

External-cause mortality after psychologic trauma: the effects of stress exposure and predisposition

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Abstract

Research suggests that exposure to psychologic trauma is associated with mortality from external causes, including homicide, suicide, drug overdoses, and unintended injury. However, the etiology of this association is unclear. We examined the survival time and cause of death among a national sample of 15 288 US Army veterans by posttraumatic stress disorder (PTSD) status 30 years after military service. In these analyses, we included demographic (age, race, marital status, service entry age, and birthplace), predisposing (army volunteer status, discharge status, history of drug abuse, early-age alcohol use, and intelligence), and combat exposure variables. After adjusting for demographic and predisposing factors, all-cause mortality was associated with PTSD for all veterans combined (hazards ratio [HR] = 2.1, $P < .001$), as well as for era veterans without Vietnam service (HR = 2.0, $P = .001$) and theater veterans with Vietnam service (HR = 2.1, $P < .001$). For theater veterans, PTSD remained significant for all-cause mortality, even after controlling for demographic, predisposition, and combat exposure measures (HR = 2.1, $P < .001$). For external mortality, the adjusted results indicated that PTSD was associated with death for all veterans combined (HR = 2.3, $P < .001$) and for theater veterans separately (HR = 2.2, $P = .002$). For era veterans, the adjusted external mortality results also approached statistical significance (HR = 2.2, $P = .068$). Among theater veterans, PTSD remained significant for external mortality, even after controlling for all variables and combat exposure (HR = 2.2, $P = .002$). Combat exposure was not associated with external mortality once all variables were controlled. In addition, theater veterans who volunteered for Vietnam and those with dishonorable discharges were at increased risk for external-cause mortality.

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1. Introduction

Research suggests that having a history of posttraumatic stress disorder (PTSD) or exposure to traumatic stressors is associated with higher rates of morbidity [1-7]. Studies also suggest that PTSD and traumatic stress exposures are associated with mental health disorders and diminished quality of life [8-14]. Recent reports related to personnel returning from Afghanistan and Iraq have indicated significant rates of psychologic problems among these veterans [15,16], and anecdotal reports have suggested that these personnel may be at higher risk for suicide after return [17]. Furthermore, one study that examined mental health problems among infantry units before and after deployment to Iraq or Afghanistan found significant

increases in mental health disorders, including PTSD [18]. Another study tracking personnel who had become eligible for Veterans Affairs benefits during the Iraq and Afghanistan conflicts found an increase in treatments for mental health disorders and PTSD among this population [19]. In addition, reports indicate that many of those recently wounded in combat were surviving injuries that were previously proven as fatal [20,21], likely increasing the prevalence of psychiatric casualties among these veterans [22].

Recently, investigators from the Centers for Disease Control and Prevention (CDC, Atlanta, GA) ascertained the vital status and underlying cause of death among participants in the Vietnam Experience Study (VES), a study of 18 313 male US Army veterans from the end of their military service through December 31, 2000 [23]. In this study, all-cause mortality appeared higher among Vietnam theater (those who served in Vietnam) compared with Vietnam era veterans (those who served elsewhere) during

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the 30-year follow-up [23]. Death rates from disease-related chronic conditions did not appear to differ between the theater and era veterans, despite the increasing age of the cohort and the long follow-up period. However, investigators reported that the rate of death from external causes, which included homicide, suicide, accidental poisoning, and unintended injury, was higher among theater veterans in the first 5 years after active duty [23]. After this, no difference occurred for this category overall. However, investigators found an excess of drug-related deaths among theater veterans during the entire follow-up period [23]. These findings were consistent with 2 similar studies. The Australian Vietnam veteran study assessed postservice mortality among 19205 Vietnam theater veterans and 25677 Vietnam era veterans through 1981 [24]. This study found that the death rate for Vietnam theater veterans was 1.2 times higher than for Vietnam era veterans [24]. More recently, a Marine Corps Vietnam veteran study followed 22062 veterans from discharge from active duty through 1991 [25]. Similar to the CDC study, the Marine study found an excess of all-cause mortality among Vietnam theater veterans, and this appeared to be due to external causes of death [25]. In addition, a mortality follow-up among Vietnam veterans enrolled in the Agent Orange Registry found that those with an *International Classification of Diseases, Ninth Revision*, diagnosis of 309.81 (indicating that PTSD was recorded in the medical record) had a higher risk of death from suicide and accidental poisoning [26]. However, the most convincing evidence linking PTSD to external mortality comes from recent analyses of the VES cohort data [27]. In this study, which included a national sample of 15288 Vietnam veterans, Cox proportional hazards regressions were used to examine survival time and external cause of death 16 years after a telephone survey (about 30 years after military service). These analyses adjusted for army entry age, race, age at interview, volunteer status, discharge status, history of drug abuse, and intelligence. Results indicated that postwar mortality from external causes was associated with PTSD among Vietnam theater veterans ($n = 7924$), with a hazards ratio (HR) of 2.3 ($P = .001$) [27]. Also noteworthy was that deaths from other causes, such as cancer and cardiovascular diseases, were also elevated [27].

There are at least several reasons to expect a link between PTSD and external mortality [28]. First, this could be due to common psychiatric comorbidities that have been associated with PTSD [9,29], such as major depression or substance abuse disorder, both of which have been associated with suicidal behavior [30]. Second, this could be due to exposure to combat independent of PTSD [2], such as an altered sense of risk taking or a change in perceived vulnerability after combat experiences [28]. Third, this could be due to self-selection, whereby those who ended up with PTSD and external-cause mortality might have had certain character traits, such as extroverted personalities or lower intelligence levels [2]. These individuals might be

more likely to be “selected out” for combat service and, thus, more likely to have PTSD [2]. However, the association between PTSD and external mortality would be spurious in this situation because it was the character trait that was related to external mortality, not PTSD [28].

