ORIGINAL ARTICLE



Risk factors for suicide in the Vietnam-era twin registry

Christopher W. Forsberg¹ | Santiago A. Estrada¹ | Aaron Baraff¹ | Kathryn M. Magruder² | Viola Vaccarino³ | Brett T. Litz^{4,5} | Matthew J. Friedman^{6,7} | Jack Goldberg^{1,8} | Nicholas L. Smith^{1,8}

¹Seattle Epidemiologic Research and Information Center Department of Veterans Affairs, Seattle, Washington, USA
 ²Department of Psychiatry, Medical University of South Carolina, Charleston, South Carolina, USA
 ³Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA
 ⁴Massachusetts Veterans Epidemiological Research and Information Center, US Department of Veteran Affairs, Boston, Massachusetts, USA
 ⁵Department of Psychiatry, Boston University, Boston, Massachusetts, USA
 ⁶Department of Psychiatry, Dartmouth Geisel School of Medicine, Hanover, New Hampshire, USA
 ⁷National Center for PTSD, U.S. Department of Veterans Affairs, Washington, District of Columbia, USA
 ⁸Department of Epidemiology, University of Washington, Seattle, Washington, USA

Correspondence

Nicholas L. Smith, Seattle Epidemiologic Research and Information Center, VA Puget Sound Health Care System, 1600 S. Columbian Way, Seattle WA 98108, USA. Emails: Nicholas.Smith@va.gov; nlsmith@u.washington.edu

Funding information

This study was supported by the Cooperative Studies Program (CSP) of the United States Department of Veterans Affairs (VA) Office of Research & Development, which has provided financial support for the development and maintenance of the Vietnam Era Twin (VET) Registry. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the VET Registry, VA, or the United States Government. Numerous organizations have provided invaluable assistance in the conduct of this study, including: Department of Defense; National Personnel Records Center, National Archives and Records Administration; the Internal Revenue Service; National Institutes of Health; National Opinion Research Center; National Research Council, National Academy of Sciences; and the Institute for Survey Research, Temple University. Most importantly, the authors gratefully acknowledge

Abstract

Background: The risk of suicide among Veterans is of major concern, particularly among those who experienced a combat deployment and/or have a history of PTSD.

Design and methods: This was a retrospective cohort study of post-discharge suicide among Vietnam-era Veterans who are members of the Vietnam Era Twin (VET) Registry. The VET Registry is a national sample of male twins from all branches of the military, both of whom served on active duty between 1964 and 1975. Military service and demographic factors were available from the military records. Service in-theater was based on military records; combat exposure and PTSD symptoms were assessed in 1987 by questionnaire. Mortality follow-up, from discharge to 2016, is identified from Department of Veterans Affairs, Social Security Administration, and National Death Index records; suicide as a cause of death is based on the International Classification of Death diagnostic codes from the death certificate. Statistical analysis used Cox proportional hazards regression to estimate the association of Vietnam-theater service, combat exposure, and PTSD symptoms with suicide while adjusting for military service and demographic confounding factors.

Results: From the 14,401 twins in the VET Registry, there were 147 suicide deaths during follow-up. In adjusted analyses, twins who served in the Vietnam theater were at similar risk of post-discharge suicide compared with non-theater Veterans; there was no association between combat and suicide. An increase in severity of PTSD symptoms was significantly associated with an increased risk of suicide in adjusted analyses (hazard ratio = 1.13 per five-point increase in symptom score; 95% CI: 1.02-1.27).

Published 2022. This article is a U.S. Government work and is in the public domain in the USA.

the past and continued cooperation and participation of the members of the VET Registry and their families. Without their contribution, this research would not have been possible

Conclusions: Service in the Vietnam theater is not associated with greater risk of suicide; however, PTSD symptom severity poses a degree of risk of suicide in Vietnam-era Veterans. Adequate screening for PTSD in Veterans may be promising to identify Veterans who are at increased risk of suicide.

