdose had noticeably higher rates of death compared to other Veterans, specifically for deaths associated with drugs (aHR 6.85 95 % CI: 5.79–8.09), viral hepatitis (aHR 3.22, 95 % CI: 2.11–4.93), cirrhosis and alcoholic liver

disease (aHR 3.05, 95 % CI 2.38–3.90). These findings suggest excess mortality among Veterans with a nonfatal overdose can be largely attributed to substance misuse. Further, mortality suggest polysubstance use among Veterans given the elevated alcohol-related deaths among Veterans described further in Tables 1 and 2. Additional research is needed to understand the intersection of comorbid substance use, mental health, and other structural factors (e.g., homelessness) that could influence the relationship between overdose risk and subsequent mortality among Veterans.

4.2. Comparison to other research

There were some distinct differences when comparing results from this study to an existing study examining mortality following a nonfatal overdose among a sample of Medicaid enrollees (Olfson et al., 2018). The all-cause SMR and drug-related deaths were similar between both the Veteran population and Medicaid enrollees. In general, the cause-specific deaths listed in both studies were elevated among the Veteran population and HIV was the only cause-specific death in both studies that was lower among the Medicaid population. The most notable difference in our study was the SMR for alcohol-related deaths, the Veteran population had an SMR more than seven times higher than the Olfson article. However, deaths from an opioid overdose appeared to be slightly lower among those Veterans with a prior nonfatal overdose compared to a Medicaid cohort with a prior opioid overdose (Goldman-Mellor et al., 2020). Deaths associated with cirrhosis and alcoholic liver disease were more than four times higher and deaths associated with viral hepatitis were more than three times higher. This finding may be attributed to high rates of HCV among Veterans from the Vietnam Era (Backus et al., 2013; Dominitz et al., 2005; Mishra et al., 2003). Further, elevated alcohol-related deaths underscore the need for tailored treatment approaches and the complex treatment needs for veterans who misuse substances. Additional research is needed to understand the period of substance use to determine ways to develop appropriate treatment approaches. In addition, external factors such as financial hardship, housing instability, social pressures should be further examined in conjunction with clinical characteristics to determine the influence of overdose risk and subsequent mortality (Grant et al., 2004).

These findings parallel previous research suggesting a deeper understanding of the complex relationship between overdose and selfharm (Bohnert et al., 2013, 2010; Bohnert et al., 2017; Rockett et al., 2010). Importantly, deaths from suicide were markedly higher among our cohort of Veterans with a prior opioid overdose compared to the general population and a random sample of Veterans from the VHA using population. This finding alone suggests the need for continued support and comprehensive services aimed at reducing suicide among Veterans. These findings parallel previous research among a California population with a prior nonfatal overdose which show a higher risk of suicide death (Goldman-Mellor et al., 2020). These results highlight the potential impact of integrated mental health services, such as post-discharge psychiatric care, which may benefit patients with history a nonfatal overdose (Bohnert et al., 2018; Vallersnes et al., 2018, 2019). A documented overdose may provide opportunities to initiate treatment or other prevention programs such as naloxone distribution or provide mental health screening given the elevated mortality associated with suicide and substance-related deaths in clinical settings.

4.3. Strengths and limitations

Although this study utilized data from one of the nation's largest healthcare networks, analyses were contingent on patients seeking medical care for healthcare needs such as an overdose. The large sample size provided the statistical power needed to detect differences in risk for mortality. Despite the large sample size, this study had several limitations. Previous studies have shown that barriers often impede healthcare treatment for OUD, which could influence findings from this study (Gordon et al., 2011). Results from this study may underestimate the magnitude of nonfatal overdoses and subsequent mortality among Veterans (Di Rico et al., 2018). Furthermore, these results may not be generalizable to the US population given the heterogeneous composition of Veterans seeking healthcare (Department of Veterans Affairs, 2017; Dursa et al., 2016; Young et al., 2000).

5. Conclusion

Given the rise in opioid overdoses across the US, there is an urgent need to understand excess mortality among people who experience a nonfatal overdose to inform future clinical and public health efforts. Veterans with a history of nonfatal overdose are significantly more likely to die from any cause, specifically deaths associated with substance use and suicide. Additional research is needed to determine the relationship between psychiatric diagnoses, substance use and overdose risk over time. These findings underscore the need for coordinated health care, with particular emphasis on mental health care among those with a prior overdose.

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Table 1

Mortality rate (per 10,000 person-years) among veterans with a nonfatal index OD (n = 8370) compared to a 5 % stratified random sample of veterans (n = 325,073).[a]