In the current article, we expand upon an earlier study [27], which did not examine the impact of combat exposure or specifically assess the role of predisposing factors in external mortality. In the current study, our main hypothesis was that external mortality was principally due to PTSD [2], not combat exposure, per se, or predisposing character traits. This is important because, as suggested, exposure to combat violence itself or self-selection could explain the associations found, not the PTSD.

2. Data and methods

In this study, we examined the impact of PTSD on external mortality among Vietnam veterans through an assessment of postservice mortality among those in the VES cohort who completed telephone interviews conducted by Research Triangle Institute (RTI). Subjects for the study included 17867 US Army veterans known to be alive in December 1983. Starting in January 1985, these men were contacted to complete telephone interviews. Altogether, 15288 (86%) were located and surveyed. The interviews included questions related to PTSD symptoms, health status, substance abuse, combat exposure, demographic data, and military history information. Data from the veteran’s military record also were available.

The population for the current study was composed of men who served in the US Army during the Vietnam War. These men were identified through a random sample of 48513 service records selected from the National Personnel Records Center. Of these, 18581 veterans met the criteria for study eligibility. These criteria included entering the military between 1965 and 1971, serving only 1 term of enlistment, having at least 16 weeks of active service time, and having a pay grade no higher than E5. Participants were classified as Vietnam theater veterans if they served at least 1 tour of duty in Vietnam or as Vietnam era veterans, if they never served in Vietnam, and if they served at least 1 tour of duty elsewhere. The final sample in the current study included 7924 Vietnam theater and 7364 era veterans, for a total of 15288 men who were known not to be deceased and who completed the RTI telephone survey. Further details regarding this study design have been published elsewhere [23,27,31–33]. The CDC Human Subject Review Committee approved the study protocols for all phases of this study, which included all aspects of informed consent. The study subjects were also given a special assurance of confidentiality in accordance with Sections 304, 306, and 308 of the Public Health Service Act (42 USC 242b, 242k, and 242m). Additional details related to human subject protection and informed consent have been published elsewhere [34].

2.1. Ascertainment of vital status and cause-specific mortality

We assessed vital status from the date of completion of the telephone interviews starting in January 1985 until the end of the mortality follow-up on December 31, 2000. In an effort to reduce false matches and to achieve the most complete results, vital status was ascertained using 3 mortality databases: the Department of Veterans Affairs Beneficiary Identification Record Locator Subsystem death file, the Social Security Administration Death Master File, and the National Death Index Plus (NDI Plus) [23]. Investigators also manually reviewed the potential matches from each data source separately and classified the matches as true, false, or questionable [23]. The final determination of vital status was obtained by combining information from all 3 mortality sources. As needed, additional information, such as actual death certificates, was ascertained to confirm vital status. Veterans who had a true match on at least 1 of the 3 national databases were determined to be deceased. All veterans whose vital status was uncertain because of a lack of data to resolve questionable matches or who were not identified through any of the 3 national databases used were assumed to be living as of December 31, 2000.

Underlying cause-of-death codes were obtained from the NDI Plus, the only national mortality database with cause-of-death information. Cause of death was coded according to the *International Classification of Diseases (ICD)* revision in place at the time of death: the *Ninth Revision (ICD-9)* for deaths between January 1, 1979, and December 31, 1998, and the *Tenth Revision (ICD-10)* for deaths between January 1, 1999, and December 31, 2000. For cases in which cause-of-death codes were not available from the NDI Plus, investigators obtained official copies of death certificates, which were then coded by an experienced nosologist at the National Center for Health Statistics (Hyattsville, MD) [23]. In the current study, our main outcome of interest was mortality due to external causes, which included homicide, suicide, drug overdoses, accidental poisoning, unintended injury, and injury of undetermined intent [35].

2.2. Ascertainment of PTSD status

As previously reported [27], we conducted analyses using a subset of VES participants who completed *both* the telephone surveys and personal interviews ($n = 4462$). We did this because although the PTSD measure used in the RTI survey had been implemented in several previous studies [34,36,37], this scale had not been clinically evaluated. Consequently, we compared the results of the RTI-PTSD scale to those obtained by the *Diagnostic Interview Schedule—Version III (DIS-III)* PTSD, based on the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III)* [38–40]. In the VES, DIS-PTSD diagnoses were available for the past 30 days and for lifetime [31,40]. For the personal interviews, a random subsample was selected by the CDC investigators among

the 15288 interviewed by telephone. Altogether, 75% of selected theater veterans ($n = 2490$) and 63% of the era veterans ($n = 1972$) completed the personal interviews (overall participation rate = 69%). The personal interviews were administered at Lovelace Medical Foundation, Albuquerque, NM, between June 1985 and September 1986. On average, the time from combat exposure in Vietnam to the telephone surveys and personal interviews was about 17 years [1]. During the telephone survey, the veterans were asked to report on 15 PTSD-related symptoms that could have occurred in the past 6 months. Consistent with *DSM-III*, a veteran was classified as having current PTSD if he reported at least 1 criterion B symptom (reexperiencing), at least 1 criterion C symptom (avoidance), and at least 2 criterion D symptoms (hyperarousal). The *DSM-III* criterion A (exposure) was not explicitly used in the RTI-PTSD scale but was implicitly used because some of the symptoms included in the B and D criteria referred explicitly to army experiences (eg, “in the past 6 months, had dreams or nightmares of Army experiences”) [34]. We also compared the RTI-PTSD results for theater veterans with results for the combat exposure scale (CES) used in personal interviews [10], a scale shown to be a valid measure of combat experiences and used in previous studies [10,41].