K E Y W O R D S

PTSD, suicide and self-harm, veterans

INTRODUCTION

Nearly nine million Veterans served during the Vietnam conflict with a third of these having served in the Vietnamtheater of operations. Several studies have examined whether military service in Vietnam leads to an increased risk of suicide. The evidence to date is decidedly mixed, with several studies finding no association (Centers for Disease Control Vietnam Experience Study, 1987; Kang et al., 2015; Thomas et al., 1991), others demonstrating that Vietnam Veterans had a reduced risk of post-discharge suicide (Breslin et al., 1988), and still others finding an increased risk of suicide (Fett et al., 1984; Watanabe & Kang, 1996). However, it is challenging to synthesize these diverse findings because they vary in the specific populations examined, how risk factors and outcomes were assessed, and duration of follow-up. For example, studies examined suicide in a random sample of Army Veterans followed from the date of military discharge (Centers for Disease Control Vietnam Experience Study, 1987), while other studies examined suicide among Vietnam Veterans seen at VA hospitals with a diagnosis of depression or PTSD (Bullman et al., 2018). Many studies failed to adjust adequately for pre-military service factors, such as family environment, that might be associated with both deployment to Vietnam and the risk of suicide. Several studies also failed to consider co-morbid depression, which may be a stronger predictor of suicide compared with PTSD alone (Gradus, 2018). Therefore, there is no clear evidence to date that PTSD is associated with an increased risk of suicide. This area needs rigorous investigation. If such an association is demonstrated, these data would be helpful for the development of interventions designed to mitigate such risk.

The Vietnam Era Twin Registry was constructed as a scientific resource to study the health of Vietnam-era Veterans (Eisen et al., 1987; Tsai et al., 2013). This unique cohort includes male-male twin pairs from all branches who both served in the military during the Vietnam era (1965–1975) and provides the most complete and representative sample to date of Vietnam Era male veterans. Other strengths to the VET Registry include the long follow-up (over 30 years since the baseline Survey of Health data collection), the availability of non-military factors, and the potential to control for familial confounders. To date, the post-discharge suicide mortality experience of this cohort has not been examined.

The purpose of this study is to examine the association between Vietnam-theater service, combat exposure, and PTSD with suicide following discharge from the military among a cohort of Vietnam-era Veterans.

METHODS

Subjects

The VET Registry was constructed from computerized military discharge records and is a national sample of male-male twins from all branches who served on active duty between 1965 and 1975 and were alive at discharge (Eisen et al., 1987). Members of the Registry were born between 1939 and 1957. The process of identifying twins involved a matching algorithm based on last name, date of birth, and similar Social Security numbers. A military record search then confirmed an individual was a member of a twin pair by matching parental names and place of birth. A complete description of the VET Registry is available (Goldberg et al., 2002; Henderson et al., 1990). The VA Office of Research & Development Central Institutional Review Board approved the study protocol.

Measures

Information from the military records

At the time the VET Registry was assembled in the 1980s, information on military service and demographics was obtained manually from the military service records. These data were abstracted and included the following: deployment to Vietnam, award of combat medals, dates of enlistment and discharge, branch of service, rank at discharge, type of discharge, Armed Forces Qualifying Test score (a measure of IQ at enlistment), date of birth, race, and educational attainment at the time of enlistment.

632

Information from the 1987 VET registry survey of health

In 1987, an initial health survey, the Survey of Health, invited the twins to participate in the VET Registry and obtained a broad array of sociodemographic, lifestyle, and health characteristics. The mailed survey also included information about service in SE Asia, combat exposure and PTSD symptoms. Regrettably information on depression was not collected as part of this survey. We created a combat exposure index, which has excellent reliability and validity, based on the sum of 18 specific combat experiences (Janes et al., 1991). For this study, three categories of combat exposure were considered as follows: persons who were not deployed to the Vietnam theater, those who were deployed and had little to no combat experience, and those who were deployed and had medium to high combat experience. The VET-R 15-item PTSD scale assessed the frequency of symptoms in the previous 6 months. The items were derived based on the Diagnostic and Statistical Manual of Mental Disorders-Third Edition-Revised (DSM-III-R) criteria; symptoms were asked of all twins, as related to "military service experiences." Response options ranged on a 5-point ordinal scale from "never" (scored 1) to "very often" (scored 5). The sum of these items produced the total VET-R PTSD score that ranges from 15 to 75. The total scale demonstrated excellent internal consistency (Chronbach's $\alpha = 0.9$), and the test-retest reliability was 0.6 (Roy-Byrne et al., 2004). In a recent report, the VET-R PTSD scale was shown to be highly correlated with both the PTSD Checklist (r = 0.90) and a diagnosis of PTSD using the Composite International Diagnostic Interview (Area Under the Curve = 87.7%) (Magruder et al., 2015).

