

Causes of Excess Mortality in Veterans Treated for Posttraumatic Stress Disorder



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Introduction: Published research indicates that posttraumatic stress disorder (PTSD) is associated with increased mortality. However, causes of death among treatment-seeking patients with PTSD remain poorly characterized. The study objective was to describe causes of death among Veterans with PTSD to inform preventive interventions for this treatment population.

Methods: A retrospective cohort study was conducted for all Veterans who initiated PTSD treatment at any Department of Veterans Affairs Medical Center from fiscal year 2008 to 2013. The primary outcome was mortality within the first year after treatment initiation. In 2018, collected data were analyzed to determine leading causes of death. For the top ten causes, standardized mortality ratios (SMRs) were calculated from age- and sex-matched mortality tables of the U.S. general population.

Results: A total of 491,040 Veterans were identified who initiated PTSD treatment. Mean age was 48.5 (± 16.0) years, 90.7% were male, and 63.5% were of white race. In the year following treatment initiation, 1.1% (5,215/491,040) died. All-cause mortality was significantly higher for Veterans with PTSD compared with the U.S. population (SMR=1.05, 95% CI=1.02, 1.08, $p < 0.001$). Veterans with PTSD had a significant increase in mortality from suicide (SMR=2.52, 95% CI=2.24, 2.82, $p < 0.001$), accidental injury (SMR=1.99, 95% CI=1.83, 2.16, $p < 0.001$), and viral hepatitis (SMR=2.26, 95% CI=1.68, 2.93, $p < 0.001$) versus the U.S. population. Of those dying from accidental injury, more than half died of poisoning (52.3%, 325/622).

Conclusions: Veterans with PTSD have an elevated risk of death from suicide, accidental injury, and viral hepatitis. Preventive interventions should target these important causes of death.

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INTRODUCTION

Posttraumatic stress disorder (PTSD) is a condition that develops after exposure to a traumatic event.¹ Symptoms include intrusive re-experiencing of the traumatic event, avoidance of trauma-related stimuli, negative alterations in cognition and mood, and changes in arousal and reactivity.¹ PTSD affects 8.3% of Americans² and is marked by significant symptom-related distress and functional impairment.³ In addition to the decreased quality of life,³ individuals with PTSD have a higher prevalence of cardiovascular,⁴ metabolic,⁵ and autoimmune disorders⁶ when compared with those without PTSD. These factors taken in aggregate arguably make PTSD an important

contributor to mortality and therefore, a priority for preventive health care.

Although literature strongly supports the assertion that patients with PTSD have increased overall

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mortality, the exact causes of that excess mortality have been more elusive. Understanding these causes may help elucidate potential targets for prevention. Most studies evaluating mortality in PTSD have been conducted in U.S. military Veterans. Though Veterans with PTSD have been documented to have twice the risk of death as those without PTSD, the causes remain unknown.⁷ Published reports frequently demonstrate causes of death attributed to cardiovascular complications^{7–12} and malignancy,^{7,12} but studies comparing Vietnam Veterans with PTSD with the general population have not found increased cardiovascular or malignancy-related deaths.^{13,14} Other studies have reported a high prevalence of external-cause mortality^{7,13–15} among patients with PTSD. However, with the exception of suicide mortality,^{7,13–18} a detailed analysis of specific external causes of death in this population has not been published yet.

Most published reports about external causes of death focus on Vietnam Veterans with PTSD.^{7,12,14,17,19,20} However, the limited research on external causes of death in other cohorts of Veterans has been less clear.^{17,20} Veterans with PTSD who served in Operation Enduring Freedom, Operation Iraqi Freedom, or Operation New Dawn have not been widely studied. These contemporary cohorts have higher percentages of young Veterans and women,²¹ both of which may influence causes of death.²² With advances in medicine and technology, Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn Veterans are more likely to survive combat injuries than previous generations, thereby increasing the prevalence of PTSD,^{17,21} pain disorder,²³ and pain-related opioid use²³ among survivors. Evaluating mortality across a diverse sample of Veterans may provide more inclusive data on causes of death related to PTSD.

In addition, causes of death among patients engaged in clinical treatment for PTSD are not well described. Although published reports demonstrate an elevated all-cause mortality risk among treatment-seeking U.S. Veterans with PTSD,^{13,24} the treatment settings are rarefied (e.g., residential¹³ and inpatient¹⁸) and generalizability to a larger PTSD treatment population may be limited. Furthermore, between 2004 and 2013, the Veterans Health Administration underwent a clinical paradigm shift in the management of PTSD²⁵ by incorporating more individualized evidence-based psychotherapy into treatment plans.²⁶ Given the wide array of clinical manifestations and comorbidities associated with PTSD, access to tailored treatment modalities may have improved health outcomes among treatment-seeking Veterans by addressing individual needs.¹⁸

Finally, the relationship between age and cause of death among patients with PTSD is not well known.