Using the B through D criteria and a 6-month prevalence period, the RTI-PTSD scale classified 10.6% of the theater veterans and 2.9% of the era veterans as having current PTSD (odds ratio [OR] = 3.9, $P < .001$). When we compared these PTSD results with those who were reinterviewed and administered the *DIS-III*, the results were as follows: Of those who met the *DIS-III* criteria for current PTSD in the past month for combat ($n = 54$), 61% were classified as having PTSD on the RTI-PTSD scale; of those classified as negative on the *DIS-III* for combat PTSD, 93% were classified as negative on the RTI-PTSD scale, for an OR of 22.3 (95% confidence interval [CI] = 12.7–39.1). For those who met the *DIS-III* criteria for current PTSD in the past month for *any* trauma ($n = 72$), the results were similar [27]. Of those that met the *DSM-III* criteria for lifetime PTSD based on combat exposure ($n = 377$), 30% were classified as having PTSD on the RTI-PTSD scale; of those classified as negative for lifetime DIS-PTSD for combat, 95% were negative on the RTI-PTSD scale, for an OR of 7.9 (95% CI = 6.1–10.2). For those who met the *DIS-III* criteria for lifetime PTSD for *any* trauma ($n = 446$), the results, again, were similar [27]. Furthermore, for the combat exposure comparison among the theater veterans, there was a dose-response relationship between having low, moderate, high, and very high combat exposure (classified by quartiles) and meeting the criteria on the RTI-PTSD measure, with 7%, 17%, 24%, and 52% positively diagnosed, respectively (χ^2_1 trend test = 123.5, $P < .0001$). We also compared results on the RTI-PTSD scale with both self-reported health status and mental health treatment seeking in the past 12 months among all participants in

the telephone survey ($n = 15288$). These results indicated that those reporting poor current health or recent mental health visits were significantly more likely (both P 's $< .001$) to be PTSD positive on the RTI scale [27]. Finally, we also compared RTI-PTSD results to the Keane PTSD scale from the Minnesota Multiphasic Personality Inventory also administered during the personal interviews [10]. Again, these results were consistent with the concurrent validity results reported above [27]. Although there are limitations that we note below, these findings suggested that a positive diagnosis on the RTI-PTSD scale was generally consistent with a diagnosis of PTSD [27].

2.3. Assessment of demographic, trauma exposure, and predisposing factors

In the current study, we included the following demographic variables in our analyses: age, race, marital status, army entry age, and place of birth [1,4,38]. We also included specific variables as indicators of predisposing character traits potentially associated with antisocial or thrill-seeking personality types [42,43], including army volunteer status, Vietnam volunteer status, discharge status, history of illicit drug use, early-age alcohol consumption, and intelligence [1,4,38]. For trauma exposure, our study included a measure of combat exposure in Vietnam. *Age* was based on the veteran's age at time of the interview and was used as a continuous variable. *Race* was based on the veteran's reported race (white, 82%; black, 11%; Hispanic, 5%; other, 2%) and coded as a 2-category indicator variable (white vs nonwhite). *Army entry age* was the age at military induction and was based on the military record. *Marital status* was based on whether the veteran was married or not when separated from military service and was taken from the military record. *Place of birth* was classified as *foreign* vs *United States* and was taken from the military record. *Army volunteer status* was based on whether the veteran volunteered for military service, classified as *volunteer* vs *drafted*, and was based on the military record. *Vietnam volunteer status* was based on whether the veteran reported volunteering for Vietnam service and pertains to theater veterans only. *Discharge status* was classified as *honorable* vs *dishonorable/other discharge* and was from the military record. *History of illicit drug use* was classified as *present* if the veteran reported use of illicit drugs (eg, narcotics, barbiturates, amphetamines, hallucinogens, or marijuana) while in the army. *Early-age alcohol use* was based on reported alcohol consumption at 14 years or younger. *Intelligence* was taken from the military record and was based on the General Technical Examination at military induction [10]. This measure was used as a continuous variable. Assessing these variables is important because Vietnam veterans were reported to come from higher risk groups [44,45], factors associated with poorer health outcomes and a higher prevalence of risk-prone behaviors [46]. In addition, we also assessed combat exposure status among the theater

veterans. As noted, we did this because we wanted to determine whether the observed outcomes were due to combat exposure, generally, or PTSD more specifically. Thus, in our study, the RTI-CES was used, which was based on 5 combat-related questions asked in the telephone survey (eg, frequency of exposure to snipers, mortar fire, ambushes, mines, and firefights). This measure was similar to the full CES used in the personal interviews [10]. In addition, the RTI-CES was highly correlated with the full CES (eg, $r = 0.76$, $P < .0001$) [10,41]. In the current study, we used the RTI-CES as a binary scale, whereby theater veterans that scored in the highest quintile were classified as high-combat exposure veterans.

