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Posttraumatic Stress Disorder and Mortality Among U.S. Army Veterans 30 Years After Military Service

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PURPOSE: Research suggests that posttraumatic stress disorder (PTSD) may be associated with later medical morbidity. To assess this, we examined all-cause and cause-specific mortality among a national random sample of U.S. Army veterans with and without PTSD after military service.
METHODS: We used Cox proportional hazards regressions to examine the causes of death among 15,288 male U.S. Army veterans 16 years after completion of a telephone survey, approximately 30 years after their military service. These men were included in a national random sample of veterans from the Vietnam War Era. Our analyses adjusted for race, Army volunteer status, Army entry age, Army discharge status, Army illicit drug abuse, intelligence, age, and, additionally—for cancer mortality— pack-years of cigarette smoking.
RESULTS: Our findings indicated that adjusted postwar mortality for all-cause, cardiovascular, cancer, and external causes of death (including motor vehicle accidents, accidental poisonings, suicides, homicides, injuries of undetermined intent) was associated with PTSD among Vietnam Theater veterans ($N = 7{,}924$), with hazards ratios (HRs) of 2.2 ($p < 0.001$), 1.7 ($p = 0.034$), 1.9 ($p = 0.018$), and 2.3 ($p = 0.001$), respectively. For Vietnam Era veterans with no Vietnam service ($N = 7{,}364$), PTSD was associated with all-cause mortality (HR = 2.0, $p = 0.001$). PTSD-positive era veterans also appeared to have an increase in external-cause mortality as well (HR = 2.2, $p = 0.073$).
CONCLUSIONS: Our study suggests that Vietnam veterans with PTSD may be at increased risk of death from multiple causes. The reasons for this increased mortality are unclear but may be related to biological, psychological, or behavioral factors associated with PTSD and warrant further investigation.
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KEY WORDS: Mortality, Survival, Cause-of-death, Posttraumatic Stress Disorder, PTSD, Cardiovascular Disease, Malignant Neoplasms/Cancer, External Mortality.

INTRODUCTION

Research suggests that having a history of posttraumatic stress disorder (PTSD) or traumatic stress exposure is associated with higher rates of morbidity and disease (1–7). Research among Vietnam combat veterans, in particular, suggests higher rates of postwar mental health disorders and medical conditions than is found in noncombat veterans or comparable nonveterans (1, 8–10). In addition, research suggests that the postwar health problems experienced by these veterans, at least in part, were due to combat-related PTSD, not selection bias or confounding (11). For example, when the postwar health status of Vietnam veterans was recently examined by whether they had PTSD, the positive veterans had substantially higher postwar rates for many chronic conditions, including circulatory, nervous system, digestive, musculoskeletal, and respiratory diseases, even after controlling for the major risk factors for these conditions (1).

The evidence linking traumatic stress exposure to cardiovascular disease is extensive (2). In addition to Vietnam veteran studies (1, 4), a population study involving World War II and Korean War veterans has found higher rates of physician-diagnosed cardiovascular disease among PTSD-positive veterans (12). Another study among Dutch Resistance Fighters found increased rates of reported angina pectoris among those with PTSD (13). A large-scale civilian population study also found an increase in ischemic heart disease based on medical exams among adults exposed to childhood traumas (14). Furthermore, a study of adults exposed to the Chernobyl disaster indicated that these individuals had increased rates of reported heart disease 8–10 years after this event (7). In addition, studies related to the Beirut Civil War and the Croatia War found increases in arteriographically confirmed coronary heart disease, cardiovascular disease mortality, and increases in acute myocardial infarctions (AMIs) associated with exposure to these conflicts (15–17). Finally, numerous studies have documented persistent increases in basal cardiovascular activity

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among PTSD victims that could facilitate the onset of disease (18). Since coronary heart disease has been associated with PTSD and this condition is now considered an "inflammatory" disease (19), it recently has been suggested that PTSD-positive veterans may be at risk for a host autoimmune diseases as well (2). For example, while there have been inconsistencies (20), investigations have found that individuals who developed PTSD, particularly men exposed to combat, appeared to have lower plasma cortisol concurrent with higher catecholamine levels (21–24). One study reported that Vietnam veterans with current PTSD not only had lower cortisol, but that this had an inverse "dose-response" relationship with combat exposure (11, 21). In addition, research has indicated that Vietnam veterans with current PTSD had clinically elevated leukocyte and T-cell counts (25) and similar findings have been reported in nonveteran studies as well (26, 27). Consistent with these clinical findings, it has been reported recently that PTSD was in fact associated with several autoimmune diseases, including rheumatoid arthritis and psoriasis (2).

