Substance use disorders and the risk of suicide mortality among men and women in the US

Veterans Health Administration

Kipling M. Bohnert, PhD^{1,2}, Mark A. Ilgen, PhD^{1,2}, Samantha Louzon, MPH³, John F.

McCarthy, PhD^{1,2,3}, Ira R. Katz, MD, PhD⁴

1. Center for Clinical Management Research, Department of Veterans Affairs, Ann Arbor, MI,

48109 USA

2. Department of Psychiatry, University of Michigan, Ann Arbor, MI, 48109 USA

3. Serious Mental Illness Treatment Resource and Evaluation Center, Office of Mental Health

Operations, Department of Veterans Affairs, Ann Arbor, MI, 48109 USA

4. Office of Mental Health Services, Department of Veterans Affairs, Washington, DC, USA

Corresponding Author: Kipling M. Bohnert, PhD, Center for Clinical Management Research,

Department of Veterans Affairs and Department of Psychiatry, University of Michigan Medical

School, North Campus Research Complex, 2800 Plymouth Rd, Building 16, Ann Arbor, MI

48109 (kiplingb@med.umich.edu).

Declaration of interests

None.

Word Count: 3685.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/add.13774

This article is protected by copyright. All rights reserved.

Abstract

Background and Aims

Limited information is available regarding links between specific substance use disorders (SUDs) and suicide mortality; however, the preliminary evidence that is available suggests that suicide risk associated with SUDs may differ for men and women. This study aimed to estimate associations between SUDs and suicide for men and women receiving Veterans Health Administration (VHA) care.

Design

A cohort study using national administrative health records.

Setting

National VHA system, USA.

Participants

All VHA users in fiscal year (FY) 2005 who were alive at the beginning of FY 2006 (n=4,863,086).

Measurements

The primary outcome of suicide mortality was assessed via FY 2006-FY 2011 National Death Index (NDI) records. Current SUD diagnoses were the primary predictors of interest, and were assessed via FY 2004- FY 2005 VHA National Patient Care Database (NPCD) records.

Findings

In unadjusted analyses, a diagnosis of any current SUD and the specific current diagnoses of alcohol, cocaine, cannabis, opioid, amphetamine, and sedative use disorders were all significantly associated with increased risk of suicide for both males and females (hazards ratios [HRs] ranging from 1.35 for cocaine use disorder to 4.74 for sedative use disorder for men, and

Authorl

3.89 for cannabis use disorder to 11.36 for sedative use disorder for women). Further, the HR estimates for the relations between any SUD, alcohol, cocaine, and opioid use disorders and suicide were significantly stronger for women than men (p<0.05). After adjustment for other factors, most notably comorbid psychiatric diagnoses, associations linking SUDs with suicide were markedly attenuated and the greater suicide risk among females was only observed for any SUD and opioid use disorder (p<0.05).

Conclusions

Current substance use disorders (SUDs) signal increased suicide risk, especially among women, and may be important markers to consider including in suicide risk assessment strategies.

Nonetheless, other co-occurring psychiatric disorders may partially explain associations between SUDs and suicide, as well as the observed excess suicide risk associated with SUDs among women.

Introduction

Suicide is a significant global public health concern, responsible for an estimated one million deaths annually [1]. In the United States (US), suicide is one of the leading causes of death [2]. The US Veterans Health Administration (VHA) is the largest integrated health care system in the US, and serves a diverse patient population with elevated suicide risk compared with the general US population [3, 4]. Although crude suicide rates are greater for male than female VHA patients, sex-specific, age-adjusted standardized mortality ratios (SMRs) indicate that suicide rates among female VHA patients are particularly high relative to women in the general US population [4, 5]. Consequently, understanding and addressing suicide risk, especially among women receiving VHA care, is an important priority.

In previous analyses regarding diagnostic factors associated with suicide among VHA patients, a substance use disorder (SUD) diagnosis was identified as a salient marker of suicide risk, especially among women [6, 7]. For example, a report by Ilgen and colleagues found that having any SUD diagnosis was associated with a 2.47 times greater risk of completed suicide (95% Confidence Interval [CI] 2.30-2.64) [6]. Furthermore, an SUD diagnosis was associated with a greater risk of suicide among females than males, with associated hazard ratios (HRs) of 6.62 (95% Confidence Interval [CI] 4.27-9.29) and 2.27 (95% CI 2.11-2.45), respectively [6]. Nonetheless, it is currently unknown whether the observed sex difference in suicide risk is uniform across all types of SUDs. In addition, prior analyses have not adjusted for important potential confounding factors, in particular co-occurring psychiatric conditions, which are more common among individuals with SUD [8, 9]. To inform VHA suicide risk assessment strategies and suicide prevention activities, a greater understanding of the sex-specific associations between SUDs and suicide is needed.