2.4. Statistical methods

First, we described the differences found by veteran and by PTSD status. Next, we used Cox proportional hazards regression to calculate both crude (bivariate) and adjusted (multivariate) HRs predicting all-cause and external-cause mortality by PTSD status, hierarchically assessing the variables discussed as a group for demographic, predisposing, and exposure status measures. For all veterans combined, and for era veterans separately, we first adjusted for demographic and then for demographic and predisposition measures. For theater veterans, we first adjusted for demographic, then demographic plus predisposition measures, and then demographic plus predisposition plus combat exposure measures. We use the likelihood ratio χ^2 test to assess the combined effects of predisposing factors "nested" within in the final models [49]. Because PTSD was assessed in the 1985 survey, we only included those who were alive and completed the 1985 telephone interviews. Thus, our analyses examined survival time from interview completion starting in January, 1985, through December 31, 2000, a period of 16 years. For these analyses, we evaluated the main proportional hazards assumption [47], controlled for confounding, and tested for effect modification. We also assessed the linearity assumption for covariates treated as continuous. Statistical analyses for our study were performed using Stata, version 9.1 (College Station, Tex) [48]. For cause-specific mortality, we only included the specific death being considered. For example, if the veteran died of another cause other than external-cause mortality, his survival time was counted until the time of death from the other cause and then exited from the analysis, which is a conservative estimation method and adjusts for differences in relative mortality [49]. All P values presented were based on the 2-tail test, with statistical significance defined as a P value lower than .05. However, given that our survey sample size was large ($n = 15288$), for descriptive statistics, we only highlighted major differences in terms of demographic variables because differences of only 2% were usually significant. Finally, we also examined differences in specific external mortality classifications by PTSD and veteran status.

3. Results

Our descriptive statistics indicated that theater veterans not only had higher rates of PTSD (10.6% vs 2.9%), but also were younger at the 1985 follow-up survey (17.7% vs 22.3%, older than 39 years) and had dishonorable discharges less often (1.9% vs 6.3%) (Table 1). Also noteworthy was that 21% of the theater veterans volunteered for Vietnam service. In terms of PTSD status, the differences were more striking. For example, not only were the PTSD-positive veterans more likely to have died since the 1985 survey (11.8% vs 4.9%), but they also were notably different in terms of other measurements (Table 2). For example, PTSD-positive veterans were more likely to have been nonwhite (30% vs 16.4%), in the lowest intelligence quintile (37.3% vs 18%), and to have had entered the service at a younger age (25% vs 12.6%). They were also more likely to have had a history of illicit drug use (8.1% vs 1.7%), more likely to have had consumed alcohol at an early age (8.5% vs 5.1%), less likely to have been drafted (57% vs 66.4%), and more likely to have had a dishonorable discharge (8.7% vs 3.6%). As expected, PTSD was also associated with high combat exposure (28.9% vs 9.5% overall), as well as with volunteering for Vietnam service (25% vs 9.6% overall).

Table 3 presents the crude and adjusted mortality results, respectively, for all-cause and external-cause mortality, as well as the number of deaths and the total person-years at risk for all veterans combined and for each veteran stratum. As can be seen, the unadjusted all-cause mortality for PTSD-positive veterans for all veterans and era veterans

Table 1
Profile of Vietnam theater veterans vs Vietnam era veterans (n = 15288)

| Variable | Vietnam theater veteran (%) | Vietnam era veteran (%) | P* |
|--|-----------------------------|-------------------------|-------|
| Deceased at follow-up | 5.5 | 5.2 | .39 |
| PTSD at interview | 10.6 | 2.9 | <.001 |
| <i>Demographic factors</i> | | | |
| Aged ≥40 years at interview | 17.7 | 22.3 | <.001 |
| Nonwhite race | 16.8 | 18.0 | .054 |
| Foreign born | 3.3 | 4.6 | <.001 |
| Married at discharged | 27.3 | 30.1 | <.001 |
| Entered service at 18 or less | 14.2 | 12.6 | .004 |
| <i>Predisposition factors</i> | | | |
| Intelligence—lowest quintile | 20.8 | 17.8 | <.001 |
| History of illicit drugs in service | 2.5 | 1.8 | .004 |
| Regular drinking at ≤14 years old | 5.5 | 5.2 | .43 |
| Volunteered for military service | 32.8 | 35.6 | <.001 |
| Volunteered for Vietnam service ^a | 20.5 | 0.0 | <.001 |
| Dishonorable discharge | 1.9 | 6.3 | <.001 |
| <i>Combat exposure</i> | | | |
| Very high combat exposure ^a | 20.9 | 0.0 | <.001 |
| n | 7924 | 7364 | – |

^a Vietnam era veterans coded as “no/none” for this variable.

* Two-sided χ^2_1 test.

Table 2

Profile of PTSD-negative vs PTSD-positive Vietnam veterans (n = 15288)

| Variable | PTSD negative (%) | PTSD positive (%) | P* |
|--|-------------------|-------------------|-------|
| Deceased at follow-up | 4.9 | 11.8 | <.001 |
| <i>Demographic factors</i> | | | |
| Aged ≥40 years at interview | 20.4 | 13.0 | <.001 |
| Nonwhite race | 16.4 | 30.0 | <.001 |
| Married at discharge | 28.6 | 29.0 | .753 |
| Entered service at ≤18 years old | 12.6 | 25.0 | <.001 |
| Foreign born | 3.8 | 5.3 | .013 |
| <i>Predisposition factors</i> | | | |
| Intelligence—lowest quintile | 18.0 | 37.3 | <.001 |
| History of illicit drugs in service | 1.7 | 8.1 | <.001 |
| Regular drinking at ≤14 years old | 5.1 | 8.5 | <.001 |
| Volunteered for military service | 33.6 | 43.0 | <.001 |
| Volunteered for Vietnam service ^a | 9.6 | 25.0 | <.001 |
| Dishonorable discharge | 3.6 | 8.7 | <.001 |
| <i>Combat exposure</i> | | | |
| Very high combat exposure ^a | 9.5 | 28.9 | <.001 |
| n | 14238 | 1050 | – |

^a Vietnam era veterans coded as “no/none” for this variable.