Recently, investigators from the Centers for Disease Control and Prevention (CDC) ascertained the vital status and underlying cause-of-death among participants in the Vietnam Experience Study (VES), a longitudinal study of 18,313 male U.S. Army veterans from the end of their military service through December 31, 2000 (28). In this study, all-cause mortality appeared higher among Vietnam theater (i.e., those who served in Vietnam) compared with Vietnam era veterans (i.e., those who served elsewhere) during the 30-year follow-up period. The excess mortality among Vietnam veterans, however, appeared isolated to the first 5 years after discharge from active duty and appeared to have resulted from an increase in external causes of death (i.e., due to motor vehicle accidents, accidental poisonings, suicides, homicides, and injuries of undetermined intent). Cause-specific analyses revealed no difference in disease-related mortality by veteran status. Vietnam theater veterans, however, experienced an excess in unintentional poisoning and drug-related deaths throughout the follow-up period. Death rates from disease-related chronic conditions—including malignant neoplasms and circulatory diseases—did not appear to differ between the theater and era veterans, despite the increasing age of the cohort (mean age, 53 years) and the long follow-up period (average, 30 years). In the current study, we examine vital status and underlying cause-of-death by posttraumatic stress disorder for the theater and era veterans combined and separately, which had not been done in the previous study.

Research suggests that the majority of Vietnam veterans with PTSD developed this disorder due to combat experiences in Vietnam (21,29–31). In addition, available research suggests that a significant proportion of these veterans still suffer from this disorder (8). Given these factors, the long-term health consequences of PTSD among Vietnam veterans—if they exist—should be detectable in large population sample of these veterans. Given the previous research noted, we expected PTSD to be associated with a higher rate of cardiovascular and external causes of deaths, but not cancer-related deaths.

Data and Methods

The focus of this study was to examine the effects of PTSD among Vietnam veterans through an assessment of post-service mortality among those in the VES cohort who completed telephone interviews conducted by Research Triangle Institute (RTI) in the mid-1980s. Potential subjects for the current study included 17,867 U.S. Army veterans known to be alive in December 1983. Starting in January 1985, these men were contacted by RTI to complete telephone interviews. Altogether, 15,288 of these men (86%) were located and completed the RTI survey. The interviews included questions related to PTSD symptoms, self-reported health status, history of substance abuse, and history of cigarette smoking, as well as demographic data and military history information. Data from the veteran's original military records also were included. These military data included discharge status, general aptitude test results at Army induction, service rank, and other service-related information.

The study population for the current study comprised of men who served in the U.S. Army during the Vietnam War. The cohort was identified through a random sample of 48,513 service records selected from the nearly 5 million records on file at the National Personnel Records Center. Of these, 18,581 veterans met the criteria for study eligibility, which were chosen to increase comparability between men who served in Vietnam and men who served elsewhere. These inclusion criteria consisted of: entering the military service for the first time between 1965 and 1971; serving only 1 term of enlistment; having at least 16 weeks of active service time; earning a military occupational specialty other than "trainee" or "duty soldier;" and having a pay grade no higher than E5 on discharge. Qualified participants were classified as Vietnam Theater veterans if they served at least one tour of duty in Vietnam, or as Vietnam Era veterans if they never served in Vietnam during this period but served at least one tour of duty in the United States, Germany, or Korea. The final completed sample in the current study included 7924 Vietnam theater and 7364 Vietnam era veterans, for a total of 15,288 men who were known not to be deceased and who completed the RTI telephone survey. Further details regarding participant selection and study design have been published elsewhere (1, 9, 10, 28, 32).

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Ascertainment of Vital Status and Cause-specific Mortality

For the current study, 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. Vital status was ascertained using 3 national mortality databases: the Department of Veterans Affairs Beneficiary Identification Record Locator Subsystem (VA BIRLS) death file, the Social Security Administration Death Master File (SSADMF), and the National Death Index Plus (NDI Plus) (28). Investigators also manually reviewed the potential matches from each data source separately and classified the matches as true, false, or questionable (28). The final determination of vital status was obtained by combining information from all three mortality sources. As needed, additional information, such as actual death certificates were ascertained, to confirm vital status. Veterans who had a true match on at least one of the three 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 by any of the national databases were assumed to be living as of December 31, 2000.

