The association between substance use disorders and mortality among a cohort of Veterans with posttraumatic stress disorder: Variation by age cohort and mortality type

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ABSTRACT

Background: Prior studies of Veterans have linked posttraumatic stress disorder (PTSD) with an increased risk of mortality. Other studies of Veterans have found that substance use disorders (SUDs) are associated with an excess risk of mortality among those with psychiatric disorders. It is not known whether having an SUD increases the risk of mortality among Veterans with PTSD, and whether the association differs by mortality type or varies by age cohort.
Methods: A cohort of patients who received Veterans Health Administration services during fiscal year (FY) 2004 and diagnosed with PTSD (n = 272,509) were followed from FY 2005 through FY 2007 for the main outcomes of mortality and cause of death.
Results: SUD was positively associated with mortality during follow-up (adjusted hazards ratio: 1.70; 95% confidence interval: 1.64, 1.77). SUD was a stronger predictor of non-injury-related mortality for the <45 years group compared with the 45–64 or ≥65 group. SUD predicted injury-related mortality for all age groups.
Conclusions: Among Veterans with PTSD, the association between SUD and mortality was most pronounced for the youngest age group, which included Iraq/Afghanistan Veterans. For older age groups, which included Vietnam-era Veterans, SUD was a greater predictor of injury-related mortality. The findings could be useful for identifying PTSD patients at excess risk of mortality.

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1. Introduction

In the United States, studies of Vietnam-era Veterans have reported an association linking posttraumatic stress disorder (PTSD) with an increased risk of mortality (Boscarino, 2006a,b; Bullman and Kang, 1994). This line of research has received renewed attention as Veterans return from recent conflicts in Iraq and Afghanistan, many of whom suffer from PTSD (Hoge et al., 2006, 2004). Despite the increased interest, potential risk factors associated with mortality among individuals with PTSD are poorly understood, and little is known about whether or not the impact of these risk factors differs for younger Veterans from a different era. Preliminary evidence suggests that comorbid substance use disorders (SUDs) may play a salient role in predicting mortality among Veterans with PTSD (Crawford et al., 2009).

The association between PTSD and SUDs has been well documented in previous epidemiological and clinical studies (Bremner et al., 1996; Creamer et al., 2001; Kessler et al., 1995). Although individual variability certainly exists in the temporal ordering and onset of these two conditions, evidence suggests that PTSD increases the risk for subsequent SUDs, which may reflect self-medication; whereas, prior work does not support the hypothesis that SUDs increase the risk for PTSD (Breslau et al., 2003; Chilcoat and Breslau, 1998; Hien et al., 2010; Jacobsen et al., 2001). Nonetheless, relatively little is known about the potential influence of co-occurring SUDs on other health-related outcomes, particularly risk of mortality, among individuals with PTSD.

In previous research on psychiatric disorders and mortality, SUDs have been consistently linked with an increased risk of death. For example, in a recent report examining psychiatric illness and mortality in a large cohort of United States Veterans, SUDs were the

strongest psychiatric predictors of death over the nine-year follow-up interval, with hazards ratios (HRs) ranging from 1.79 to 1.97 (Chwastiak et al., 2010). There is additional evidence suggesting that, among individuals with psychiatric disorders, SUDs may contribute to excess mortality (Rosen et al., 2008). Other research has examined the association with specific types of mortality and found that Veterans with alcohol use disorders (AUDs) were at an even greater risk of injury-related mortality than non-injury-related mortality (Fudalej et al., 2010). Similarly, prior reports found that Vietnam-era Veterans with PTSD were more likely to die from external causes, which included injuries and drug-related causes, than from other medical causes (Boscarino, 2006a,b). Therefore, it is particularly important to examine whether SUDs differentially predict injury versus non-injury-related mortality among Veterans with PTSD. The results of such research may inform more appropriate prevention and treatment efforts by shaping the content of tailored interventions designed to target subgroups at elevated risk for non-injury-related and injury-related mortality.

Furthermore, Vietnam-era Veterans (typically ages 50–65 years) account for the majority of PTSD patients treated by United States Department of Veterans Affairs (VA) (Rosenheck and Fontana, 2007). Nonetheless, the prevalence of PTSD is also high and the absolute number of cases is growing among Iraq and Afghanistan Veterans, most of whom are under age 45 (Seal et al., 2007). It is unknown whether the association between SUDs and the risk of mortality are similar among these different Veteran cohorts.

Therefore, in order to better understand the role of SUDs in predicting mortality among individuals with PTSD, the aims of the present study are to: (a) estimate the predictive association between SUDs and the risk of mortality among a cohort of Veterans Health Administration (VHA) patients with PTSD, (b) test whether the hypothesized association is greater for injury-related than for non-injury-related mortality, and (c) examine whether age group moderates the hypothesized association between SUDs and injury-related and non-injury related mortality.

2. Methods

2.1. Sample, design, and data sources

The study cohort was defined as all VHA patients who received services in fiscal year (FY) 2004, had a diagnosis of PTSD in their medical records during FY 2004, and were alive at the start of FY 2005. A FY for a given year encompasses the period of time from 1 October of the previous calendar year through 30 September of that calendar year (e.g., FY 2004 is 1 October 2003 through 30 September 2004). Based on the stated criteria, a resulting study cohort of 272,509 individuals was obtained among the 4,751,668 patients who received services in FY 2004 and were alive at the start of FY 2005. The study follow-up interval used to analyze mortality began at the start of FY 2005 and continued through the end of FY 2007 (i.e., three years).