* Two-sided χ^2_1 test.

separately was higher for both these groups, with HRs of 2.5 ($P < .001$) and 2.6 ($P < .001$), respectively. Although reduced somewhat, the results remained significant for all-cause mortality for these groups when demographic and predisposition measures were added hierarchically (for all veterans, HR = 2.1, $P < .001$; for era veterans, HR = 2.0, $P = .001$). For all veterans combined, the results for external mortality were similar to all-cause mortality (for crude, HR = 2.7, $P < .001$; for adjusted, HR = 2.3, $P < .001$). In terms of the external-cause mortality for era veterans, these PTSD-positive veterans had a crude HR of 2.9 ($P < .001$) and an adjusted HR of 2.2 ($P = .068$) (Table 3). The result for theater veterans indicated that the crude result for PTSD-positive veterans was significant for both all-cause and external-cause mortality (for all-cause, HR = 2.5, $P < .001$; for external-cause, HR = 2.6, $P < .001$) (Table 4). When the theater veteran results were adjusted hierarchically, the HRs for these veterans for all-cause and external-cause mortality were reduced somewhat, but remained significant (for all-cause, HR = 2.1, $P < .001$; for external-cause, HR = 2.2, $P = .002$).

Noteworthy was that for the theater veterans, combat exposure was significant neither in the all-cause (HR = 1.2, $P = .15$) nor the external-cause mortality (HR = 1.0, $P = .883$) model (Table 4). In contrast, as a block, the predisposition measures were clearly significant in most models assessed based on the likelihood ratio χ^2 test, except for external-cause mortality for era veterans ($P = .522$). In the external mortality model for theater veterans, these approached significance when combat was included ($P = .064$). However, when combat was excluded from the full model, predisposing factors were significant ($P = .039$)

Table 3
Cox proportional hazards regressions: crude and adjusted hazards ratio models for all-cause and external-cause mortality by all veterans combined and era veterans

| | All veterans—all-cause and external-cause mortality (n = 15 288, person risk years = 229 565, total PTSD cases = 1050) | | | | | | | | | | | | | | | | | |
|--|--|---------|-------|---------|---------|-------|---|---------|-------|---|---------|-------|---------|---------|-------|---|---------|-------|
| | All-cause mortality—total deaths = 820 | | | | | | | | | External-cause mortality—total deaths = 175 | | | | | | | | |
| | Model 1 | | | Model 2 | | | Model 3 | | | Model 1 | | | Model 2 | | | Model 3 | | |
| | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P |
| PTSD | 2.5 | 2.1-3.0 | <.001 | 2.4 | 1.9-2.9 | <.001 | 2.1 | 1.7-2.6 | <.001 | 2.7 | 1.8-4.0 | <.001 | 2.5 | 1.6-3.8 | <.001 | 2.3 | 1.5-3.5 | <.001 |
| <i>Demographic factors</i> | | | | | | | | | | | | | | | | | | |
| Age | — | | | 1.1 | 1.0-1.1 | .001 | 1.1 | 1.0-1.1 | <.001 | — | | | 1.0 | 0.9-1.1 | .621 | 1.0 | 0.9-1.1 | .943 |
| Nonwhite race | — | | | 1.5 | 1.3-1.8 | <.001 | 1.3 | 1.1-1.6 | .003 | — | | | 1.0 | 0.7-1.5 | .963 | 0.9 | 0.6-1.3 | .576 |
| Married | — | | | 0.9 | 0.7-1.1 | .217 | 0.9 | 0.8-1.1 | .292 | — | | | 0.8 | 0.6-1.1 | .191 | 0.8 | 0.6-1.1 | .234 |
| Entered service at 19-22 years old ^a | — | | | 0.7 | 0.5-0.8 | <.001 | 0.7 | 0.5-0.8 | .001 | — | | | 0.6 | 0.4-1.0 | .036 | 0.6 | 0.4-0.9 | .026 |
| Entered service at ≥23 years old ^a | — | | | 0.7 | 0.5-1.0 | .049 | 0.7 | 0.5-1.0 | .043 | — | | | 0.7 | 0.3-1.5 | .378 | 0.6 | 0.3-1.4 | .241 |
| Foreign born | — | | | 0.6 | 0.4-1.0 | .031 | 0.6 | 0.4-1.0 | .035 | — | | | 1.2 | 0.6-2.4 | .688 | 1.2 | 0.5-2.3 | .746 |
| <i>Predisposing factors</i> | | | | | | | | | | | | | | | | | | |
| Intelligence | — | | | — | | | 1.0 | 1.0-1.0 | <.001 | — | | | — | | | 1.0 | 1.0-1.0 | .390 |
| History of illicit drug use | — | | | — | | | 1.6 | 1.3-2.0 | <.001 | — | | | — | | | 1.3 | 0.8-2.1 | .327 |
| Early-age drinking | — | | | — | | | 1.0 | 0.8-1.4 | .939 | — | | | — | | | 1.5 | 0.9-2.6 | .111 |
| Service volunteer | — | | | — | | | 0.8 | 0.7-1.0 | .040 | — | | | — | | | 0.7 | 0.5-1.0 | .057 |
| Dishonorable discharge | — | | | — | | | 1.4 | 1.2-1.9 | .013 | — | | | — | | | 1.8 | 1.0-3.2 | .035 |
| Assessment of predisposing factors within full model | — | | | — | | | Likelihood ratio, $\chi^2_7 = 92.97$, $P > .001$ | | | — | | | — | | | Likelihood ratio, $\chi^2_7 = 21.06$, $P = .004$ | | |