Prior research from other settings has also documented associations between SUDs and increased risk of suicidal behaviors [10-12]. Such studies have predominantly investigated nonfatal suicide outcomes, namely, suicidal ideation, plans, and attempts; relatively few have focused on the specific outcome of suicide death. Among the studies that have examined suicide mortality, the majority have assessed links between alcohol use disorder and suicide, with a smaller number of studies exploring the potential role of other SUDs [13]. Notably, the suicide risk associated with other common SUDs, including cannabis use disorder and cocaine use disorder, remains largely unknown. Furthermore, the minimal information regarding the suicide risk associated with particular SUDs comes from studies estimating individual associations between one type of substance and suicide (e.g., only assessing the risk of suicide associated with opioid use disorder). This lack of data on the suicide risk for more than one type of SUD from the same data source greatly diminishes the ability to evaluate the extent to which risk varies across different types of SUDs, due to differences in populations, study designs, and measures between studies. Preliminary evidence from other settings also suggests that the suicide risk associated with SUDs may differ between males and females [6, 13]. Two prior meta-analyses found that suicide-specific standardized mortality ratios (SMRs) associated with alcohol use disorder were larger for females than males [13, 14]. However, there were an insufficient number of studies to estimate similar sex-stratified SMRs for other SUDs. Consequently, VHA suicide analyses may have broad public health relevance.

In the present investigation, we constructed a cohort that included all VHA users who obtained care in the VHA system within a single fiscal year (FY), and aimed to: 1) estimate the overall and SUD-specific suicide rates among the entire cohort, as well as by sex; 2) estimate associations between current SUD diagnoses and the risk of suicide in the six years of follow-up

using a series of sex-stratified proportional hazards models; 3) calculate, and compare by SUD diagnosis status and sex, percentages of method of suicide among cohort members who died by suicide during follow-up. Analyses were stratified by sex because of the published a-priori evidence regarding sex-differences in the suicide risk associated with SUD.

Methods

Design and Data

To address the aims of the present study, we conducted a retrospective cohort study in the VHA population using national administrative databases. The study cohort included all VHA users who received services in FY 2005 and were alive at the beginning of FY 2006 (n=4,863,086). A FY begins on October 1st of the previous calendar year and ends on September 30th of the calendar year. The cohort was then assessed for suicide from the beginning of FY 2006 through the end of FY 2011 (i.e., a six-year follow-up).

Data for the cohort were drawn from the VHA National Patient Care Database (NPCD) and the VHA Suicide Data Repository, which includes search results from the Centers for Disease Control and Prevention's National Death Index (NDI). The NPCD is a national VHA patient medical records database that contains demographic, diagnostic, and treatment information for all VHA inpatient and outpatient clinical encounters. Diagnoses in the NPCD are based on clinical judgment, and correspond to the International Classification of Diseases Ninth Revision Clinical Modification (ICD-9-CM). The NDI includes data on the date and cause of death for all deaths that occur within the United States, and classifies causes of death according to the International Classification of Diseases Tenth Revision Clinical Modification (ICD-10-CM). The NDI records are based on death certificates filed to state vital statistics offices. Prior research has shown that the NDI is the most sensitive population-based vital status data source in the United States [15]. The study dataset was created using established procedures, and the approach of the present investigation parallels those of previous VHA suicide-related evaluation efforts [4, 16, 17]. The project was approved by the VA Ann Arbor Institutional Review Board.

Measures

Suicide. The primary study outcome of interest was suicide during the six years of follow-up (i.e., FY 2006- FY 2011). Deaths by suicide were identified from NDI data using the ICD-10-CM codes X60-X84 and Y87.0. In addition, date of death and method of suicide were obtained from the NDI data.

SUDs. The main predictors of interest were current SUD diagnoses in FY 2004- FY 2005, which were assessed via NPCD records using ICD-9-CM diagnosis codes. Major classes of SUDs included alcohol, cocaine, cannabis, opioid, amphetamine or other psychostimulant, and sedative, hypnotic or anxiolytic use disorders. In addition, a composite indicator of any current SUD was also examined that included any of the aforementioned SUDs, as well as hallucinogen use disorder and/or any other/multiple SUDs. All current SUD diagnoses were based on clinical judgment and recorded by VHA healthcare providers (e.g., clinical psychologists) during clinical encounters.