Underlying cause-of-death codes were obtained from 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, CDC investigators obtained official copies of death certificates, which were then coded by an experienced nosologist at the CDC's National Center for Health Statistics (NCHS) (28).

RTI-PTSD Scale Validation Study

In addition to our mortality study, we conducted a separate analysis using a subset of VES participants who completed both the telephone survey *and* personal interviews after the telephone survey was completed (N = 4462). This was necessary because, while the PTSD measure used in the RTI survey had been implemented in several previous studies and had content validity (33–35), this version of the 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 scale, derived from the *Diagnostic and Statistical Manual of Mental Disorders—Version III* (DSM-III) (36). DIS-III is a standardized questionnaire designed to assess the presence of psychiatric conditions consistent with DSM-III (36–38). In the VES, DIS-III PTSD diagnoses were available for the past 30 days and for lifetime (39). For the personal interviews, a random sub-sample was selected by the CDC investigators among the 15,288 interviewed by telephone. Altogether, 75% of the 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, New Mexico, 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 15 PTSD-related symptoms experienced in the past 6 months. Consistent with DSM-III nomenclature and based on symptoms reported "often" or "very often," a veteran was classified as having current PTSD if he reported at least one criterion B symptom (reexperiencing), at least one criterion C symptom (avoidance), and at least two criterion D symptoms (hyperarousal). The DSM-III criterion A (exposure) was not explicitly used in the RTI-PTSD scale, but it was used implicitly, since some of the symptoms included in the B and D criteria referred to Army experiences (e.g., "in past 6 months, had dreams or nightmares of Army experiences") (34). Using the DIS-III criteria employed in the personal interviews, PTSD was diagnosed as *current* if the veteran met the criteria for criterion A through D in the past 30 days. However, because of the way RTI-PTSD was defined, for comparison purposes, the A criterion for exposure in the DIS-III PTSD measure was defined in two ways: for combat experiences only and for *any* traumatic exposures. Because of the differences in timeframes and exposure criteria for these measures, we also compared the RTI-PTSD scale to lifetime DIS-III PTSD, both related to combat and to *any* trauma exposures. Finally, we compared the RTI-PTSD results for Vietnam theater veterans to results for the Combat Exposure Scale (CES) used in the personal interviews (39). The CES has been shown to be a valid measure of combat exposure and has been used in several previous studies (39, 40).

Using the B though 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 with current PTSD (odds ratio [OR] = 3.9, $p < 0.001$). When we compared these PTSD results among those who were reinterviewed and administered the DIS-III during the personal interviews, 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, 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 (OR = 17.1, 95% CI = 10.6–27.6). Of those that met the DIS-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-III 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 (OR = 7.3, 95% CI = 5.6–9.3). Furthermore, for the combat exposure comparison among the Vietnam theater veterans, there was a clear "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 (Chi-square trend test = 123.5, df = 1, $p < 0.0001$). In addition, Cronbach's alpha was high for the RTI-PTSD scale items (alpha = 0.92), as was the Guttman split-half coefficient (0.91), suggesting internal reliability (41). Finally, we also compared results on the RTI-PTSD scale to both self-reported health status and mental health treatment seeking in the past 12 months among all participants in the telephone survey (N = 15,288). These results indicated that 39% of those reporting "poor" current health had current PTSD on the RTI scale, compared with only 6% reporting otherwise (OR = 9.7, $p < 0.001$). Similarly, 23% of men who sought mental health treatment in the past 12 months were PTSD positive on the RTI scale, compared with only 5% among the nontreatment seekers (OR = 5.4, $p < 0.001$). While there are limitations that we note below due to the difference in metrics involved (e.g., different timeframes and use of the A criterion), these findings suggest that a positive diagnosis on the RTI-PTSD scale is generally consistent with a diagnosis of PTSD.