Mortality follow-up

Mortality follow-up occurred from the date of discharge from the military to date of death or December 31, 2016 whichever came first. We used multiple sources to identify deaths among VET Registry members based on matching name, state of birth, date of birth, and Social Security number. In the period from discharge to prior to 1979, we used both the VA Beneficiary Identification and Record Location Subsystem and the Social Security Administration Death Master File to identify individual deaths. After 1979, we were able to use the National Center for Health Statistics National Death Index (NDI) to identify deaths. For each death identified from our computerized linkage, we reviewed the matches to confirm the accuracy of each match. For each death identified prior to 1979, we attempted to obtain a hard copy death certificate from individual states to confirm the date and cause of death; after 1979, we used the *NDI Plus* system to confirm date of death and underlying cause.

We classified cause of death according to International Classification of Disease (*ICD-9*) after using the appropriate cross-walk between ICD 8, 9 and 10 codes. Suicides were identified using the ICD External cause of death codes of E950-E959.

Analytic dataset and statistical analysis

Two separate analytical approaches were used. The primary analyses were based on twins-as-individuals and accounting for the non-independence of the twins through the use of clustering by pair. The full-cohort analytic dataset is based on the number of twin pairs that we confirmed from the military record who were both alive at discharge from the military. For the secondary analyses, we formed an analytic co-twin control dataset based on twin pairs who were discordant for suicide, meaning one member of the pair had died as a result of suicide and the co-twin had not died by suicide (i.e., was either alive or had died from a cause other than suicide).

Statistical analysis was conducted in several stages. The initial twins-as-individuals approach used the fullcohort and examined the association between Vietnamtheater service and suicide mortality from the date of military discharge through December 2016 (n = 14,401); we first examined Kaplan-Meier mortality curves and estimated the strength of association using the hazard ratio along with 95% confidence intervals, after accounting for clustering by twin pair. In subsequent regression analyses, we examined the risk of suicide based on military service and demographic factors using Cox proportional hazards regression. We also performed a twins-as-individuals analysis among all those twin pairs who responded to the 1987 VET Registry Survey of Health (n = 10,445), as this survey contained information about PTSD symptoms where the military records did not. This analysis examined risk of suicide starting from the date of survey response until the end of 2016 and allowed us to incorporate survey-based exposure measures of combat and the 1987 VET-R PTSD symptom scale and service in Southeast Asia as risk factors.

In the analyses of the full cohort from the time of discharge, we simultaneously adjusted for potential confounders, including military service factors and demographic factors available from the military records. Military service factors included the following: service in Vietnam, award of combat medal, branch of service, type of discharge (Specifically, for "other than honorable" the types were as follows: dishonorable (n = 4), unfitness (n = 439),

and misconduct (n = 406)), year of entry into service, and year of discharge. Demographic factors included the following: age at enlistment (classified into a binary variable of below or above median age at enlistment), educational level at enlistment (HS grad vs less than HS grad), and race (white vs non-white). In the analysis of the co-twin control dataset, we used univariate conditional logistic regression to estimate the within-pair association of potential risk factors with suicide. Given the modest number of suicides in the 1987 follow-up cohort, we could not simultaneously adjust for all potential confounding factors. Thus, only univariable analyses were conducted. The 1987 follow-up cohort additionally included the military service risk factors, combat exposure index and VET-R PTSD score, which were not available from the military records data. The PTSD score was modeled in quintiles and also continuously.