Sex. The stratification variable of male or female sex was ascertained via NPCD demographic records.

Covariates. Several other variables that might confound the relation between SUD and the risk of suicide were included as covariates in the adjusted study analyses. Age in years was ascertained via NPCD demographic records, and was divided into the following categories: 18 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69, 70 to 79, or 80 years or older. Similar to other studies

using these data, reliable information on other demographic variables (e.g., race/ethnicity, marital status, and employment) was not available, and was consequently not included in analyses (e.g., [6]). The Charlson Comorbidity Index is an established metric that was used to assess current non-psychiatric medical comorbidity, including heart disease and cancers, and is based on ICD-9-CM clinical diagnostic codes obtained from FY 2004-2005 NPCD records [18]. Charlson Comorbidity Index scores were recoded into the following categories: 0, 1, or 2 or greater. Current psychiatric diagnoses, which have been shown previously to be associated with suicide risk, were assessed via FY 2004-2005 NPCD diagnostic records. These included the presence or absence of each of the following: depression, schizophrenia, bipolar disorder, posttraumatic stress disorder, and other anxiety disorders.

Statistical Analysis

Analyses were conducted on the cohort of 4,863,086 individuals who had VHA encounters in FY 2005 and were alive at the beginning of FY 2006. To begin, we calculated the number and percentage of current SUD diagnoses for the entire cohort, as well as by sex. Next, we estimated the overall and SUD-specific suicide rates per 100,000 person-years for the cohort, and separately for males and females. A series of sex-stratified Cox proportional hazards regression models was then used to estimate associations between each category of SUD, as well as the composite indicator of any SUD, and the risk of suicide, with analyses yielding HRs and corresponding 95% confidence intervals (CIs) as the estimates of association [19]. Risk time for all cohort members began on the first day of FY 2006 and ended on their recorded date of suicide or the last day of FY 2011, if alive. Cohort members who died from other causes during the follow-up interval were censored at the recorded date of their death. In addition, all proportional

Author N

hazards models used covariance sandwich estimators to take into account the clustered nature of the data, with patients nested within VHA facilities. The first model in the series estimated the unadjusted, bivariate relationship between the given SUD category and risk of suicide mortality. The second model adjusted for age group and Charlson Comorbidity. The third model expanded upon the two previous models, with additional adjustment for each of the following co-occurring psychiatric conditions: depression, schizophrenia, bipolar disorder, posttraumatic stress disorder, and other anxiety disorders. In additional post-hoc analyses, male-female differences in associations between SUDs and suicide were tested using sex by SUD interaction terms in non-stratified hazards models (i.e., models using the full cohort). As a final analytic step, we calculated percentages of method of suicide among all suicide decedents in the cohort, as well as by current SUD status and sex, and performed chi-square analyses to test differences between groups. All data analyses were conducted using SAS 9.3.

Results

Table 1 displays age group and current SUD diagnostic characteristics of the cohort, overall, as well as by sex. Consistent with the VHA patient population, a majority of the FY 2005 cohort members were male (n=4,460,447; 91.7%); 402,639 (8.3%) were female. Age distributions varied between men and women, with greater percentages of women in younger age groups (p<0.001). SUD diagnoses also varied by sex, with a greater percentage of males than females with at least one SUD diagnosis (males=8.4%; females=3.4%; p<0.001). Similarly, with respect to specific SUD diagnoses, greater percentages of males had current alcohol, cocaine, cannabis, opioid, amphetamine, and sedative use disorder diagnoses than females.

Table 2 presents suicide information for the entire cohort, as well as stratified by sex. During the six year follow-up interval, 9,087 cohort members died by suicide; the overall suicide rate was 34.7 per 100,000 person-years. Suicide rates were approximately three-fold greater for men than women. The suicide rate among individuals with an SUD diagnosis was 75.6 per 100,000 person-years; 76.1 per 100,000 person-years for males and 63.4 per 100,000 person-years for females. With respect to specific SUDs, the suicide rate associated with sedative use disorder was largest, followed by amphetamine, opioid, cannabis, alcohol, and cocaine use disorders. Specific SUD-associated suicide rates followed the same pattern for men. Among women the order differed, with the highest suicide rate observed for sedative use disorder followed by opioid, amphetamine, alcohol, cocaine, and cannabis use disorders.