Study Control Variables

Our main research focus was to determine if PTSD was associated with postservice mortality. To achieve this, we developed multivariate models predicting survival, which were adjusted for obvious confounders and potential selection biases. To do this, we adjusted our model for the following variables: race, Army volunteer status, Army entry age, Army discharge status, Army illicit drug use, intelligence, and age at interview (1, 4, 25). In addition, for cancer mortality, we also controlled for pack-years of cigarette smoking at interview. We needed to control for these variables, because we wanted to examine the association between PTSD and survival, unconfounded by potential selection biases or confounders, such as race, intelligence, volunteer status (42, 43). With the exception of cancer mortality, where we controlled for a key behavioral risk factor (e.g., pack-years of cigarette smoking), we did not control for other behavioral risk factors such as illicit drug use or marital status at the time of the interview. We did this because we wanted to avoid "over controlling" for behavioral variables potentially in the causal chain of events linking PTSD to mortality (2). *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. non-White). *Army volunteer status* was based on whether the veteran volunteered for military service and was classified as "volunteer" versus "draftee" and based on the military record. *Army entry age* was the age at induction and was based on the military record. *Army discharge status* was classified as honorable versus dishonorable/other discharge and was from the military record. *Army illicit drug use* was classified as present if the veteran reported use of illicit drugs (e.g., narcotics, barbiturates, amphetamines, hallucinogens, or marijuana) while in the Army. *Intelligence* was based on the General Technical (GT) Examination Test at military induction, which is considered a good measure of mental aptitude (39). This scale was used as a continuous variable. *Age at interview* was based on the veteran's age at time of the interview and was used as a continuous variable. For our cancer analyses, *pack-years of cigarette smoking* was based on the average number of cigarette packs smoked per day and the number of years smoked and used as a 6-category indicator variable (none, 1–9, 10–18, 19–29, 30+ pack-years, primarily pipe or cigar smoker). Controlling for these variables are important because Vietnam veterans are reported to come from higher risk groups (44), factors often associated with poorer health outcomes (45). In addition to the above variables, our descriptive analyses comparing veteran status and PTSD status also included the following variables: level of education, marital status, heavy drinking, and illicit drug use. These variables were defined as follows: *Marital status* was based on vital status at interview and classified as married versus not married. *Alcohol abuse* was classified as present if the veteran reported drinking an average of 5 or more drinks per day in the past 30 days when interviewed. *Drug abuse* was classified as present if the veteran reported regular use of narcotics, barbiturates, amphetamines, or hallucinogenic drugs in the past year when interviewed. *Educational attainment* was based on total years of education achieved at the time of interview and used as dichotomous variable, coded as high school or less versus more than high school.

Statistical Methods

First, we describe the differences found by veteran status and by PTSD status. Next, we use Cox proportional hazards

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regression to calculate both crude (bivariate) and adjusted (multivariate) hazards ratios (HRs) using the control variables discussed for all-cause mortality, cardiovascular mortality, cancer mortality, and mortality due to all external causes combined, which included homicide, suicide, accidental poisoning, and unintended injury. Since another study examined survival from Army discharge about 30 years previous (28) and we only included those who were alive and completed the 1985–1986 telephone interviews, our analyses examine survival time from interview completion stating in January 1985 through to December 31 2000, a period of 16 years. For these analyses, we evaluated the main proportional hazards assumption (46), 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 8 (Stata Corp., College Station, TX). For all-cause mortality, we included all deaths for the time period. For cause specific mortality, we only included the specific death being considered. For example, with cancer mortality, if the veteran died of another cause of death other than cancer, then his survival time was counted until the time of death from the other cause and then he exited from the analysis, which is a conservative estimation method (47). All p-values presented were based on the 2-tail test.

RESULTS

Given that our survey sample size was large (N = 15,288), we only highlight major differences here in terms of descriptive statistics for veteran status and PTSD status, since differences of 2% were generally significant. These findings indicate that theater veterans had not only higher rates of PTSD (10.6% vs. 2.9%), but also were younger at follow up (17.7% vs. 22.3%, over 39 years of age), had lower educational attainment (53.7% vs. 49.5%, high school or less), had lower intelligence (20.8% vs. 17.8%, lowest quintile), were heavier smokers (34.1% vs. 31.2%, 19+ pack-years), and had nonhonorable discharges less often (1.9% vs. 6.3%, nonhonorable) (Table 1). 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 1985–1986 survey (11.8% vs. 4.9%), but they were notably different on a number of other measures (Table 2). For example, PTSD-positive veterans were more likely to have been non-White (30% vs. 16.4%), in the lowest intelligence quintile (37.3% vs. 18%), heavy drinkers (22.8 vs. 8%), users of narcotics or other hard drugs (8.1% vs. 1.7%), and to have entered the service at a younger age (25% vs. 12.6%).