Early research suggests that patients with PTSD may have accelerated cellular aging as evidenced by shorter telomere lengths²⁷ and may therefore be at increased risk for death. This may be related to chronic stress states compounded over many years.¹³ In a 6-year longitudinal study of Vietnam Veterans with PTSD, hyperarousal symptoms were found to significantly increase over time.¹⁸ It is plausible that this hyperarousal could increase rates of cardiovascular disease and death among older patients with chronic PTSD. Evaluating causes of death relative to age in patients with PTSD may be important for developing targeted interventions.

No study has comprehensively investigated specific causes of death by age group among contemporary treatment-seeking Veterans with PTSD and compared mortality rates with an age- and sex-matched U.S. general population. Stratifying causes of death by age may help determine if mortality related to chronic stress states appears later in life. The purpose of this study was to better understand the relationship between PTSD and mortality among a national sample of treatment-seeking Veterans with PTSD. The primary objectives were as follows: (1) to document the relative mortality for Veterans engaging in PTSD treatment compared with the U.S. population and (2) to determine the specific causes of death contributing to this mortality, thereby informing preventive interventions for patients and providers.

METHODS

Department of Veterans Affairs Medical Center (VA) users with new PTSD treatment episodes between the fiscal years (FY) 2008 and 2013 were identified using the VA Corporate Data Warehouse. Patient demographic information, encounter, and diagnostic data were obtained from the Corporate Data Warehouse. The Veterans IRB of Northern New England approved the study.

Study Population

Patients were drawn from an existing retrospective cohort of Veterans entering PTSD treatment at a VA facility (VA users) between October 1, 2008 and September 30, 2013.^{28,29} To avoid misclassification of PTSD status in VA administrative data, VA users included those who received a primary diagnosis of PTSD at two or more outpatient visits, at least one of which occurred in a mental health setting, over the course of 90 days. Requiring at least two PTSD diagnoses^{30,31} and using PTSD diagnoses made in mental health settings are both strategies to increase the positive predictive value of diagnostic data.³⁰ However, as access to individualized evidence-based psychotherapy for PTSD has only increased in clinical practice since 2008,³² this data set was restricted to Veterans with new episodes of VA PTSD treatment in FY 2008 or later. When Veterans met inclusion criteria multiple times over the 6-year period, only the first episode was included. Qualifying Veterans were followed up for 1 year after index PTSD diagnosis.

Measures

To describe the cohort, patient and healthcare utilization characteristics were measured for FY 2008–2013. Patient characteristics included demographics, medical and psychiatric comorbidities, and military service. Healthcare utilization characteristics included percentage of patients receiving outpatient visits to primary care, general mental health, specialized PTSD clinics, substance abuse specialty clinics, as well as residential PTSD programs, substance abuse programs, and acute inpatient psychiatry settings.

To assess mortality, vital status was obtained using the VA Vital Status File, which is linked to the Corporate Data Warehouse. All deaths identified within 1 year of index PTSD diagnosis were assessed for cause of death using the VA–Department of Defense Suicide Data Repository, which links VA decedents to the Centers for Disease Control and Prevention (CDC) National Death Index.³³ Cause of death was classified using ICD-10 definitions from the CDC National Center for Health Statistics.

To allow for statistical comparison with the general population, mortality rates for the 2014 U.S. population were extracted from CDC's Wide-ranging Online Database for Epidemiologic Research (WONDER).³⁴ The CDC WONDER comparison population was classified by sex and three age categories (18–34 years, 35–64 years, and ≥65 years). For all-cause mortality and leading causes of death present in the study population, reference rates were obtained for age- and sex-specific strata to facilitate calculation of age- and sex-adjusted standardized mortality ratios (SMRs).

Statistical Analysis

The collected data were analyzed in two parts between September 4, 2018 and November 2, 2018. Counts of death were generated for all causes of death for Veterans in the first year of VA PTSD treatment from FY 2008 to 2013. Following National Death Index data standards, categories were suppressed where counts of death dropped below ten. This method resulted in the presentation of up to 15 leading causes of death for the study population overall and for each age group. To compare the observed mortality among PTSD Veterans with the U.S. population, age- and sex-adjusted SMRs were calculated for only the top ten leading causes to ensure stable rates in the substrata. To generate a consistent comparison with CDC's WONDER,³⁴ all deaths were counted for Veterans who initiated VA PTSD treatment in calendar years 2008–2013. However, this time frame shift did not change the rank order of the leading causes of death.