Results from the sex-stratified proportional hazards regression models estimating prospective associations between current SUDs and the risk of suicide during the follow-up interval are displayed in Table 3. In the unadjusted models (Model 1), all current SUDs, as well as any current SUD, were significantly associated with increased risk of suicide among both men

and women; however, the strength of the association was approximately two-to-three-fold greater for women than men. In post-hoc tests, substance-specific estimates for alcohol, cocaine, and opioid use disorders, as well as the estimate for any SUD, were significantly greater for women than men (p<0.05). After adjustment for age group and Charlson Comorbidity (Model 2), the HR estimates associated with SUDs were marginally attenuated for men and more moderately attenuated for women, yet all remained statistically significant. Furthermore, although the same substance-specific HR estimates remained significantly greater for women than men in post-hoc tests (p<0.05), the magnitude of the difference was not as pronounced as in Model 1. In the third set of regressions, additional adjustment was made for current co-occurring psychiatric diagnoses (Model 3), which further attenuated the SUD HRs. For men, cocaine use disorder became inversely associated with suicide, and for women significant associations remained only for alcohol and opioid use disorders, as well as any SUD. In addition, post-hoc analyses revealed that male-female differences were no longer significant for alcohol use disorder in Model 3.

Figure 1 displays method of suicide among all individuals in the cohort who died by suicide during the follow-up interval, as well as by current SUD status and sex. Overall, firearm use was the most common method of suicide. Firearm use was more common among decedents without a current SUD diagnosis at baseline than among those with a current SUD diagnosis. It was also more common among males than females. Poisoning was more common among decedents with a current SUD than those without one, as well as more common among women than men.

Discussion

In this investigation, we estimated associations between current SUDs and risk of suicide in over 4.8 million men and women who used VHA services in FY 2005. In unadjusted analyses, a current diagnosis of any SUD and the specific current diagnoses of alcohol, cocaine, cannabis, opioid, amphetamine or other psychostimulant, and sedative, hypnotic or anxiolytic use disorders were all associated with elevated risk of suicide for both males and females.

Further, the relative risk estimates for the relations between any SUD, alcohol, cocaine, and opioid use disorders and suicide were markedly stronger for women than men. However, after adjustment for other factors, most notably comorbid psychiatric diagnoses, associations linking current SUDs with suicide were attenuated and male-female differences observed in the unadjusted models were diminished.

Although links between SUDs and nonfatal suicide outcomes have been reported in the literature, only a limited number of prior studies have examined suicide mortality. The few studies investigating suicide mortality have noted individual associations between any SUD, alcohol use disorder, and opioid use disorder and suicide [13]. The present investigation is one of the first to provide estimates of the suicide risk associated with current cannabis, cocaine, amphetamine, and sedative use disorders in a broad population cohort. Furthermore, to the best of our knowledge, prior work has not concurrently examined links between specific SUDs and suicide mortality within the same data source. Consequently, previous studies have not allowed for comparisons in the magnitude of risk associated with specific types of SUDs. Nor have these comparisons been made separately for men and women, despite evidence of sex-differences in the risk factors for suicide and the need for greater understanding of SUD and suicide among women [13, 20-22]. Findings from the present investigation indicate that associations between

SUDs and risk of suicide vary by sex as well as type of SUD. Among men, the unadjusted suicide HRs ranged from 1.35 for cocaine use disorder to 4.74 for sedative use disorder. Among women, there was greater variation in the suicide risk estimates by type of SUD, with HRs ranging from 3.89 for cannabis use disorder to 11.36 for sedative use disorder. Such differences may be important for clinicians and health systems to consider when providing care for patients with SUDs, and could help inform suicide prevention efforts. The sizable risk of suicide among women with a current opioid use disorder is especially noteworthy, and may be important for clinicians to be aware of when treating such patients.

The marked differences between males and females in the crude SUD-suicide associations, as well as the variability in suicide risk between specific types of SUDs, were appreciably attenuated after adjustment for co-occurring psychiatric diagnoses. For instance, the HR for suicide associated with a current alcohol use disorder was reduced from 2.26 to 1.64 for men and from 4.72 to 1.57 for women after adjustment. In the case of cocaine use disorder among males, the direction of the association was reversed after including other psychiatric diagnoses such that cocaine use disorder was associated with a 26% reduction in suicide risk. Among women, HRs associated with cocaine and cannabis use disorders approached the null and were non-significant after the inclusion of comorbid psychiatric diagnoses. Previous work has found that co-occurring psychopathology may be especially salient among those with a cocaine use disorder who attempt suicide [23, 24], and our finding of an inverse association among men might be due in part to collinearity between cocaine use disorder and other psychiatric conditions; however, further research is needed to better understand suicide mortality among those with a cocaine use disorder. In general, few prior prospective studies examining links between SUDs and suicide mortality have taken into account comorbid psychiatric conditions,