	Nonfatal OD		Control group		Hazard ratio of mortality	95 % CI Hazard Ratio	Adjusted Hazard ratio of mortality[b]	95 % CI Adjusted Hazard Ratio[b]	p-value[c]
Cause of death	**No. of deaths**	**Crude mortality rate**	**No. of deaths**	**Crude mortality rate**					
Opioid overdose	59	15.05		–	–	–	–	–	–
External Cause of death	69	17.60	1509	10.15	1.74*	(1.36–2.21)	1.82*	(1.43–2.32)	**<0.001**
Suicide	39	9.95	651	4.38	2.27*	(1.65–3.14)	2.24*	(1.62–3.10)	**<0.001**
Homicide	5	1.28	98	0.66	1.93	(0.79–4.75)	1.71	(0.70–4.23)	0.24
Accidents	25	6.38	760	5.11	1.25	(0.84–1.86)	1.43	(0.96–2.13)	0.08
Substance-related	223	56.88	1474	9.91	5.74*	(4.98–6.61)	5.03*	(4.36–5.80)	**<0.001**
Drug-related	169	43.10	871	5.86	7.36*	(6.24–8.68)	6.85*	(5.79–8.09)	**<0.001**
Alcohol-related	54	13.77	603	4.06	3.40*	(2.57–4.49)	2.73*	(2.06–3.61)	**<0.001**
Infectious	55	14.03	1393	9.37	1.50*	(1.14–1.96)	1.89*	(1.44–2.49)	**<0.001**
Viral hepatitis	24	6.12	203	1.37	4.48*	(2.94–6.84)	3.22*	(2.11–4.93)	**<0.001**
HIV	8	2.04	83	0.56	3.66*	(1.77–7.56)	2.63*	(1.27–5.44)	**0.01**
Circulatory system	388	98.96	18,312	123.17	0.80*	(0.73–0.89)	1.29*	(1.16–1.42)	**<0.00**1
Respiratory system	191	48.72	6730	45.27	1.08	(0.93–1.24)	1.87*	(1.61–2.16)	**<0.001**
Influenza & pneumonia	23	5.87	1219	8.20	0.72	(0.47–1.08)	1.32	(0.87–2.00)	0.19
Chronic respiratory disease	139	35.45	4051	27.25	1.30*	(1.10–1.54)	2.18*	(1.83–2.58)	**<0.001**
Digestive system	109	27.80	2036	13.69	2.03*	(1.68–2.46)	2.27*	(1.87–2.75)	**<0.001**
Cirrhosis & alcoholic liver disease	70	17.85	763	5.13	**3.48***	(2.72–4.44)	3.05*	(2.38–3.90)	**<0.001**
Cancers	280	71.42	14,585	98.10	0.73*	(0.65–0.82)	1.00	(0.88–1.12)	0.97
Lung & bronchus	80	20.40	4347	29.24	0.70*	(0.56–0.87)	0.90	(0.72–1.13)	0.38
Liver & intrahepatic bile duct	43	10.97	699	4.70	2.33*	(1.71–3.17)	2.31*	(1.69–3.16)	**<0.001**
Digestive system	42	10.71	2780	18.70	0.57*	(0.42–0.78)	0.77	(0.57–1.05)	0.09
Lymphoma & leukemia	9	2.30	1116	7.51	0.31*	(0.16–0.59)	0.47*	(0.24–0.90)	**0.03**
Other cancers	106	27.04	5643	37.96	0.71*	(0.59–0.86)	1.06	(0.88–1.29)	0.55
Any type of death	1453	370.59	57,099	384.06	0.97	(0.92–1.02)	1.46*	(1.39–1.54)	**<0.001**

Abbreviations: No, Number; CI, Confidence Interval; SMR, Standardized Mortality Rate Ratio; OD, overdose; HIV, human immunodeficiency virus.

[a] For those with a nonfatal OD there were 39,207 person-years follow-up. A control group was constructed using a 5 % random sample of veterans, stratified by sex and age stratum.

[b] Analyses were adjusted for age and sex.

[c] Statistical differences between mortality rates of Veterans with a prior nonfatal OD was compared to Veterans without a prior OD (control group).

Table 2

Standardized Mortality Ratios, observed, and expected number of deaths for veterans with a nonfatal index overdose for all causes and selected causes, 2011-2015.

Cause of death	Nonfatal OD		US Age-adjusted rates[a] Expected number of deaths [b]	Standardized Mortality Rate Ratio (95 % CI)	
	No. of deaths	Crude mortality rate		SMR [b]	95 % CI
Opioid overdose	59	15.05	0.91	64.73	(48.29–81.38)
External Cause of death	69	17.60	4.19	16.47	(12.58–20.35)
Suicide	39	9.95	1.34	29.01	(19.97–38.24)
Homicide	5	1.28	0.54	9.25	(1.14–17.38)
Accidents	25	6.38	2.30	10.85	(6.61–15.13)
Substance-related	223	56.88	1.96	113.96	(98.84–128.71)
Drug-related	169	43.10	1.21	139.25	(118.62–160.73)
Alcohol-related	54	13.77	0.74	72.65	(53.51–92.44)
Infectious	55	14.03	1.65	33.36	(24.52–42.14)
Viral hepatitis	24	6.12	0.22	107.39	(65.45–152.74)
HIV	8	2.04	0.23	34.88	(10.68–58.89)
Circulatory system	388	98.96	15.27	25.41	(22.88–27.94)
Respiratory system	191	48.72	5.40	35.40	(30.35–40.39)
Influenza & pneumonia	23	5.87	0.94	24.45	(14.47–34.47)
Chronic respiratory disease	139	35.45	3.35	41.48	(34.59–48.39)
Digestive system	109	27.80	2.41	45.15	(36.74–53.72)
Cirrhosis & alcoholic liver disease	70	17.85	1.07	65.29	(50.09–80.75)
Cancer	280	71.42	15.29	18.32	(16.17–20.46)
Lung & bronchus	80	20.40	4.17	19.20	(14.98–23.39)
Liver & intrahepatic bile duct	43	10.97	0.63	68.23	(47.85–88.65)
Digestive system	42	10.71	3.14	13.36	(9.33–17.42)
Lymphoma & leukemia	9	2.30	1.06	8.47	(2.94–14.04)
Other cancers	106	27.04	6.14	17.27	(13.98–20.55)
Any type of death	1453	370.59	55.41	26.22	(24.87–27.57)

Abbreviations: No, Number; CI, Confidence Interval; SMR, Standardized Mortality Rate Ratio.

[a] Mortality for US population was from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research data (CDC WONDER).

[b] Mortality rates and expected counts is by using age-adjusted mortality rates among 15–84 year olds.