RESULTS

Between FY 2008 and 2013, a total of 491,040 Veterans with PTSD met inclusion criteria for treatment initiation (Table 1). The mean age of Veterans was 48.5 (±16.0) years, 90.7% were male, 63.5% were white, and 60.1% were middle-aged (35–64 years). In the year after index PTSD diagnosis, 60.3% were diagnosed with comorbid depression, 39% with nicotine dependence, 22.6% with alcohol dependence, and 3.2% with opioid dependence. More than one third served in Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn

Table 1. Profile of VA Users With New Episodes of PTSD Care Between FY 2008–2013

Variable	VA PTSD Veteran cohort, ^a n (%)
Demographic characteristics at index PTSD diagnosis	
Age at time of care, years	
18–34	133,965 (27.28)
35–64	295,034 (60.08)
≥65	62,041 (12.63)
Sex	
Male	445,583 (90.7)
Female	45,457 (9.3)
Race	
White	311,756 (63.5)
Black	93,666 (19.1)
Hispanic	39,827 (8.1)
Married	258,764 (52.7)
Rural	171,644 (35.0)
Homeless	26,574 (5.4)
VA disability level ≥70	273,242 (55.7)
Comorbidities during year after index PTSD diagnosis	
Pain disorder	318,802 (64.9)
Headache disorder	123,441 (25.1)
TBI and cognitive disorders	65,834 (13.4)
Depressive mood disorders	296,071 (60.3)
Non-PTSD anxiety disorders	139,779 (28.5)
Bipolar mood disorders	30,560 (6.2)
Substance use disorders during year after index PTSD diagnosis	
Nicotine dependence	191,712 (39.0)
Alcohol dependence	111,027 (22.6)
Opioid dependence	15,903 (3.2)
Military characteristics	
OEF/OIF/OND Veteran	171,364 (34.9)
Combat exposure	140,344 (28.6)
Military sexual trauma	45,803 (9.3)
Service utilization during year after index PTSD diagnosis	
Any primary care visits	453,051 (92.3)
Any outpatient general mental health visits	490,511 (99.9)
Any outpatient specialized PTSD clinic visits	218,827 (44.6)
Any outpatient substance abuse/detox visits	71,513 (14.6)
Any residential PTSD treatment	10,375 (2.1)
Any residential substance abuse treatment	12,723 (2.6)
Any inpatient mental health treatment	34,386 (7.0)

^an=491,040.

FY, fiscal year; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom; OND, Operation New Dawn; PTSD, posttraumatic stress disorder; TBI, traumatic brain injury; VA, U.S. Department of Veterans Affairs.

(34.9%) and many experienced combat (28.6%). Almost all utilized primary care (92.3%) and outpatient general mental health services (99.9%). Nearly half of Veterans

Table 2. Causes of Death Among VA Users During First Year of PTSD Treatment Between FY 2008–2013

Rank	Overall (n=5,215)		Age 18–34 years (n=417)		Age 35–64 years (n=2,875)		Age ≥65 years (n=1,923)	
	Cause of death	n	Cause of death	n	Cause of death	n	Cause of death	n
1	Heart disease	1,243	Unintentional injury	202	Heart disease	671	Heart disease	552
2	Malignant neoplasms	1,126	Suicide	115	Malignant neoplasms	659	Malignant neoplasms	457
3	Unintentional injury	622	Heart disease	20	Unintentional injury	345	Chronic lower respiratory disease	161
4	Suicide	311	Homicide	12	Suicide	174	Unintentional injury	75
5	Chronic lower respiratory disease	297	Malignant neoplasms	10	Chronic lower respiratory disease	134	Diabetes mellitus	68
6	Diabetes mellitus	194	— ^a	—	Diabetes mellitus	125	Cerebrovascular	56
7	Liver disease	130	— ^a	—	Liver disease	107	Influenza and pneumonia	50
8	Cerebrovascular	118	— ^a	—	Cerebrovascular	60	Alzheimer disease	42
9	Influenza and pneumonia	79	— ^a	—	Viral hepatitis	56	Nephritis	32
10	Viral hepatitis	58	— ^a	—	Septicemia	30	Septicemia	22
11	Septicemia	52	— ^a	—	Influenza and pneumonia	27	Liver disease	22
12	Nephritis	51	— ^a	—	Hypertension	24	Suicide	22
13	Alzheimer disease	44	— ^a	—	Nephritis	19	Pneumonitis	20
14	Homicide	35	—	—	Homicide	19	Parkinson disease	19
15	Hypertension	32	—	—	Aortic aneurysm	15	Benign neoplasms	12

^aEight causes suppressed: <10 cases.

FY, fiscal year; PTSD, posttraumatic stress disorder; VA, U.S. Department of Veterans Affairs.

with PTSD visited outpatient specialized PTSD clinics (44.6%), with a smaller percentage entering residential PTSD treatment (2.1%) or inpatient mental health (7%).

During the first year of VA PTSD treatment, 5,215 Veterans died (Table 2). The top three causes of death were heart disease, malignant neoplasms, and unintentional injury. The leading causes of death for young Veterans (aged 18–34 years) were unintentional injury and suicide. The leading causes of death for middle-aged Veterans (35–64 years) and older Veterans (aged ≥65 years) were heart disease and malignant neoplasms.

Given that 622 Veterans with PTSD died of unintentional injury during their first year of treatment, these injury-related deaths were described further (Table 3). In the entire population, the top three causes of unintentional injury deaths were poisoning, motor vehicle traffic, and falls. The leading causes of unintentional injury deaths in young Veterans and middle-aged Veterans were poisoning and motor vehicle traffic. The leading causes of unintentional injury deaths in older Veterans were falls and motor vehicle traffic.