possibly due to additional sample size requirements beyond those that are already necessary to study the rare event of suicide. However, the previous investigations that have included adjustment for other covariates have also noted that underlying psychiatric comorbidity may partially explain associations between SUDs and suicide [25]. Collectively, these findings highlight the potentially confounding role of comorbid psychiatric illness in SUD-suicide associations. Hence, assessment and treatment of comorbid psychiatric conditions may be important in lowering the risk of suicide among individuals with co-occurring SUDs and other psychopathology. Nonetheless, findings from the present investigation suggest that even after statistical adjustment for comorbid psychiatric conditions SUDs (in particular, alcohol and opioid use disorders) may independently confer excess risk for suicide mortality. Therefore, SUD treatment, including integrated or additional SUD-specific treatment for those with co-occurring psychiatric conditions, with assessment and management of suicidal behaviors may be important for suicide prevention. In addition, the findings from the present study regarding method of suicide among decedents with SUD highlight the importance of developing strategies to prevent intentional poisoning, as well as include firearm safety in suicide prevention efforts, for individuals with SUDs.

Theoretical models regarding suicide risk among individuals with SUDs posit that proximal risk for suicide is driven by ongoing substance use, psychiatric symptoms, and interpersonal stress [11]. In the present study, the presence of a clinical diagnosis of a co-occurring psychiatric condition likely reflects a combination of symptoms and distress/impairment. Unfortunately, no data are available on the extent of substance use in the present cohort. However, in the absence of such data, it is possible that much of the risk is carried by this clinically significant symptom impairment. Ideally, future work would be able to

model fluctuations in psychiatric symptoms and substance use that might drive suicidal behaviors in those with SUDs, as well as the extent to which these fluctuations can be modified by treatment.

There are several limitations that should be considered when interpreting findings from the present investigation. First, the study cohort included all patients who used VHA services in a given year. Previous research has found that individuals who use VHA services may have poorer physical and mental health functioning, as well as higher rates of suicide, than those in the US general population [4, 26, 27]. Web-based analyses of national injury data from the US Centers for Disease Control and Prevention's (CDC's) Web-based Injury Statistics Query and Reporting System (WISQARs) show that the crude suicide rate was 15.56 per 100,000 person years for adults aged 20 years and older, and 25.33 per 100,000 person years for males and 6.39 per 100,000 person years for females, during the same time period as study follow-up (i.e., 2006-2011)[28]. These crude rates for the US population are lower than those found among our VHA cohort. Consequently, findings may not be generalizable to patient populations from other health settings. Second, although death data are from the NDI, which is the "gold standard" for ascertainment of mortality in the US [15], cause of death may still be subject to misclassification. In particular, distinguishing between suicide and accidental overdose may be problematic among individuals with SUDs, especially among those with opioid use disorders (e.g., [29]). Third, current SUD and other psychiatric diagnoses were obtained from administrative records in the NPCD. Diagnoses are based on VHA providers' clinical assessment and judgment. As such, the validity and reliability of these current diagnoses are unknown. Fourth, administrative data used in study analyses do not contain information on level of severity of SUDs, which may be important to consider in future studies. It is also possible that the level of severity of SUDs that

were diagnosed by providers may have differed between men and women. Such differences could have had an impact on the observed associations between SUDs and suicide. Fifth, analyses were limited to the investigation of suicide risk associated with current SUD diagnoses; specific information regarding the extent of drug use including poly drug use is also unavailable in VHA administrative data. Nonetheless, research regarding levels of drug use and poly drug use is an important area of suicide research that requires further study [12]. Sixth, given the observational, non-randomized nature of the study design, incomplete adjustment for confounding factors, measured or unmeasured, is a potential limitation. Such factors may include unreliable or unmeasured demographic variables that were omitted from study analyses. We were also unable to account for comorbid SUD diagnoses in analyses due to power concerns, especially among women. Therefore, findings should be interpreted within the context of this limitation, and additional research regarding the potential role of co-occurring SUDs on suicide is required. Seventh, study analyses compared individuals with current SUD diagnoses to those without current SUD diagnoses. We were unable to further categorize those without current SUD diagnoses into former SUD and never SUD groups. Further research is needed to examine the potential impact of remitted SUDs on suicide risk.

Despite these limitations, this investigation provides novel and important data regarding current SUDs and the risk of suicide. SUDs may be important markers of suicide risk, especially among women, and may be important factors for health systems and clinicians to consider including in suicide risk assessment strategies. Nevertheless, other co-occurring psychiatric disorders may partially explain associations between SUDs and suicide, as well as the observed excess suicide risk associated with SUDs among women.