Secondary analyses used the co-twin control design to examine within-pair differences in exposure among suicide-discordant twin pairs. Paralleling our approach to the full cohort analysis, we first examined all suicidediscordant pairs from the date of military discharge and then examined suicide-discordant twin pairs for those twins who both responded to the 1987 Survey of Health. In the co-twin control analyses, we obtained odds ratio estimates and 95% confidence intervals from conditional logistic regression for matched pairs. These analyses adjusted for the same risk factors as the primary analysis.

All analyses used two-sided tests and set significance levels at p < 0.05. Data analyses used R, version 4.02.

RESULTS

Sample characteristics

The VET Registry consists of 14,401 Vietnam-era Veterans who were alive at discharge from the military and contributed a total of 600,420 person-years of follow-up. Table 1 shows that 2966 of the Registry twins have died since discharge through the end of December 2016. A larger proportion of deaths from suicide tended to occur closer to the time of discharge from active military service compared with all-cause mortality. In total, there were 147 suicides (5.0 percent) among the 2966 deaths. Four of the suicides were within two twin pairs, and the remaining 139 suicides occurred in only one twin in a given twin pair. The 139 suicides form the co-twin control analytic dataset. Among those who completed the Survey of Health (circa 1987), there were a total of 1727 deaths and 446,100 person-years of follow-up. A total of 48 suicides occurred following the Survey of Health. There were 37 suicidediscordant twin pairs among twins who both responded to the Survey of Health.

Distribution of risk factors

In the full VET Registry cohort, the distribution of military service factors was generally similar in suicide deaths compared with those who did not die by suicide (Table 2). For example, 32.7 percent of the Veterans who died by suicide served in the Vietnam-theater, whereas 35.9 percent

TABLE 1 All deaths and suicide deaths in the Vietnam Era Twin Registry through December 2016

Time interval	All deaths	Suicide deaths	Proportional mortality ratio (per 100 deaths)	Mean cohort age during time interval
	From date of military discharge Initial cohort $n = 14,742$			
1965–1969	3	1	33.3	21–22
1970–1979	188	25	13.3	22-30
1980–1989	256	39	15.2	31-40
1990–1999	452	30	6.6	41-50
2000-2009	965	40	4.1	51-60
2010-2016	1,102	12	1.1	61–67
Total	2966	147	5.0	
	From completion of the Survey of Health Questionnaire (circa 1987) Initial cohort $n = 10,980$			
1987–1989	50	6	12.0	38-40
1990–1999	286	17	5.9	41-50
2000-2009	618	21	3.4	51-60
2010-2016	773	4	0.5	61–67
Total	1727	48	2.8	

TABLE 2 Military service and demographic factors for suicide in the full Vietnam-Era Twin Registry cohort and among responders to the Survey of Health

	Time interval from Discharge through 2016		Time interval from Survey of health (circa 1987) through 2016	
Military service and demographic factors	Suicide deaths $(n = 147)$	Alive at discharge ^a $(n = 14,401)$	Suicide deaths $(n = 48)$	Alive in 1987 ^a ($n = 10,445$)
Military service				
Service in Vietnam theater (%)	32.7	35.9	25.0	35.4
Award of Combat Medal (%)	11.6	14.6	6.2	15.4
PTSD symptom score (mean ±SD)			29.4 (10.6)	26.2 (10.3)
Quintiles: Q1			10.4	15.9
Q2			10.4	19.6
Q3			20.8	24.1
Q4			25.0	19.9
Q5			33.3	20.5
Combat exposure (%)				
No Service in Vietnam theater			68.8	60.3
Service with no or low combat exposure			18.8	18.8
Service with medium or high combat exposure			12.5	20.9
Branch of Service (%)				
Army	56.8	52.4	54.2	52.1
Navy	23.1	22.4	20.8	23.4
Air Force	12.2	17.1	10.4	17.1
Marines	8.2	8.1	14.6	7.5
Type of discharge (%)				
Non-honorable	14.3	5.7	14.6	4.0
Honorable	85.7	94.3	85.4	96.0
Discharge rank (%)				
Officer	0.7	2.8	0.0	3.2
Enlistment	99.3	97.2	100.0	96.8
Year of entry into service (%)				
<1969	41.5	47.8	35.4	49.3
≥1969	58.5	52.2	64.6	50.7
Year of discharge (%)				
<1970	12.2	19.1	10.4	19.1
≥1970	87.8	80.9	89.6	80.9
Demographics				
Age at enlistment (mean \pm SD)	19.1 (1.4)	19.7 (1.6)	19.3 (1.6)	19.8 (1.4)
Education at enlistment (%)				
<high graduate<="" school="" td=""><td>29.9</td><td>19.3</td><td>29.2</td><td>16.0</td></high>	29.9	19.3	29.2	16.0
High school graduate	59.9	62.7	58.3	63.8
>High school graduate	10.2	18.0	12.5	20.2
Race (%)				
White	95.9	90.1	97.9	92.6
Non-white	4.1	9.9	2.1	7.4