Between calendar years 2008 and 2013, a total of 473,803 Veterans entered VA PTSD treatment and 4,782 died within 1 year. Based on the age- and sex-matched U.S. population, 4,553.7 deaths were expected because of any cause. Therefore, there was evidence of excess

mortality among Veterans with PTSD compared with the U.S. population (SMR=1.05, 95% CI=1.02, 1.08, $p<0.001$).

Veterans with PTSD had a significant increase in mortality compared with the U.S. population for several causes of death (Table 4), including diabetes mellitus (SMR=1.29, 95% CI=1.11, 1.49, $p<0.001$) and chronic liver disease (SMR=1.34, 95% CI=1.11, 1.59, $p<0.01$). In addition, Veterans with PTSD had a twofold increase in mortality compared with the U.S. population for suicide (SMR=2.52, 95% CI=2.24, 2.82, $p<0.001$), unintentional injury (SMR=1.99, 95% CI=1.83, 2.16, $p<0.001$), and viral hepatitis (SMR=2.26, 95% CI=1.68, 2.93, $p<0.001$). Conversely, among those with PTSD, there were fewer-than-expected deaths from cerebrovascular disease (SMR=0.54, 95% CI=0.44, 0.65, $p<0.001$) and malignant neoplasms (SMR=0.90, 95% CI=0.85, 0.96, $p<0.001$).

DISCUSSION

This study outlines specific causes of excess mortality among Veterans with PTSD and stratified those causes of death by age. Compared with the U.S. population, VA users engaging in PTSD treatment had a 5% excess risk for death resulting from any cause. Accidents, suicide, and viral hepatitis were most elevated as causes of death

Table 3. Unintentional Injury Deaths Among VA Users During First Year of PTSD Treatment FY 2008–2013

Rank	Overall (n=622)		Age 18–34 years (n=202)		Age 35–64 years (n=345)		Age ≥65 years (n=75)	
	Cause of death	n	Cause of death	n	Cause of death	n	Cause of death	n
1	Poisoning	325	Poisoning	130	Poisoning	183	Fall	30
2	MV traffic	149	MV traffic	63	MV traffic	72	MV traffic	14
3	Fall	53	— ^b	—	Fall	22	Poisoning	12
4	Other deaths ^a	23	— ^b	—	Drowning	16	— ^c	—
5	Drowning	22	— ^b	—	Other deaths ^a	15	— ^c	—
6	Suffocation	17	— ^b	—	Suffocation	13	— ^c	—
7	Pedestrian	10	— ^b	—	— ^d	—	— ^c	—
8	— ^e	—	—	—	— ^d	—	— ^c	—
9	— ^e	—	—	—	— ^d	—	— ^c	—
10	— ^e	—	—	—	— ^d	—	—	—
11	— ^e	—	—	—	— ^d	—	—	—
12	— ^e	—	—	—	— ^d	—	—	—
13	— ^e	—	—	—	— ^d	—	—	—

^aOther deaths include accidental injury by firearm, fire/burn, machinery, natural/environment, struck by or against.

^b5 causes suppressed: <10 cases.

^c6 causes suppressed: <10 cases.

^d7 causes suppressed: <10 cases.

^e6 causes suppressed: <10 cases.

FY, fiscal year; MV, motor vehicle; PTSD, posttraumatic stress disorder; VA, U.S. Department of Veterans Affairs.

in Veterans with PTSD compared with the U.S. population, with SMRs indicating a twofold increase in mortality for each cause of death. Diabetes mellitus and chronic liver disease were also significantly elevated as causes of death in Veterans with PTSD compared with the U.S. population. During the first year of VA treatment, young Veterans with PTSD were more likely to die of unintentional injury and suicide, whereas middle-aged and older Veterans were more likely to die of cardiovascular disease and malignant neoplasms.

The overall results support prior literature demonstrating an association between PTSD and excess mortality. However, the findings in this study showing a 5% excess mortality were smaller than the twofold elevated risk reported by Schlenger et al.,⁷ and the 58% elevated risk found by Meier and colleagues.¹⁵ This divergence may be attributed to the selection of all-era Veterans, including a large proportion of young Veterans, across a range of PTSD treatment settings. Veterans seeking treatment for PTSD may be more inclined

Table 4. Leading Causes of Death Among VA Users Compared With the General U.S. Population^a

Rank	Cause of death	General population		Observed deaths	Expected deaths	SMR ^b (95% CI)
		VA PTSD cohort Rate per 100,000	Rate per 100,000			
1	Diseases of heart	243.1	255.1	1,152	1,137.3	1.01 (0.96, 1.07)
2	Malignant neoplasms	214.9	242.8	1,018	1,129.0	0.90 ^{***} (0.85, 0.96)
3	Unintentional injury (accidents)	120.5	50.0	571	286.5	1.99 ^{***} (1.83, 2.16)
4	Intentional self-harm (suicide)	61.4	15.9	291	115.3	2.52 ^{***} (2.24, 2.82)
5	Chronic lower respiratory disease	56.1	60.0	266	239.9	1.11 (0.98, 1.25)
6	Diabetes mellitus	38.0	30.4	180	139.3	1.29 ^{***} (1.11, 1.49)
7	Chronic liver disease and cirrhosis	24.9	13.9	118	87.9	1.34 ^{**} (1.11, 1.59)
8	Cerebrovascular disease	22.0	54.8	104	191.2	0.54 ^{***} (0.44, 0.65)
9	Influenza and pneumonia	15.2	22.5	72	88.9	0.81 (0.63, 1.01)
10	Viral hepatitis	10.6	3.3	50	22.1	2.26 ^{***} (1.68, 2.93)

Note: Boldface indicates statistical significance (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

^aVA users were followed after initiation of PTSD treatment between calendar year 2008 and 2013.