Era veterans—all-cause and external-cause mortality (n = 7,364, person risk years = 110,553, total PTSD cases = 214)

| | All-cause mortality—total deaths = 383 | | | | | | | | | External-cause mortality—total deaths = 78 | | | | | | | | |
|--|--|---------|-------|---------|---------|-------|---|---------|-------|--|---------|-------|---------|---------|-------|--|---------|------|
| | Model 1 | | | Model 2 | | | Model 3 | | | Model 1 | | | Model 2 | | | Model 3 | | |
| | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P |
| PTSD | 2.6 | 1.7-3.8 | <.001 | 2.4 | 1.6-3.6 | <.001 | 2.0 | 1.3-3.0 | .001 | 2.9 | 1.3-6.7 | <.001 | 2.5 | 1.1-5.9 | <.032 | 2.2 | 0.9-5.3 | .068 |
| <i>Demographic factors</i> | | | | | | | | | | | | | | | | | | |
| Age | — | | | 1.1 | 1.0-1.1 | .007 | 1.1 | 1.0-1.1 | .001 | — | | | 1.0 | 0.9-1.1 | .816 | 1.0 | 0.9-1.1 | .704 |
| Nonwhite race | — | | | 1.4 | 1.1-1.9 | .003 | 1.1 | 0.9-1.5 | .382 | — | | | 1.3 | 0.7-2.2 | .423 | 1.0 | 0.5-1.7 | .904 |
| Married | — | | | 0.9 | 0.7-1.2 | .469 | 0.9 | 0.7-1.2 | .510 | — | | | 0.9 | 0.6-1.6 | .812 | 0.9 | 0.6-1.6 | .842 |
| Entered service at 19-22 years old ^a | — | | | 0.7 | 0.5-1.0 | .053 | 0.7 | 0.5-1.1 | .101 | — | | | 0.7 | 0.3-1.3 | .210 | 0.6 | 0.3-1.3 | .178 |
| Entered service at ≥23 years old ^a | — | | | 0.7 | 0.4-1.2 | .218 | 0.8 | 0.5-1.3 | .333 | — | | | 0.4 | 0.1-1.3 | .133 | 0.4 | 0.1-1.4 | .145 |
| Foreign born | — | | | 0.7 | 0.4-1.2 | .149 | 0.7 | 0.4-1.1 | .138 | — | | | 0.8 | 0.2-2.5 | .664 | 0.7 | 0.2-2.3 | .557 |
| <i>Predisposing factors</i> | | | | | | | | | | | | | | | | | | |
| Intelligence | — | | | — | | | 1.0 | 1.0-1.0 | <.001 | — | | | — | | | 1.0 | 1.0-1.0 | .021 |
| History of illicit drug use | — | | | — | | | 1.8 | 1.3-2.6 | <.001 | — | | | — | | | 1.1 | 0.5-2.4 | .850 |
| Early-age drinking | — | | | — | | | 0.9 | 0.6-1.5 | .780 | — | | | — | | | 1.9 | 0.9-3.9 | .101 |
| Service volunteer | — | | | — | | | 0.8 | 0.6-1.0 | .098 | — | | | — | | | 0.7 | 0.4-1.2 | .164 |
| Dishonorable discharge | — | | | — | | | 1.3 | 0.9-1.8 | .253 | — | | | — | | | 1.3 | 0.6-2.8 | .565 |
| Assessment of predisposing factors within full model | — | | | — | | | Likelihood ratio, $\chi^2_7 = 29.23$, $P < .001$ | | | — | | | — | | | Likelihood ratio, $\chi^2_7 = 6.15$, $P = .522$ | | |

HR = hazards ratio; CI = confidence interval; PTSD = posttraumatic stress disorder.

^a Reference is entered military service at age 18 years or younger.

Table 4
Cox proportional hazards regressions: crude and adjusted hazards ratios for all-cause and external-cause mortality by theater veterans

| Theater veterans—all-cause mortality (n = 7924, person risk years = 119453, total PTSD cases = 836) | | | | | | | | | | | | |
|---|---------|---------|-------|---------|---------|-------|---------|---------|-------|--|---------|-------|
| All-cause mortality—total deaths = 437 | | | | | | | | | | | | |
| | Model 1 | | | Model 2 | | | Model 3 | | | Model 4 | | |
| | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P |
| PTSD | 2.5 | 2.0-3.2 | <.001 | 2.4 | 1.9-3.0 | <.001 | 2.1 | 1.7-2.7 | <.001 | 2.1 | 1.7-2.7 | <.001 |
| <i>Demographic factors</i> | | | | | | | | | | | | |
| Age | — | | | 1.1 | 1.0-1.1 | .052 | 1.1 | 1.0-1.1 | .009 | 1.1 | 1.0-1.1 | .009 |
| Nonwhite race | — | | | 1.6 | 1.3-2.0 | <.001 | 1.5 | 1.2-1.9 | .001 | 1.5 | 1.2-1.9 | .001 |
| Married | — | | | 0.9 | 0.7-1.1 | .291 | 0.9 | 0.7-1.1 | .435 | 0.9 | 0.7-1.1 | .419 |
| Entered service at 19-22 years old ^a | — | | | 0.6 | 0.5-0.8 | .001 | 0.6 | 0.5-0.9 | .004 | 0.6 | 0.5-0.9 | .005 |
| Entered service at ≥23 years old ^a | — | | | 0.7 | 0.4-1.1 | .159 | 0.7 | 0.4-1.1 | .142 | 0.7 | 0.4-1.2 | .154 |
| Foreign born | — | | | 0.6 | 0.3-1.1 | .109 | 0.6 | 0.3-1.2 | .138 | 0.6 | 0.4-1.2 | .148 |
| <i>Predisposing factors</i> | | | | | | | | | | | | |
| Intelligence | — | | | — | | | 1.0 | 1.0-1.0 | .163 | 1.0 | 1.0-1.0 | .166 |
| History of illicit drug use | — | | | — | | | 1.5 | 1.1-2.0 | .009 | 1.5 | 1.1-2.0 | .009 |
| Early-age drinking | — | | | — | | | 1.1 | 0.7-1.6 | .690 | 1.1 | 0.7-1.6 | .709 |
| Service volunteer | — | | | — | | | 0.8 | 0.7-1.1 | .174 | 0.9 | 0.7-1.1 | .205 |
| Vietnam volunteer | — | | | — | | | 1.1 | 0.9-1.4 | .343 | 1.1 | 0.9-1.4 | .338 |
| Dishonorable discharge | — | | | — | | | 1.9 | 1.2-3.0 | .006 | 1.9 | 1.2-3.0 | .006 |
| <i>Stress exposure</i> | | | | | | | | | | | | |
| High combat exposure | — | | | — | | | — | | | 1.2 | 0.9-1.5 | .151 |
| Assessment of predisposing factors within full model with combat | | | | | | | | | | Likelihood ratio, $\chi^2_8 = 65.52, P < .001$ | | |
| Assessment of predisposing factors within full model without combat | | | | | | | | | | Likelihood ratio, $\chi^2_7 = 63.50, P < .001$ | | |