Table 3 presents the crude and adjusted mortality results, respectively, for all-cause, cardiovascular, cancer, and external cause-of-death, as well as the number of deaths and the total person-years at risk for each group. As can be seen, the crude (unadjusted) all-cause mortality for PTSD-positive veterans was higher for both the era and the theater veterans, with hazards ratios (HRs) of 2.6 and 2.5, respectively (both p-values < 0.001) (Table 3). For cardiovascular and cancer mortality, however, only PTSD-positive theater veterans had crude hazards ratios that were significant for these outcomes, with HRs of 1.8 ($p = 0.015$) and 2.2 ($p = 0.003$), respectively. This was not the case for external-cause mortality, however (Table 3). For this outcome, PTSD-positive era veterans had a crude HR of 2.9 ($p = 0.012$) and PTSD-positive theater veterans had a crude HR of 2.6 ($p < 0.001$).

TABLE 1. Profile of Vietnam theater veterans vs. Vietnam era veterans

Variable	Vietnam Theater Veteran (%)	Vietnam Era Veteran (%)	P-value*
PTSD at interview	10.6	2.9	<0.001
Deceased at follow up	5.5	5.2	0.39
Age 40+ at interview	17.7	22.3	<0.001
Non-white race	16.8	18.0	0.054
High school or less education	53.7	49.5	<0.001
Married at interview	74.1	74.5	0.59
Intelligence—lowest quintile	20.8	17.8	<0.001
19+ cigarette pack years	34.7	31.2	<0.001
Heavy drinking at interview	9.9	8.0	<0.001
Used hard drugs at interview	2.5	1.8	0.004
Drafted into military service	64.4	67.2	<0.001
Entered service at 18 or less	14.2	12.6	0.004
Less than honorable discharge	1.9	6.3	<0.001
N =	7924	7364	–

PTSD = posttraumatic stress disorder.
*2-sided chi-square test, df = 1.

TABLE 2. Profile of PTSD negative vs. PTSD positive Vietnam Veterans

Variable	PTSD Negative (%)	PTSD Positive (%)	P-value*
Deceased at follow-up	4.9	11.8	<0.001
Age 40+ at interview	20.4	13.0	<0.001
Non-White race	16.4	30.0	<0.001
High school or less education	50.9	62.9	<0.001
Married at interview	75.3	60.1	<0.001
Intelligence—lowest quintile	18.0	37.3	<0.001
19+ cigarette pack years	32.7	38.3	<0.001
Heavy drinking at interview	8.0	22.8	<0.001
Used hard drugs at interview	1.7	8.1	<0.001
Drafted into military service	66.4	57.0	<0.001
Entered service at 18 or less	12.6	25.0	<0.001
Less than honorable discharge	3.6	8.7	<0.001
N =	14,238	1050	–

PTSD = posttraumatic stress disorder.
*2-sided chi-square test, df = 1.

TABLE 3. Cox proportional hazards regressions: crude and adjusted hazard ratios (HRs) by veteran and PTSD status

	All-cause mortality (Total deaths = 820)			Cardiovascular mortality (Total deaths = 241)			Cancer mortality (Total deaths = 188)			External-cause mortality (Total deaths = 175)		
Veteran Status	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
All Veterans (N = 15,288)												
(Person risk years = 229,565)												
(Total PTSD cases = 1050)												
PTSD—unadjusted	2.5	2.1–3.0	<0.001	1.7	1.1–2.6	0.010	1.8	1.1–2.8	0.013	2.7	1.8–4.0	<0.001
PTSD—adjusted*	2.1	1.7–2.6	<0.001	1.6	1.1–2.4	0.027	1.5	1.0–2.4	0.075	2.3	1.5–3.5	0.001
Vietnam Era Veteran (N = 7364)												
(Person risk years = 110,553)												
(Total PTSD cases = 214)												
PTSD—unadjusted	2.6	1.7–3.8	<0.001	1.3	0.5–3.6	0.57	1.1	0.4–3.6	0.84	2.9	1.3–6.7	0.012
PTSD—adjusted*	2.0	1.3–3.0	0.001	1.2	0.4–3.4	0.69	0.9	0.3–3.1	0.92	2.2	0.9–5.2	0.073
Vietnam Theater Veteran (N = 7924)												
(Person risk years = 119,453)												
(Total PTSD cases = 836)												
PTSD—unadjusted	2.5	2.0–3.2	<0.001	1.8	1.1–2.8	0.015	2.2	1.3–3.7	0.003	2.6	1.6–4.1	<0.001
PTSD—adjusted*	2.2	1.7–2.7	<0.001	1.7	1.0–2.7	0.034	1.9	1.1–3.3	0.018	2.3	1.4–3.9	0.001