^bReference is age- and sex-matched general U.S. population rates available from 2014 CDC WONDER.

CDC, Centers for Disease Control and Prevention; PTSD, posttraumatic stress disorder; SMR, standardized mortality ratio; VA, U.S. Department of Veterans Affairs.

to seek treatment for other medical conditions, thereby mitigating potential risk factors associated with mortality.

The finding that Veterans with PTSD were at elevated risk for death by suicide is consistent with prior literature.¹⁶ Although this finding was potentially mediated by elevated rates of depression and substance abuse,³⁵ it does not change the fact that Veterans with PTSD were at risk for suicide. This study also demonstrated that excess mortality in patients with PTSD was largely attributed to unintentional injuries, especially among young Veterans. This relationship has not been well explored previously. Though Meier et al.¹⁵ found that patients with PTSD had a significantly higher mortality risk because of external causes, they did not distinguish between accidents and suicide. Most unintentional injury deaths observed in this study were the result of poisoning. Given the ongoing concerns regarding potential misclassification of suicides, especially overdose deaths,³⁶ it may be that some of the unintentional poisonings in this cohort were in fact misclassified suicides.

Veterans with PTSD were at significantly elevated risk for death because of diabetes mellitus and chronic liver disease, which is consistent with mounting evidence supporting that PTSD may be associated with metabolic disorders.^{8,9} Patients with PTSD are prone to engage in unhealthy behaviors (22.6% of this cohort had alcohol dependence) that increase their risk for liver disease. Similar to Bullman and colleagues¹⁴ and Drescher et al.¹³ who used general population comparators, this study did not find a significantly elevated risk for death resulting from cardiovascular disease or malignancy among Veterans with PTSD compared with the U.S. population.

Although Veterans with PTSD were at elevated risk for death from viral hepatitis compared with the U.S. population, there has been relatively little study of the relationship between bloodborne pathogens and PTSD. Yet, similar to this study, Essock and colleagues³⁷ reported that PTSD was associated with a significant risk for HIV as well as hepatitis B and C. This finding may correlate with increasing frequency of opioid use disorder among Veterans (3.2% of this cohort had opioid dependence) with PTSD.^{23,29} This is relevant given the documented association between opioid injection and hepatitis C.³⁸

This study has important implications for preventive medicine. Although screening benefits must be weighed against the probability of adverse outcomes without screening,³⁹ patients with PTSD require greater utilization of health care⁴⁰ because of impaired functionality and comorbid medical and psychiatric illness.⁴¹ It may therefore be less costly to intervene early. The VA

currently has a PTSD screening process in place⁴² and valid measures of PTSD diagnosis^{30,31,43}; however, less consensus regarding PTSD screening exists in the civilian population.⁴⁴ Research is needed to determine if screening instruments, such as the VA Primary Care PTSD Screen,⁴² can help identify at-risk civilians. Moreover, research is needed to address the comorbidities that contribute to mortality in patients with PTSD.

The intersection of pain and PTSD may have significant clinical and programmatic implications, particularly for Veterans with PTSD. Although CDC recently issued guidelines emphasizing nonpharmacologic treatments for pain disorder,⁴⁵ Veterans with PTSD and comorbid pain may be at risk for opioid use disorder.²³ In addition to increasing the risk for hepatitis, opioids may play a role in unintentional injury and suicide, especially among Veterans with PTSD who are aged 18–34 years. Preventive efforts may need to focus on pain control as a possible target for PTSD treatment in this age group.

Treatment-seeking patients with PTSD may also benefit from more seamless transitions between care settings.¹³ Among Vietnam Veterans in residential PTSD treatment, Drescher et al.¹³ found that the average time from discharge to death was only 4 years. Close follow-up, cross-provider communication, and community integration⁴¹ may be effective strategies to prevent PTSD-related deaths. However, more research is needed to determine if evidence-based PTSD care impacts mortality in this population.

Limitations

This study has several limitations, primarily related to sample selection and follow-up. First, the approach did not account for relevant confounders including race/ethnicity, psychiatric and medical comorbidity, and treatment. Although the cohort was started in 2008 to account for changes in VA delivery of evidence-based PTSD care, this study did not address patient-level treatment characteristics and was not designed to determine whether PTSD care affects mortality. Additional multi-year longitudinal cohorts are required to assess whether implementation of evidence-based psychotherapy for PTSD had an effect on mortality outcomes for VA users with PTSD.