^aExcludes suicide deaths.

of the Veterans who did not die by suicide served in the Vietnam-theater. However, among Veterans who died by suicide, there was a higher proportion of non-honorable discharges, and this group tended to be discharged earlier. Demographic factors were also similar in those who did and did not die by suicide with a mean age of enlistment of 19 years in both groups, except education was generally lower among Veterans who died by suicide. Among responders to the 1987 Survey of Health, the overall mean total PTSD symptom severity score was 26.2, with the majority responding that they had minimal symptoms. The distribution of military service and demographic factors was similar to the full VET Registry cohort. The overall level of combat exposure was lower, and the mean and distribution PTSD symptom level was higher among persons who died by suicide compared with those who did not. The Kaplan-Meier curve for these data are shown in Figure 1. Over the 30 years of follow-up, those in the highest quintile of PTSD symptom severity scores had lowest suicide-free survival. In the secondary co-twin control samples of suicide-discordant pairs, military service and demographic characteristics were comparable in twins who did and did not die by suicide in both the cohort followed from discharge and the 1987 cohort followed from the completion of the Survey of Health (Table S1).

Primary analysis with twins-asindividuals design

The overall incidence rate of suicide was 24.1 suicides per 100,000 person-years (95% CI: 20.2–28.1) in the full VET Registry. Suicide mortality in the full VET Registry cohort from the time of military discharge through the close of follow-up in 2016 was not different in Vietnam theater and non-theater Veterans. Figure 1 provides the Kaplan-Meier survival curve of suicide mortality by theater service and Table 3 provides an adjusted hazard ratio of 0.98 (95% CI: 0.65-1.49). Of the military service factors examined in the full cohort, only type and year of discharge were associated with significant increased risk of post-discharge suicide: those with a discharge other than honorable (dishonorable, unfitness, inaptitude, unsuitability, and misconduct) were 2.05 times more likely to die by suicide compared with those with an honorable discharge (95% CI: 1.20-3.49) (Table 3). Those with a later discharge date (i.e., later than 1970) had an elevated risk of suicide (HR = 1.86; 95% CI: 1.04–3.33). The only demographic factor significantly associated with suicide in the full cohort was age of enlistment, with greater risk found in Veterans who were below the median age of enlistment in the cohort (HR = 1.73; 95% CI: 1.18-2.54). We tested the global assumption of proportional hazards using the Schoenfeld residuals, and it was not violated (p = 0.114).

In the 1987 cohort based on respondents to the Survey of Health, suicide was not significantly associated with Southeast Asia service or receipt of a combat medal (Table 3). For PTSD, Figure 2 provides the Kaplan–Meier survival curve of suicide mortality by PTSD symptom score quintiles. In an adjusted model and when modeled continuously (Table 3), PTSD symptom score was associated with increased risk of suicide (HR = 1.13 per 5-unit change in score, 95% CI: 1.02–1.27). Due to the low number of events, there was limited power, the confidence intervals were correspondingly wide for the quintiles of PTSD symptom score, and the increasing risk trend appeared



Full Cohort - Discharge through 2016

FIGURE 1 Kaplan-Meier survival curves of suicide mortality in full VET Registry cohort, from date of military discharge until end of 2016, stratified by Southeast Asia theater service

TABLE 3Hazard ratios for theassociation of military service anddemographic factors with suicide