Acknowledgments

This work was supported by the Department of Veterans Affairs (VA) Office of Mental Health Services and the VA Office of Mental Health Operations. Data were acquired for program planning and evaluation purposes—not for research. Input from senior mental health leadership at the VHA Central Office helped shape the design and conduct of the study; the collection, management, analysis, and interpretation of the data; and the preparation, review, and approval of the manuscript. In addition, Dr. Bohnert is supported by a VA Health Services Research & Development Career Development Award (CDA 11-245).

The views expressed in this report are those of the authors and do not necessarily represent those of the VA.

References

- The Global Burden of Disease: 2004 Update Geneva, Switzerland: World Health Organization; 2008.
- 2. Kochanek K. D., Xu J., Murphy S. L., Minino A. M., Kung H. Deaths: Final Data for 2009. *National Vital Statistics Reports* 2011; **60**.
- 3. Blow F. C., Bohnert A. S., Ilgen M. A., Ignacio R., Mccarthy J. F., Valenstein M. M. et al. Suicide mortality among patients treated by the Veterans Health Administration from 2000 to 2007. *Am J Public Health* 2012; **102 Suppl 1**: S98-104.
- 4. Mccarthy J. F., Valenstein M., Kim H. M., Ilgen M., Zivin K., Blow F. C. Suicide mortality among patients receiving care in the veterans health administration health system. *Am J Epidemiol* 2009; **169**: 1033-1038.
- 5. Hoffmire C. A., Kemp J. E., Bossarte R. M. Changes in Suicide Mortality for Veterans and Nonveterans by Gender and History of VHA Service Use, 2000-2010. *Psychiatr Serv* 2015; **66**: 959-965.
- 6. Ilgen M. A., Bohnert A. S., Ignacio R. V., Mccarthy J. F., Valenstein M. M., Kim H. M. et al. Psychiatric diagnoses and risk of suicide in veterans. *Arch Gen Psychiatry* 2010; **67**: 1152-1158.
- 7. Ilgen M. A., Mccarthy J. F., Ignacio R. V., Bohnert A. S., Valenstein M., Blow F. C. et al. Psychopathology, Iraq and Afghanistan service, and suicide among Veterans Health Administration patients. *J Consult Clin Psychol* 2012; **80**: 323-330.
- 8. Kessler R. C., Chiu W. T., Demler O., Merikangas K. R., Walters E. E. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005; **62**: 617-627.

- 9. Trivedi R. B., Post E. P., Sun H., Pomerantz A., Saxon A. J., Piette J. D. et al.

 Prevalence, Comorbidity, and Prognosis of Mental Health Among US Veterans. *Am J Public Health* 2015; **105**: 2564-2569.
- 10. Borges G., Loera C. R. Alcohol and drug use in suicidal behaviour. *Curr Opin Psychiatry* 2010; **23**: 195-204.
- 11. Conner K. R., Ilgen M. A. Substance use disorders and suicidal behaviour. In: The international handbook of suicide prevention: research, policy and practice, Oxford, UK: Wiley-Blackwell; 2011, p. 93-108.
- 12. Borges G., Walters E. E., Kessler R. C. Associations of substance use, abuse, and dependence with subsequent suicidal behavior. *Am J Epidemiol* 2000; **151**: 781-789.
- 13. Wilcox H. C., Conner K. R., Caine E. D. Association of alcohol and drug use disorders and completed suicide: an empirical review of cohort studies. *Drug Alcohol Depend* 2004; **76 Suppl**: S11-19.
- 14. Harris E. C., Barraclough B. Suicide as an outcome for mental disorders. A metaanalysis. *Br J Psychiatry* 1997; **170**: 205-228.
- 15. Cowper D. C., Kubal J. D., Maynard C., Hynes D. M. A primer and comparative review of major US mortality databases. *Ann Epidemiol* 2002; **12**: 462-468.
- 16. Bohnert K. M., Ilgen M. A., Mccarthy J. F., Ignacio R. V., Blow F. C., Katz I. R. Tobacco use disorder and the risk of suicide mortality. *Addiction* 2014; **109**: 155-162.
- 17. Sohn M. W., Arnold N., Maynard C., Hynes D. M. Accuracy and completeness of mortality data in the Department of Veterans Affairs. *Popul Health Metr* 2006; **4**: 2.