Data for the present study come from two sources: the VHA National Patient Care Database (NPCD) and the Centers for Disease Control and Prevention National Death Index (NDI). The NPCD is a comprehensive medical records database that contains information on all clinical contact within the VHA system. Specifically, it contains demographic and diagnostic information on all patients seen in the VHA. Diagnoses are entered by VHA health care providers based on their clinical assessments, and correspond to the International Classification of Diseases Ninth Revision Clinical Modification (ICD-9-CM).

Data on vital statistics and cause of death come from the NDI. The NDI data include the date and cause of death for all deaths of US residents that occur within the US. This information is derived from death certificates that are filed in state vital statistics offices. The NDI classifies cause of death according to the International Classification of Diseases Tenth Revision Clinical Modification (ICD-10-CM). Previous research has shown the NDI to be the most sensitive population-based vital status data source in the United States (Cowper et al., 2002).

For each FY of follow-up, NDI searches were performed for the individuals in the cohort who did not receive VHA services and had no recorded encounters with the VHA during that given FY. The NDI searches included information on Social Security Number, last name, first name, race, sex, and state of residence. When multiple potential matches were identified, established procedures yielded "true" matches (Sohn et al., 2006). Since FY 1999, over 99% of deaths in the VHA user population have been matched on all nine Social Security Number digits in NDI records.

This research was approved by the VA Ann Arbor Human Subjects Committee.

2.2. Measures

For the present study, the main outcomes of interest were mortality during the follow-up interval and cause of death, which were obtained from the NDI. In accordance with methods developed by the National Center for Health Statistics (1997), causes of death were classified into 15 categories. Consistent with prior research on mortality, these 15 categories were further collapsed into injury-related and non-injury-related death (Fudalej et al., 2010). Injury-related death comprises accidents, suicide, and homicide. Non-injury-related death includes heart disease, malignant neoplasm, chronic lower respiratory disease, diabetes, cerebrovascular disease, liver disease, influenza and pneumonia, nephritis, septicemia, Alzheimer's disease, Parkinson's disease, and hypertension. An additional "other" category was created to include all other causes of death that did not fall under the specific injury-related categories.

The main explanatory variable of interest was a diagnosis of a SUD (ICD9-CM codes: 291, 303, 305.0, 304.0, 304.7, 305.5, 304.2, 305.6, 304.3, 305.2, 304.4, 305.7, 304.1, 305.4, 304.8, 305.9, 292) in FY 2004, which was determined via NPCD records. Other covariates of interest also come from FY 2004 NPCD records. These variables include: demographic information (i.e., age, sex, and race), VHA service connection, tobacco use disorder (ICD9-CM code: 305.1), psychiatric conditions (i.e., major depression (ICD9-CM codes: 296.2, 296.3), bipolar disorder (ICD9-CM codes: 296.0, 296.1, 296.4, 296.5, 296.6, 296.7, 296.8), other anxiety disorders (ICD9-CM codes: 300.00, 300.01, 300.02, 300.09, 300.10, 300.20, 300.21, 300.22, 300.23, 300.29), personality disorders (ICD9-CM codes: 301.0, 301.20, 301.22, 301.7, 301.83, 301.50, 301.81, 301.82, 301.6, 301.4, 301.9), and schizophrenia (ICD9-CM codes: 295.0, 295.1, 295.2, 295.3, 295.4, 295.6, 295.7, 295.8, 295.9)), and medical comorbidity. Medical comorbidity was assessed according to the Charlson Comorbidity Index, an established measure that classifies comorbidity according to severity (Charlson et al., 1987).

2.3. Statistical analyses

Descriptive analyses included the frequency and percentage of type of mortality (injury versus non-injury) among the cohort members who died during follow-up. Next, survival analyses with Cox proportional hazards regression modeling were used to examine the association between SUDs and risk of death (Cox, 1972). Three successive models were estimated. In the first model, the influence of having a SUD was modeled as predictor of all-cause mortality, adjusting for age, sex, race, and service connection. In the second model, the analysis was elaborated to adjust for tobacco use disorder and other psychiatric conditions (i.e., major depression, bipolar disorder, other anxiety disorders, personality disorders, and schizophrenia). In the third model, additional adjustment was made for medical comorbidity (i.e., via the Charlson Comorbidity Index). In the final analytic step, a multivariable competing risks hazards regression approach was used to test for differences in the strength of association between SUDs and injury-related mortality, and SUDs and non-injury-related mortality (Lunn and McNeil, 1995). In the competing risks approach, we also tested whether age group moderated the association between SUDs and mortality with the alpha level set at 0.05. The competing risks models adjusted for all of the variables included in the third model of the all-cause mortality analysis. All analyses were conducted using SAS 9.1.

3. Results

3.1. Description of the PTSD cohort

Table 1 provides a description of the PTSD cohort. The table includes information on SUD, demographics, service connection, tobacco use disorder, other psychiatric disorders, and medical comorbidity. As is displayed in the table, nearly one out of every five (19.33%) individuals in the PTSD cohort had a diagnosed SUD. A majority of the individuals in the cohort were 45–64 years of age (74.90%), and a majority were male (93.68%). 42.96% of the cohort had VHA service connection of 70% or greater. With respect to other health conditions, 22.66% had tobacco use disorder. Major depression was also a prevalent comorbid psychiatric condition (i.e., 21.13%). In addition, 48.45% of the cohort had at least one other medical comorbidity.

3.2. Causes of death among the PTSD cohort

During the follow-up interval from FY 2005 through FY 2007, 7.00% (n = 19,064) of the individuals in the PTSD cohort died. Table 2 presents the specific causes of death among the decedents during the follow-up interval. As shown in the table, the most frequent