Military service and	Time interval from Discharge through 2016		Time interval from Survey of Health through 2016	
demographic factors	HR ^b	95% CI	HR ^c	95% CI
Service in Vietnam theater				
No	1.0		1.0	
Yes	0.98	0.65-1.49	0.85	0.23-3.16
PTSD symptom score Continuous (per 5-pt. change)			1.13	1.02-1.27
Quintiles: Q1			1.0	
Q2			0.83	0.24-2.84
Q3			1.32	0.45-3.83
Q4			1.65	0.57-4.80
Q5			2.31	0.84-6.41
Combat Exposure				
No Service in Vietnam theater			1.0	
Service with no or low combat exposure			1.26	0.38-4.20
Service with medium or high combat exposure			0.61	0.15-2.45
Award of combat medal				
No	1.0		1.0	
Yes	0.81	0.44-1.47	0.47	0.11-2.02
Branch of service				
Army	1.0		1.0	
Navy	0.82	0.54-1.25	0.66	0.31-1.37
Air force	0.59	0.33-1.05	0.42	0.14-1.25
Marines	0.66	0.36-1.24	1.24	0.55-2.81
Type of discharge				
Honorable	1.0		1.0	
Non-honorable	2.05	1.20-3.49	2.36	0.96-5.82
Year of Entry into Service				
<1969	1.0		1.0	
≥1969	0.91	0.59-1.38	1.00	0.48-2.07
Year of discharge				
<1970	1.0		1.0	
≥1970	1.86	1.04-3.33	1.71	0.60-4.85
Median age at enlistment				
Above median	1.0		1.0	
Below median	1.73	1.18-2.54	1.59	0.86-2.95
Education at enlistment				
At least high school graduate	1.0		1.0	
<high graduate<="" school="" td=""><td>1.37</td><td>0.90-2.09</td><td>1.33</td><td>0.64-2.76</td></high>	1.37	0.90-2.09	1.33	0.64-2.76

AMERICAN

637

^bAll hazard ratios are estimated from a multivariable Cox regression model that included the complete set of military service and demographic factors in the model.

^cHazard ratios for each of the military service and demographic factors are estimated from separate univariable Cox regression models. Bold entries indicate hazard ratios significantly different from 1 at the 0.05 significance level.



TABLE 4 Hazard ratios for the interaction between PTSD and combat exposure on suicide among responders to the 1987 survey of health

Factors	HR	95% CI
PTSD Symptom score (5-unit change)		1.03-1.41
Combat exposure		
No service in Vietnam theater	1.0	
Service, no or low combat exposure	0.34	0.08-1.39
Service, medium or high combat	1.06	0.13-8.52
exposure		
PTSD by Combat Exposure interaction		
$PTSD \times No$ service in Vietnam theater	1.0	
PTSD × Service, no or low combat exposure	1.15	0.94–1.40
PTSD × Service, medium or high combat exposure	0.87	0.65-1.16

to be limited to quintile 3, 4, and 5 (Table 3). Testing for interaction of PTSD with combat exposure did not detect significant interaction (Table 4).

Secondary analysis using co-twin control design

In the co-twin control analysis of all suicide-discordant pairs with follow-up starting from the date of discharge, there was no significant association with theater service (OR = 0.79; 95% CI: 0.45–1.37) or any of the other military service risk factors. None of the demographic factors demonstrated a significant association with suicide risk. Among the 37 suicide-discordant twin pairs in whom both FORSBERG ET AL.

twins responded to the Survey of Health, there were no military service or demographic factors significantly associated with suicide. Of particular note in the matched pair analysis, the total PTSD symptom severity score did not significantly elevate the odds of suicide for any quintile of symptom score (Table S2). When this PTSD symptom score was modeled continuously, a similar point estimate to the twins-as-individuals design was observed (OR = 1.14 for a five-unit change; 95% CI: 0.86–1.50), albeit not reaching statistical significance.