- 18. Charlson M. E., Pompei P., Ales K. L., Mackenzie C. R. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373-383.
- 19. Cox D. R. Regression models and life-tables. *Journal of the Royal Statistical Society* 1972; **34**: 187-220.
- 20. Chapman S. L., Wu L. T. Suicide and substance use among female veterans: a need for research. *Drug Alcohol Depend* 2014; **136**: 1-10.
- 21. Qin P., Agerbo E., Mortensen P. B. Suicide risk in relation to socioeconomic, demographic, psychiatric, and familial factors: a national register-based study of all suicides in Denmark, 1981-1997. *Am J Psychiatry* 2003; **160**: 765-772.
- 22. Qin P., Agerbo E., Westergard-Nielsen N., Eriksson T., Mortensen P. B. Gender differences in risk factors for suicide in Denmark. *Br J Psychiatry* 2000; **177**: 546-550.
- 23. Roy A. Characteristics of cocaine-dependent patients who attempt suicide. *Am J Psychiatry* 2001; **158**: 1215-1219.
- 24. Roy A. Characteristics of cocaine dependent patients who attempt suicide. *Arch Suicide Res* 2009; **13**: 46-51.
- 25. Flensborg-Madsen T., Knop J., Mortensen E. L., Becker U., Sher L., Gronbaek M. Alcohol use disorders increase the risk of completed suicide--irrespective of other psychiatric disorders. A longitudinal cohort study. *Psychiatry Res* 2009; **167**: 123-130.
- 26. Agha Z., Lofgren R. P., Vanruiswyk J. V., Layde P. M. Are patients at Veterans Affairs medical centers sicker? A comparative analysis of health status and medical resource use. *Arch Intern Med* 2000; **160**: 3252-3257.

- 27. Kazis L. E., Miller D. R., Clark J., Skinner K., Lee A., Rogers W. et al. Health-related quality of life in patients served by the Department of Veterans Affairs: results from the Veterans Health Study. *Arch Intern Med* 1998; **158**: 626-632.
- 28. Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System. Accessed December 23, 2016, from http://www.cdc.gov/injury/wisqars/index.html.
- 29. Farrell M., Neeleman J., Griffiths P., Strang J. Suicide and overdose among opiate addicts. *Addiction* 1996; **91**: 321-323.

Table 1. Characteristics of	the cohort of I	TY05 VHA	patients alive	at the begi	nning of FY 20	006,						
total, and by sex (n=4,863,086)												
	All		Male	9	Female							
Characteristic	N	%	N	%	N	%						
Total	4,863,086	100.0	4,460,447	100.0	402,639	100.0						
Age Group												
18-29	158,967	3.3	110,376	2.5	48,591	12.1						
30-39	245,266	5.0	182,128	4.1	63,138	15.7						
40-49	514,083	10.6	410,439	9.2	103,644	25.7						
50-59	1,161,916	23.9	1,057,552	23.7	104,364	25.9						
60-69	955,689	19.7	915,564	20.5	40,125	10.0						
70-79	1,136,095	23.4	1,118,723	25.1	17,372	4.3						
80+	691,070	14.2	665,665	14.9	25,405	6.3						
Any SUD	386,238	7.9	372,717	8.4	13,521	3.4						
Alcohol Use Disorder	307,923	6.3	298,831	6.7	9,092	2.3						
Cocaine Use Disorder	83,808	1.7	80,565	1.8	3,243	0.8						
Cannabis Use Disorder	56,524	1.2	53,968	1.2	2,556	0.6						
Opioid Use Disorder	37,908	0.8	36,284	0.8	1,624	0.4						
Amphetamine or Other Psychostimulant Use Disorder	12,033	0.2	11,321	0.3	712	0.2						
Sedative, Hypnotic or Anxiolytic Use Disorder	7,301	0.2	6,779	0.2	522	0.1						

All Suicide Mortality FY 06-11		Suicide Rate per 100,000 person-years	Suic Mort among FY 0	ality Males	Male Suicide Rate per 100,000 person-years	an Fer	cides nong nales 06-11	Female Suicide Rate per 100,000 person-years	
Characteristic	N	%		N	%		N	%	
Overall	9,087	100.0	34.7	8,796	100.0	36.9	291	100.0	12.4
Any SUD	1,573	17.3	75.6	1,524	17.3	76.1	49	16.8	63.4
Alcohol Use Disorder	1,259	13.9	76.2	1,231	14.0	76.9	28	9.6	54.0
Cocaine Use Disorder	231	2.5	49.3	222	2.5	49.3	9	3.1	48.0
Cannabis Use Disorder	246	2.7	77.4	239	2.7	78.9	7	2.4	47.3
Opioid Use Disorder	177	1.9	86.9	168	1.9	86.4	9	3.1	98.6
Amphetamine or Other Psychostimulant Use Disorder	64	0.7	95.0	61	0.7	96.5	3	1.0	72.4
Sedative, Hypnotic or Anxiolytic Use Disorder	66	0.7	171.4	62	0.7	174.1	4	1.4	138.7