Second, the results were not stratified based on military service, time from military separation to index PTSD diagnosis, area of deployment, exposure to theater of war, or trauma source. It is conceivable that each of these variables may affect PTSD severity and mitigate or worsen mortality risk. Third, the results only apply to the first year after PTSD diagnosis. Therefore, the influence of PTSD on disease may appear less severe than in subsequent years. Fourth, the PTSD cohort was included

in the reference group (U.S. population) for SMR calculations. As a result, SMRs likely underestimate the differences between observed and expected deaths.

Finally, the study population was limited to U.S. Veterans. The Veteran population has demonstrated characteristics that make it unique from other PTSD populations.⁴⁶ Notably, Veterans are predominantly older and male.⁴⁶ Veterans who access the VA Health Care System are more likely to have poorer health, lower SES, and more medical conditions than the general population.⁴⁶ Therefore, these findings may not be generalizable to civilians with PTSD. It will be important that other studies replicate these results in non-Veteran populations and adjust for relevant confounders.

CONCLUSIONS

The findings suggest that Veterans with PTSD are at elevated risk for death compared with the general population, although the risk is smaller than in previous studies. Furthermore, this study fills several gaps in the literature.

The risk for death from suicide and accidents is high in Veterans with PTSD, especially among younger Veterans. Veterans with PTSD and comorbid alcohol use disorder have even greater rates of suicide.⁴⁷ Treatment of PTSD as well as co-occurring depression and substance use disorders may lessen the risk of suicide. Similarly, interventions that target PTSD and comorbid pain disorder may reduce opioid-related suicide and accidental poisoning.²³

The risk for death from diabetes, chronic liver disease, and viral hepatitis is also high in Veterans with PTSD. These conditions are associated with unhealthy lifestyle choices. Therefore, patients with PTSD should receive comprehensive education on the benefits of diet and exercise as well as the risks of chronic stress and substance use.

Finally, future studies should focus on developing and testing targeted interventions to address these risk factors to improve the overall health outcomes in patients with PTSD.

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REFERENCES

1. American Psychiatric Association. Trauma and stressor-related disorders. In: *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013: pp. 265–290.
2. Kilpatrick DG, Resnick HS, Milanak ME, et al. National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-V criteria. *J Trauma Stress*. 2013;26(5):537–547. <https://doi.org/10.1002/jts.21848>.
3. Fang SC, Schnurr PP, Kulish AL, et al. Psychosocial functioning and health-related quality of life associated with posttraumatic stress disorder in male and female Iraq and Afghanistan War Veterans: the VALOR registry. *J Womens Health (Larchmt)*. 2015;24(12):1038–1046. <https://doi.org/10.1089/jwh.2014.5096>.
4. Beristianos MH, Yaffe K, Cohen B, Byers AL. PTSD and risk of incident cardiovascular disease in aging veterans. *Am J Geriatr Psychiatry*. 2016;24(3):192–200. <https://doi.org/10.1016/j.jagp.2014.12.003>.
5. Rosenbaum S, Stubbs B, Ward PB, et al. The prevalence and risk of metabolic syndrome and its components among people with posttraumatic stress disorder: a systematic review and meta-analysis. *Metabolism*. 2015;64(8):926–933. <https://doi.org/10.1016/j.metabol.2015.04.009>.
6. O'Donovan A, Cohen BE, Seal KH, et al. Elevated risk for autoimmune disorders in Iraq and Afghanistan Veterans with posttraumatic stress disorder. *Biol Psychiatry*. 2015;77(4):365–374. <https://doi.org/10.1016/j.biopsych.2014.06.015>.
7. Schlenger WE, Corry NH, Williams CS, et al. A prospective study of mortality and trauma-related risk factors among a nationally representative sample of Vietnam Veterans. *Am J Epidemiol*. 2015;182(12):980–990. <https://doi.org/10.1093/aje/kwv217>.
8. Cohen BE, Marmar C, Ren L, Bertenthal D, Seal KH. Association of cardiovascular risk factors with mental health diagnoses in Iraq and Afghanistan War Veterans using VA health care. *JAMA*. 2009;302(5):489–492. <https://doi.org/10.1001/jama.2009.1084>.
9. Edmondson D, Cohen BE. Posttraumatic stress disorder and cardiovascular disease. *Prog Cardiovasc Dis*. 2013;55(6):548–556. <https://doi.org/10.1016/j.pcad.2013.03.004>.
10. Ahmadi N, Hajsadeghi F, Mirshkarlo HB, Budoff M, Yehuda R, Ebrahimi R. Post-traumatic stress disorder, coronary atherosclerosis, and mortality. *Am J Cardiol*. 2011;108(1):29–33. <https://doi.org/10.1016/j.amjcard.2011.02.340>.
11. Xue Y, Taub PR, Iqbal N, et al. Cardiac biomarkers, mortality, and posttraumatic stress disorder in military veterans. *Am J Cardiol*. 2012;109(8):1215–1218. <https://doi.org/10.1016/j.amjcard.2011.11.063>.
12. Boscarino JA. Posttraumatic stress disorder and mortality among U.S. Army Veterans 30 years after military service. *Ann Epidemiol*. 2006;16(4):248–256. <https://doi.org/10.1016/j.annepidem.2005.03.009>.
13. Drescher KD, Rosen CS, Burling TA, Foy DW. Causes of death among male veterans who received residential treatment for PTSD. *J Trauma Stress*. 2003;16(6):535–543. <https://doi.org/10.1023/B:JOTS.000004076.62793.79>.
14. Bullman TA, Kang HK. Posttraumatic stress disorder and the risk of traumatic deaths among Vietnam Veterans. *J Nerv Ment Dis*. 1994;182(11):604–610. <https://doi.org/10.1097/00005053-199411000-00002>.
15. Meier SM, Mattheisen M, Mors O, Mortensen PB, Laursen TM, Pennington BW. Increased mortality among people with anxiety disorders: total population study. *Br J Psychiatry*. 2016;209(3):216–221. <https://doi.org/10.1192/bjp.bp.115.171975>.