Theater veterans—external-cause mortality (n = 7,924, person risk years = 119,453, total PTSD cases = 836)

External-cause mortality—total deaths = 97

| | Model 1 | | | Model 2 | | | Model 3 | | | Model 4 | | |
|--|---------|---------|-------|---------|---------|-------|---------|---------|------|---|---------|------|
| | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P | HR | 95% CI | P |
| PTSD | 2.6 | 1.6-4.1 | <.001 | 2.4 | 1.5-4.0 | <.001 | 2.2 | 1.3-3.6 | .002 | 2.2 | 1.3-3.7 | .002 |
| <i>Demographic factors</i> | | | | | | | | | | | | |
| Age | — | | | 0.9 | 0.8-1.1 | .274 | 1.0 | 0.9-1.1 | .459 | 1.0 | 0.9-1.1 | .459 |
| Nonwhite race | — | | | 0.8 | 0.5-1.4 | .452 | 0.8 | 0.5-1.5 | .590 | 0.8 | 0.5-1.5 | .587 |
| Married | — | | | 0.7 | 0.4-1.1 | .133 | 0.7 | 0.4-1.2 | .237 | 0.7 | 0.4-1.2 | .239 |
| Entered service at 19-22 years old ^a | — | | | 0.6 | 0.4-1.1 | .106 | 0.7 | 0.4-1.3 | .246 | 0.7 | 0.4-1.3 | .244 |
| Entered service at ≥22 years old ^a | — | | | 1.3 | 0.5-3.6 | .646 | 1.3 | 0.4-3.7 | .666 | 1.3 | 0.4-3.7 | .669 |
| Foreign born | — | | | 1.6 | 0.7-4.0 | .299 | 1.7 | 0.7-4.3 | .251 | 1.7 | 0.7-4.3 | .252 |
| <i>Predisposing factors</i> | | | | | | | | | | | | |
| Intelligence | — | | | — | | | 1.0 | 1.0-1.0 | .232 | 1.0 | 1.0-1.0 | .232 |
| History of illicit drug use | — | | | — | | | 1.3 | 0.7-2.3 | .452 | 1.3 | 0.7-2.3 | .454 |
| Early-age drinking | — | | | — | | | 1.3 | 0.6-2.7 | .512 | 1.3 | 0.6-2.7 | .510 |
| Service volunteer | — | | | — | | | 0.6 | 0.4-1.0 | .058 | 0.6 | 0.4-1.0 | .057 |
| Vietnam volunteer | — | | | — | | | 2.1 | 1.3-3.3 | .001 | 2.1 | 1.3-3.3 | .001 |
| Dishonorable discharge | — | | | — | | | 3.5 | 1.6-7.9 | .002 | 3.5 | 1.6-7.9 | .002 |
| <i>Stress exposure</i> | | | | | | | | | | | | |
| High combat exposure | — | | | — | | | — | | | 1.0 | 0.6-1.6 | .883 |
| Assessment of predisposing factors within full model with combat | | | | | | | | | | Likelihood ratio, $\chi^2_8 = 14.78, P = .064$ | | |
| Assessment of predisposing factors within full model without combat | | | | | | | | | | Likelihood ratio, $\chi^2_7 = 14.76, P = .039$ | | |

HR = hazards ratio; CI = confidence interval; PTSD = posttraumatic stress disorder.

^a Reference is entered military service at age 18 years or younger.

(Table 4). Examination of specific predisposition measures for all-cause and external-cause mortality by veteran status revealed the following. For era veterans, history of drug abuse was a risk factor (HR = 1.8, $P < .001$) and lower intelligence was protective for all-cause mortality (HR = 0.99, $P < .001$); for external-cause mortality, only lower intelligence was protective for era veterans (HR = 0.99, $P = .021$). For theater veterans, history of drug abuse was a risk factor for all-cause mortality (HR = 1.5, $P = .009$), as was having a dishonorable discharge (HR = 1.9, $P = .006$); for external-cause mortality, volunteering for Vietnam was a risk factor for theater veterans (HR = 2.1, $P = .001$), as was having a dishonorable discharge (HR = 3.5, $P = .002$).

Finally, although specific external mortality classifications could not be modeled because of the small numbers involved, we qualitatively examined these by PTSD and veteran status. This examination indicated that although the overall prevalence was similar in each external death category, it appeared that PTSD-positive theater veterans were more likely to be classified as a homicide or self-inflicted death (ie, suicide, firearm, drug, or alcohol-related mortality) than the PTSD-positive era veterans for some reason (results available from author upon request).