Table 3. Cox hazards models estimating associations between current SUD and suicide mortality during the follow up interval, FY06 - FY11 (N=4,863,086)

	Model 1*					Model 2**						Model 3***						
	Males			Females			Males			Females			Males			Females		
Characteristic	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Any SUD	2.29	2.12, 2.46	<0.001	5.95	4.29, 8.26	<0.001	2.26	2.11, 2.43	<0.001	4.82	3.42, 6.79	<0.001	1.67	1.55, 1.79	<0.001	2.15	1.44, 3.21	0.001
Alcohol Use Disorder	2.26	2.10, 2.44	< 0.001	4.72	3.15, 7.06	< 0.001	2.21	2.06, 2.38	<0.001	3.73	2.48, 5.62	< 0.001	1.64	1.52, 1.76	< 0.001	1.57	1.01, 2.45	0.047
Cocaine Use Disorder	1.35	1.17, 1.55	<0.001	3.97	2.13, 7.39	<0.001	1.19	1.03, 1.36	0.014	2.88	1.50, 5.50	0.001	0.74	0.64, 0.84	< 0.001	1.10	0.57, 2.15	0.776
Cannabis Use Disorder	2.17	1.91, 2.48	< 0.001	3.89	1.80, 8.37	0.001	1.97	1.72, 2.25	< 0.001	2.90	1.34, 6.25	0.007	1.16	1.02, 1.33	0.024	1.01	0.45, 2.26	0.990
Opioid Use Disorder	2.37	1.96, 2.86	<0.001	8.19	3.74, 17.95	<0.001	2.12	1.76, 2.56	< 0.001	5.90	2.66, 13.10	<0.001	1.31	1.08, 1.58	0.005	2.33	1.05, 5.18	0.038
Amphetamine or Other Psychostimulant Use Disorder	2.63	2.06, 3.35	<0.001	5.90	2.10, 16.57	<0.001	2.32	1.82, 2.95	<0.001	4.42	1.52, 12.91	0.006	1.30	1.02, 1.64	0.032	1.50	0.52, 4.38	0.456
Sedative, Hypnotic or Anxiolytic Use Disorder	4.74	3.64, 6.17	<0.001	11.36	3.67, 35.14	<0.001	4.26	3.27, 5.56	<0.001	8.28	2.69, 25.53	<0.001	1.97	1.51, 2.57	< 0.001	2.41	0.79, 7.44	0.127

^{*}Unadjusted. Covariance sandwich estimators were used to adjust for clustering within VHA facilities.

^{**}Controlling for age and Charlson Comorbidity Index. Covariance sandwich estimators were used to adjust for clustering within VHA facilities.

^{***}Controlling for age, Charlson Comorbidity Index and psychiatric diagnoses. Covariance sandwich estimators were used to adjust for clustering within VHA facilities.

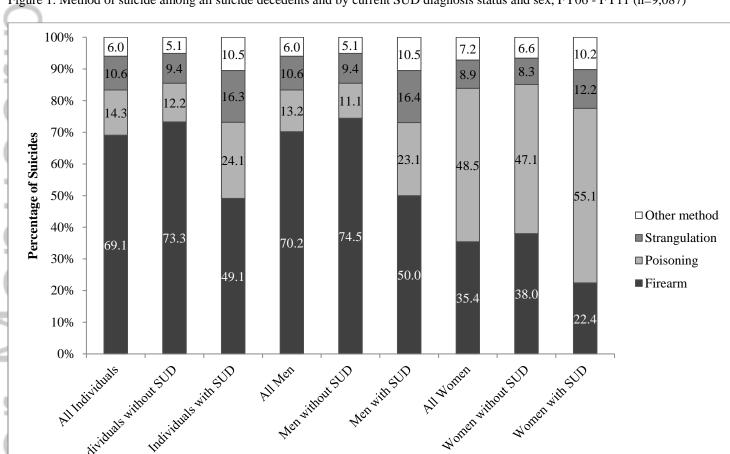


Figure 1. Method of suicide among all suicide decedents and by current SUD diagnosis status and sex, FY06 - FY11 (n=9,087)