DISCUSSION

During more than 30 years of follow-up after military discharge, Vietnam-theater Veteran twins were at no higher risk of suicide than Vietnam-era Veterans who were not deployed. This absence of association between deployment to Vietnam-theater exposure and suicide is consistent across time, as indicated by the test of proportional hazards. Yet, among VET Registry members who were alive in 1987, subsequent suicide risk was higher among those with an increased burden of PTSD symptoms, regardless of deployment to Southeast Asia or combat exposure; this increased gradient of risk, especially for those in the highest quintile of PTSD score is illustrated by the Kaplan-Meier curves, and the risk persists over 30 years until the end of follow-up. Although the point estimates appeared to approximate an increasing trend in risk of suicide with increasing PTSD quintile, we were likely underpowered to detect quintile-specific significance. Additional findings of note included an increased risk of suicide associated with military discharge other than honorable and a younger age of enlistment. Findings regarding PTSD and suicide

risk in the co-twin control analyses were similar in magnitude (though were nominally no longer significant) and suggest that after adjusting for familial and genetic factors, there may still be an association with PTSD symptom severity and suicide risk. However, we are cautious in our interpretation of these results given the modest number of suicide deaths. The sparse data are difficult to interpret, and the lack of association may be a result of insufficient power to detect statistically significant associations.

There is a substantial body of research on the risk of suicide among Veterans. The central question raised in this literature is whether military service or specific aspects of military service, such as deployment to a war zone, alter the subsequent risk of suicide. A directly related question is whether the potential increase in the risk of suicide might be due to the psychological sequalae of serving in combat. Several meta-analyses and literature reviews have attempted to summarize this diverse literature (Haney et al., 2012; Knapik et al., 2009; Pompili et al., 2013; Rozanov & Carli, 2012). Broadly, the conclusion from these reviews is that suicide risk in Veterans is highly variable and depends on the study population and specific military experiences and their consequences. A meta-analysis of several large, population-based studies of Veterans who served during the Iraq and Afghanistan conflicts found little evidence of an increased risk of suicide among those who were deployed to a war zone (Knapik et al., 2009). The evidence from studies of Vietnam-era Veterans is less clear, with some studies finding increased risk of suicide among theater Veterans (Fett et al., 1984; Watanabe & Kang, 1996) while most others found no evidence of an increase in risk related to deployment (Centers for Disease Control Vietnam Experience Study, 1987; Thomas et al., 1991). There is also the association of co-morbid depression which cannot be addressed in our sample as depression and other psychiatric comorbidities were not assessed in the 1987 VET Registry Survey of Health. The Survey of Health only contained the VET-R PTSD symptom scale. This is unfortunate as co-morbid depression may be a stronger predictor of PTSD-associated suicide than PTSD alone (Gradus, 2018).

Studies of the effects of PTSD in Veterans and the relationship to suicide risk are difficult to interpret because of the differences in how samples were defined and assembled. For example, a strong association of PTSD with suicide death is found in several large studies of VA treatment-seeking populations (Desai et al., 2008; Zivin et al., 2007). The studies of Veteran suicide most directly comparable to the VET Registry cohort are those based on the CDC Vietnam Experience Study and the Australian retrospective cohort of Vietnam-era Veterans. The CDC study, which was made up of more 17,000 enlisted Army Veterans who served a single tour, found a hazard ratio

of 0.98 (95% CI 0.58-1.65) for theater service compared with non-theater service in the follow-up period between discharge and 1983 (Centers for Disease Control Vietnam Experience Study, 1987); in a subsequent follow-up of this cohort through 2000 the hazard ratio in the first 5 years following discharge was 1.72 (95% CI 0.76-3.88) and 0.93 (95% CI 0.64-1.34) in the time period greater than 5 years after discharge (Boehmer et al., 2004). The Australian cohort of more than 45,000 Veterans found an increased risk of suicide among those who served in Southeast Asia compared with those who did not serve (HR = 1.50; 95%CI: 1.0-2.4) (Fett et al., 1987) although a later nested casecontrol study of the Australian Vietnam-era Veterans group found no significant association with Vietnam service (O'Toole & Cantor, 1995). In a study of Veterans of the Iraq and Afghanistan conflicts, hazard ratios of 0.83 (95% CI: 0.74-0.94) and 0.99 (95% CI: 0.57-1.71) were observed in Veterans who were deployed (compared with those who were not deployed), among male and female Veterans, respectively (Kang et al., 2015).