HR = hazards ratio; CI = confidence interval; PTSD = posttraumatic stress disorder.
*All models adjusted for race, Army volunteer status, Army entry age, Army discharge status, Army illicit drug use, age at interview, and intelligence. For cancer mortality, models adjusted for these variables, in addition to pack-years of cigarette smoking. (See methods section for additional information.)

As suggested, these crude survival results can be misleading, because they were not adjusted for selection bias and confounding. When these adjustments were made, they generally reduced the size of the hazard ratios (Table 3). For all-cause mortality, the hazards ratios were reduced somewhat, but remain significant, with p-values < 0.001 for both veteran groups combined (HR = 2.1). For era veterans the adjusted HR = 2.0 ($p = 0.001$) and for the theater veterans HR = 2.2 ($p < 0.001$) for all-cause mortality. For cardiovascular mortality, the adjusted results were significant for all veterans combined (HR = 1.6, $p = 0.027$), but when stratified by veteran status, this was only significant for the Vietnam theater veterans (HR = 1.7, $p = 0.034$). For cancer mortality, the adjusted results were only significant for Vietnam theater veterans, with a hazards ratio of 1.9 ($p = 0.018$). For external-cause mortality, the adjusted results were statistically significant for veterans overall (HR = 2.3. $p = 0.001$), but this was primarily because of the theater veterans (HR = 2.3, $p = 0.001$); the results were marginally significant for the era veterans (HR = 2.2, $p = 0.073$).

Since cancer mortality was significant among the PTSD-positive theater veterans, we examined the detailed cancer results in order to determine if a specific cancer site was more prevalent than another. These results were mixed. PTSD-positive theater veterans tended to have a somewhat higher rate of death from lung as well as from all other cancers combined (both 108 cases per 10,000 persons).

DISCUSSION

In the initial CDC mortality study conducted in the 1980s (32), three fourths of all deaths 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 based on the leading causes of death for U.S. men in the same age range (28, 48). However, the CDC investigators also reported no difference in disease-related mortality by veteran status during their entire 30-year follow-up period (28).

The CDC reported the rate of death from external causes was higher among Vietnam theater versus Vietnam era veterans in the first 5 years after discharge from active duty. After this, no difference occurred for this category overall; however, the rate of death from unintentional poisonings was higher among theater veterans during this period (28). The CDC investigators also found an excess of drug-related deaths among theater veterans during the entire follow-up period (28). These findings can be compared with those of two similar studies. The Australian Vietnam veteran study

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assessed postservice mortality among 19,205 Vietnam theater veterans and 25,677 Vietnam era veterans through 1981 (49). This study found that the death rate for Vietnam theater veterans was 1.2 times than for Vietnam era veterans (49). More recently, a Marine Corps Vietnam veteran study followed 22,062 veterans from discharge from active duty through 1991 (50). Similar to the CDC study, the Marine Corps study found an excess of all-cause mortality among Vietnam theater veterans versus Vietnam era veterans. This increased mortality appeared to be due principally to external causes of death (50).

Compared to the CDC study and the other two mortality studies mentioned, our analysis of cause-of-death status yields a more complete picture. As shown, PTSD was associated with an adjusted all-cause mortality for both era and theater veterans. However, for cardiovascular, cancer, and external-cause mortality, the PTSD-positive theater veteran was at an increased risk for death. The one exception was that PTSD-positive era veterans also were possibly at higher risk for external-cause mortality as well (HR = 2.2, p = 0.073).

This study has several strengths and limitations. Use of multiple sources of vital status allowed for a more complete account of postservice mortality. Thus, the CDC investigators probably identified nearly all deaths in the United States; however, they may have missed deaths that occurred elsewhere. Two additional reasons for underreporting mortality are that death certificate fields often are incomplete for transient persons, and the database matching criteria depend largely on the accuracy of the social security number. Underreporting was likely to have occurred equally among Vietnam and non-Vietnam veterans; thus, the results of this study should not be substantially biased.