16. Gradus JL. Posttraumatic stress disorder and death from suicide. *Curr Psychiatry Rep.* 2018;20(11):98. <https://doi.org/10.1007/s11920-018-0965-0>.
17. Boscarino JA. External-cause mortality after psychological trauma: the effects of stress exposure and predisposition. *Compr Psychiatry.* 2006;47(6):503–514. <https://doi.org/10.1016/j.comppsy.2006.02.006>.
18. Johnson DR, Fontana A, Lubin H, Corn B, Rosenheck R. Long-term course of treatment-seeking Vietnam Veterans with posttraumatic stress disorder: mortality, clinical condition, and life satisfaction. *J Nerv Ment Dis.* 2004;192(1):35–41. <https://doi.org/10.1097/01.nmd.0000105998.90425.6a>.
19. Boscarino JA. Psychobiologic predictors of disease mortality after psychological trauma: implications for research and clinical surveillance. *J Nerv Ment Dis.* 2008;196(2):100–107. <https://doi.org/10.1097/NMD.0b013e318162a9f5>.
20. Bullman TA, Kang HK, Watanabe KK. Proportionate mortality among U.S. Army Vietnam Veterans who served in military region I. *Am J Epidemiol.* 1990;132(4):670–674. <https://doi.org/10.1093/oxfordjournals.aje.a115708>.
21. Fulton JJ, Calhoun PS, Wagner HR, et al. The prevalence of posttraumatic stress disorder in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans: a meta-analysis. *J Anxiety Disord.* 2015;31:98–107. <https://doi.org/10.1016/j.janxdis.2015.02.003>.
22. Schnurr PP, Friedman MJ, Bernardy NC. Research on posttraumatic stress disorder: epidemiology, pathophysiology, and assessment. *J Clin Psychol.* 2002;58(8):877–889. <https://doi.org/10.1002/jclp.10064>.
23. Seal KH, Shi Y, Cohen G, et al. Association of mental health disorders with prescription opioids and high-risk opioid use in U.S. Veterans of Iraq and Afghanistan. *JAMA.* 2012;307(9):940–947. <https://doi.org/10.1001/jama.2012.234>.
24. KasproW WJ, Rosenheck R. Mortality among homeless and nonhomeless mentally ill veterans. *J Nerv Ment Dis.* 2000;188(3):141–147. <https://doi.org/10.1097/00005053-200003000-00003>.
25. Rosen CS, Matthieu MM, Wiltsey Stirman S, et al. A review of studies on the system-wide implementation of evidence-based psychotherapies for posttraumatic stress disorder in the Veterans Health Administration. *Admin Policy Ment Health.* 2016;43(6):957–977. <https://doi.org/10.1007/s10488-016-0755-0>.
26. Veterans Health Administration, Office of Quality Safety and Value. The Management of Posttraumatic Stress Disorder Working Group. VA/DoD clinical practice guidelines for the management of posttraumatic stress disorder and acute stress disorder. U.S. Departments of Veterans Affairs and Defense. www.healthquality.va.gov/guidelines/MH/ptsd/VADoDPTSDCPGFinal012418.pdf. Published 2017. Accessed October 25, 2018.
27. Li X, Wang J, Zhou J, Huang P, Li J. The association between posttraumatic stress disorder and shorter telomere length: a systematic review and meta-analysis. *J Affect Disord.* 2017;218:322–326. <https://doi.org/10.1016/j.jad.2017.03.048>.
28. Shiner B, Westgate CL, Bernardy NC, Schnurr PP, Watts BV. Anticonvulsant medication use in veterans with posttraumatic stress disorder. *J Clin Psychiatry.* 2017;78(5):e545–e552. <https://doi.org/10.4088/JCP.16m11031>.
29. Shiner B, Leonard Westgate C, Bernardy NC, Schnurr PP, Watts BV. Trends in opioid use disorder diagnoses and medication treatment among veterans with posttraumatic stress disorder. *J Dual Diagn.* 2017;13(3):201–212. <https://doi.org/10.1080/15504263.2017.1325033>.
30. Gravelly AA, Cutting A, Nugent S, Grill J, Carlson K, Spont M. Validity of PTSD diagnoses in VA administrative data: comparison of VA administrative PTSD diagnoses to self-reported PTSD Checklist scores. *J Rehabil Res Dev.* 2011;48(1):21–30. <https://doi.org/10.1682/JRRD.2009.08.0116>.
31. Frayne SM, Miller DR, Sharkansky EJ, et al. Using administrative data to identify mental illness: what approach is best? *Am J Med Qual.* 2010;25(1):42–50. <https://doi.org/10.1177/1062860609346347>.