To assess basic Cox proportional hazards assumptions, we used Schoenfeld residuals and the “stphtest” procedure in Stata to assess fit for our models [48,49]. This test is equivalent to testing that the log HR function is constant over time [48,49]. The results of the procedure indicated that all the final models used were adequate, with P values higher than .05. In addition, we also tested for effect modification within the veteran strata for PTSD by age, race, marital status, drug abuse history, discharge status, and intelligence. None of these interactions tended to be significant in the final models, so these were dropped. Next, using our final multivariate models, we plotted the external mortality survival curves by PTSD for the era and theater veterans separately. Because these survival curves did not cross, we again assumed that the main hazard assumptions for PTSD status were not violated.

4. Discussion

In the initial CDC study conducted in the 1980s [33], three fourths of all deaths among Vietnam veterans resulted from external causes. In the most recent CDC follow-up, external causes, diseases of the circulatory system, and malignant neoplasms each accounted for a substantial proportion of deaths (38.5%, 23.1%, and 17.5%, respectively), as would be expected for nonveteran men in the same age range [23,50]. In addition, as noted, a recent study of Vietnam veterans found that PTSD was significantly associated with external, cardiovascular, and cancer deaths among the theater veterans, even after controlling for potential selection bias and confounding [27]. Compared with the CDC study and the other mortality studies mentioned, our current analyses yielded much more specific

information. Consistent with previous reports [27], PTSD was associated with an adjusted all-cause mortality for both era and theater veterans. However, for external-cause mortality, PTSD-positive theater veterans appeared to have an increased risk of death. Nevertheless, PTSD-positive era veterans, without combat exposure, also appeared to be at higher risk for external-cause mortality as well (HR = 2.2, $P = .068$). However, specific cause-of-death classifications suggested that theater veterans were more likely to die of suicide, homicide, and alcohol- and drug-related causes. Given the results for era veterans and the lack of significance for combat status, our study suggests that it is PTSD that was associated with external mortality, not combat exposure, per se, but that type of external mortality (eg, intended vs unintended injury) seems to differ between veteran cohorts. In addition, our analyses suggested that predisposing traits likely contribute to these outcomes. As discussed, for era veterans, history of drug abuse was a risk factor and lower intelligence was protective for all-cause mortality; for external-cause mortality, only lower intelligence was protective. For theater veterans, history of drug abuse and a dishonorable discharge were risk factors for all-cause mortality; for external-cause mortality, volunteering for Vietnam and a dishonorable discharge were risk factors for them. In summary, these findings indicate that although the etiology of external-cause mortality among veterans appeared to be multifactorial and that PTSD was a major factor in this outcome, predisposing factors likely related to character traits also appeared to be associated with this outcome and apparently varied by veteran status. Why this was the case is unclear, but it may be related to the type of traumas experienced.

This study has several strengths and limitations. Use of multiple sources of vital status allowed for a more complete account of postservice mortality in the United States. However, investigators may have missed deaths that occurred elsewhere. In addition, underlying cause of death, as reported on the death certificate, is known to underreport alcohol- and drug-related deaths and to overreport circulatory conditions, ill-defined conditions, and respiratory conditions [23]. Furthermore, although our RTI-PTSD scale appeared to have concurrent validity and internal reliability, this was an earlier version of the PTSD nomenclature [34]. This PTSD measure also likely lacked sensitivity and specificity compared with a valid gold standard (eg, a structured diagnostic interview) with a comparable time frame. It also should be noted that the *DIS-III* used in the VES was an earlier version of the *DSM-III* PTSD nomenclature and has been found to be at variance with later PTSD measures [51]. However, given the results of our validation study [27], we conclude that the RTI-PTSD measure used in our study was generally consistent with the presence of PTSD among these men, although it had limitations. Other limitations were that our study included only men and only those who survived to participate in the survey. Our study also did not assess the impact of early life

traumas, family history, or other comorbid mental health conditions that could have affected our results. Nevertheless, study strengths were that this research was based on a large population sample, not simply persons identified through medical clinics or treatment seeking, and it included key controls for potential selection biases and confounders.

Our study suggests a link between long-term psychologic distress and death from external causes. Research among other populations also suggests an association, especially as this relates to suicidal behaviors [52,53]. A particular challenge for this research is assessing the impact of behavioral risk factors and character traits that could be related to psychologic trauma exposure, but which also could be associated with mortality (eg, alcohol abuse, drug dependence, etc) [2]. However, acquiring health-enhancing behaviors postexposure could be protective. For example, cognitive therapy is often recommended for treatment of anxiety disorders [54]. If this is effective in reducing symptoms and subsequent substance abuse, then the burden of mortality could be reduced [2,55]. In this regard, it was recently reported that victims of the World Trade Center disaster who received brief mental health interventions shortly after this event had significantly reduced postdisaster mental health and substance abuse problems [56]. This finding may have implications for returning war veterans from the current theaters of war.

We think that the findings in the current study warrant further investigation and may have long-term implications for treatment and prevention among those exposed to traumatic events [56]. Interestingly, although the overall prevalence of external mortality was similar between PTSD-positive veteran cohorts, PTSD-positive theater veterans appeared more likely classified as having a violent or self-inflicted death. Whether this was due to reporting bias or other factors is yet to be determined. Nevertheless, our study suggested that although there appears to be predisposing factors that may increase or decrease the risk of external-cause mortality among veterans, it is PTSD, not past combat exposure, that is associated with this outcome.

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