Death certificates are the most common source of underlying cause-of-death data in epidemiologic research. However, underlying cause-of-death, as reported on the death certificate, is known to underreport alcohol- and drug-related deaths and to over-report circulatory conditions, ill-defined conditions, and respiratory conditions (28). Neoplasms, in general, are the most accurately diagnosed condition on the death certificate when compared with autopsy results (28). To the extent that misclassification of the underlying cause-of-death is similar for Vietnam and non-Vietnam veterans and for the U.S. population as a whole, the findings in this study are unlikely to be biased. Another limitation relates to the PTSD scale. Although our RTI-PTSD scale appeared to have concurrent validity and excellent internal reliability, this was an earlier version of the PTSD nomenclature (34). This PTSD measure also likely lacked sensitivity compared to a valid gold standard (e.g., a structured diagnostic clinician interview) with a comparable timeframe. It should be noted that the DIS-III used in the VES was in fact an earlier version of the DSM-III PTSD nomenclature and has been found to be at variance with other later PTSD measures (51). Thus, to further assess our RTI-PTSD measure, we also compared our results to the Keane PTSD scale from the MMPI administered during the personal interview (39). Again, these results were consistent with the concurrent validity results reported above for the various measures assessed (OR = 9.9, 95% CI = 7.8–12.8). We conclude, therefore, that the RTI-PTSD measure used in our study was generally consistent with the presence of PTSD among these men. Another limitation, of course, was that a number of risk factor measures used were based on self-report and this could have introduced bias. Other limitations were that our study included only men and only those who survived to complete the baseline interview. Furthermore, it is possible that the results found were still due to other factors, such as exposure to toxic agents in the military or shared vulnerabilities (3), not PTSD per se. A major strength of our study, however, was that it was based on a large national population sample, not simply on persons identified through medical clinics and through treatment-seeking behaviors.

IMPLICATIONS

As suggested, there is growing evidence that exposure to psychologically traumatic events is related to increased medical morbidity (1). We think that our study, together with other recent epidemiologic and clinical studies, suggest a link between long-term exposure to severe psychological distress and the onset of disease. More conclusive evidence will require additional research. A particular challenge, nevertheless, will be assessing the impact of behavioral risk factors that could be related to psychological trauma exposures, but which also could result in disease (alcohol abuse, tobacco dependence, etc.). However, we suggest that the behavioral aspects of disease also may prove especially promising, because acquiring health-enhancing behaviors could be protective for disease outcomes. For example, cognitive therapy is often recommended for treatment of PTSD and other anxiety disorders (52). If this therapy is effective in reducing PTSD symptoms and such things as substance abuse, then the burden of disease may be decreased, possibly along several causal pathways, including psychological, behavioral, and/or biological conduits (2, 53). Nevertheless, PTSD appears to have a biological foundation that exists below cognitive functioning (1, 21), suggesting that a purely psychotherapeutic approaches may be limited (54). As has been previously suggested (1, 2), understanding both the physiological and the psychological aspects of traumatic phenomenon clearly seems warranted to effectively treat the sequelae associated with this

condition. The behavioral risk-factor disparities shown for PTSD status in Table 2, however, clearly point to some challenges. In addition, it is important to stress that our study population included *only* those who survived to participate in the survey, hence the force of morbidity related to PTSD is likely greater than suggested here: 485 men died *before* the baseline interviews occurred.

There is growing evidence that the development of PTSD may be related to alterations in neuroendocrine and immune system functions. In particular, given the reduced cortisol levels often found, it has been suggested that a down-regulated glucocorticoid system may result in elevations in leukocyte and other immune inflammatory activities (55). One causal pathway often cited involves alterations in the HPA stress axis concurrent with sympathetic-adrenomedullary (SAM) axis activation (56–58), which could lead to a host of diseases (52). An increase in allostatic load as a result of these biologic alterations, or efforts to relieve their adverse psychological effects through substance use, or both, could contribute to the pathophysiologic process (59). While this suggests complex interrelated biologic processes, one observer recently characterized the residual effects psychological trauma for veterans somewhat differently (60):

> The story of combat is timeless…. The extreme and terrible nature of war touches something essential about being human. For those who survive, the victors and the defeated, the battle lives in their memories and nightmares…. It survives as hundreds of searing private memories, memories of loss and triumph, shame and pride, struggles each veteran must fight each day of his life.

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