32. Maguen S, Li Y, Madden E, et al. Factors associated with completing evidence-based psychotherapy for PTSD among veterans in a national healthcare system. *Psychiatry Res.* 2019;274:112–128. <https://doi.org/10.1016/j.psychres.2019.02.027>.
33. Center of Excellence for Suicide Prevention. Joint Department of Veterans Affairs (VA) and Department of Defense (DoD) Suicide Data Repository – National Death Index (NDI). Published 2017.
34. Friede A, Reid JA, Ory HW. CDC WONDER: a comprehensive online public health information system of the Centers for Disease Control and Prevention. *Am J Public Health.* 1993;83(9):1289–1294. <https://doi.org/10.2105/AJPH.83.9.1289>.
35. Conner KR, Bossarte RM, He H, et al. Posttraumatic stress disorder and suicide in 5.9 million individuals receiving care in the Veterans Health Administration health system. *J Affect Disord.* 2014;166:1–5. <https://doi.org/10.1016/j.jad.2014.04.067>.
36. Rockett IR, Smith GS, Caine ED, et al. Confronting death from drug self-intoxication (DDSI): prevention through a better definition. *Am J Public Health.* 2014;104(12):e49–e55. <https://doi.org/10.2105/AJPH.2014.302244>.
37. Essock SM, Dowden S, Constantine NT, et al. Risk factors for HIV, hepatitis B, and hepatitis C among persons with severe mental illness. *Psychiatr Serv.* 2003;54(6):836–841. <https://doi.org/10.1176/appi.ps.54.6.836>.
38. Lake S, Kennedy MC. Health outcomes associated with illicit prescription opioid injection: a systematic review. *J Addict Dis.* 2016;35(2):73–91. <https://doi.org/10.1080/10550887.2015.1127712>.
39. Harris R, Sawaya GF, Moyer VA, Calonge N. Reconsidering the criteria for evaluating proposed screening programs: reflections from 4 current and former members of the U.S. Preventive Services Task Force. *Epidemiol Rev.* 2011;33(1):20–35. <https://doi.org/10.1093/epi-REV/mxr005>.
40. Schnurr PP, Friedman MJ, Sengupta A, Jankowski MK, Holmes T. PTSD and utilization of medical treatment services among male Vietnam Veterans. *J Nerv Ment Dis.* 2000;188(8):496–504. <https://doi.org/10.1097/00005053-200008000-00004>.
41. Wisco BE, Marx BP, Wolf EJ, Miller MW, Southwick SM, Pietrzak RH. Posttraumatic stress disorder in the U.S. Veteran population: results from the National Health and Resilience in Veterans Study. *J Clin Psychiatry.* 2014;75(12):1338–1346. <https://doi.org/10.4088/JCP.14m09328>.
42. Prins A, Bovin MJ, Smolenski DJ, et al. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): development and evaluation within a veteran primary care sample. *J Gen Intern Med.* 2016;31(10):1206–1211. <https://doi.org/10.1007/s11606-016-3703-5>.
43. Holowka DW, Marx BP, Gates MA, et al. PTSD diagnostic validity in Veterans Affairs electronic records of Iraq and Afghanistan veterans. *J Consult Clin Psychol.* 2014;82(4):569–579. <https://doi.org/10.1037/a0036347>.
44. Lang AJ, Stein MB. An abbreviated PTSD checklist for use as a screening instrument in primary care. *Behav Res Ther.* 2005;43(5):585–594. <https://doi.org/10.1016/j.brat.2004.04.005>.
45. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA.* 2016;315(15):1624–1645. <https://doi.org/10.1001/jama.2016.1464>.
46. Agha Z, Lofgren RP, VanRuiswyk JV, Layde PM. Are patients at Veterans Affairs medical centers sicker? A comparative analysis of health status and medical resource use. *Arch Intern Med.* 2000;160(21):3252–3257. <https://doi.org/10.1001/archinte.160.21.3252>.
47. Straus E, Norman SB, Haller M, Southwick SM, Hamblen JL, Pietrzak RH. Differences in protective factors among U.S. Veterans with posttraumatic stress disorder, alcohol use disorder, and their comorbidity: results from the National Health and Resilience in Veterans Study. *Drug Alcohol Depend.* 2019;194:6–12. <https://doi.org/10.1016/j.drugalcdep.2018.09.011>.