Our study has several limitations. The VET Registry is a sample of twin pairs and it is possible that being a twin could alter the risk for suicide. However, research from the Nordic twin registries suggests major physical and mental health disorders are similar to that found among the general population (Christensen et al., 2011). Our study was restricted to male Veteran twins as the VET Registry does not include female twins, who were a small portion of the military during the Vietnam-era. The issue of exposure measurement in this cohort is challenging. Deployment to Vietnam could be determined from the military records, but as with previous studies of Vietnam-era Veterans (Centers for Disease Control Vietnam Experience Study, 1987), there were no measures of combat exposure or indicators of PTSD or psychological well-being from the records; our PTSD symptom scale was obtained in 1987 based on survey responses, which was more than a full decade after the official end of the Vietnam conflict and well after the many of suicides in this cohort had occurred. The 1987 VET-R PTSD symptom scale which we used in the current study is a measure of PTSD symptom burden and is strongly correlated with the more widely used Post Traumatic Stress Disorder Checklist (PCL) (Magruder et al., 2015) and the formal DSM-IV diagnosis of PTSD using the Composite International Diagnostic Instrument (Kessler & Ustun, 2004). As previously noted, the 1987 VET Registry Survey of Health did not obtain any measures of depression or other psychiatric disorders and contained only the PTSD symptom scale. The association between suicide and less than honorable discharge may reflect an association between suicide and substance abuse (which also predicts suicide) which, like depression, was not assessed during the 1987 survey. Unfortunately,

despite widespread belief among clinicians that many "bad papers" were due to substance abuse, there is little unclassified documentation of such an association. Finally, it is possible that there was non-response bias in those who completed the Survey of Health and those did not participate. Our analysis only examined direct effects of PTSD and deployment with suicide. It could be that PTSD mediates the relationship between deployment and suicide. The number of suicide deaths was too small to conduct a formal mediation analysis; thus, this should be the object of future investigation. Clearly, a number of key questions remain for future research about direct and indirect associations between suicide and PTSD, depression, substance use, pre-deployment/deployment factors and other variables. Ideally, measures of all of the abovementioned variables would be assessed at the time of discharge for a more extensive follow-up of Veterans as they separate from military service. The risk of death from suicide might be greatest immediately following separation from the military and/or deployment.

Statistical power for analyses based on exposures from the Survey of Health was limited due to the small number of suicides. This also impacted the stability of our estimates, particularly for the co-twin control analyses, and limited our ability to perform multivariable confounder adjustment. We defined suicide based solely on ICD codes contained on death certificates, which might be subject to misclassification. It is possible that some suicides were missed because they were classified as other forms of external cause mortality, such as single-car crashes. However, death certificates were universally available, and it was not feasible to obtain additional supporting medical documentation on each death that took place during the more than 30 years of follow-up.

A major strength of our study is the use of the VET Registry cohort, which is national in scope, includes all branches and ranks, and is unselected with respect to treatment seeking. We used several large computerized files of deaths from the VA, SSA, and CDC in an attempt to completely identify vital status throughout the follow-up period. Our analysis looked at suicide risk across a prolonged time interval and this permitted us to examine the association with both theater service (from the time of discharge) and PTSD symptoms (from 1987). To refine our inferences, we also conducted a co-twin control study that controls for age and other potential unmeasured familial and genetic confounding factors (McGue et al., 2010).

In summary, suicide risk is elevated among aging Vietnam-era Veterans with a history of PTSD, particularly those with the heaviest burden of symptoms. This association appeared to persist throughout follow-up, but there was no evidence that risk of suicide depends on previous combat exposure. Given the persistence of PTSD among Vietnam Veterans, targeted intervention programs and outreach for those Veterans with PTSD, *regardless of military experiences*, may reduce risk of suicide (Marmar et al., 2015).

REFERENCES

- Boehmer, T. K. C., Flanders, W. D., McGeehin, M. A., Boyle, C., & Barrett, D. H. (2004). Postservice mortality in Vietnam veterans: 30-year follow-up. *Archives of Internal Medicine*, *164*(17), 1908– 1916. https://doi.org/10.1001/archinte.164.17.1908
- Breslin, P., Kang, H. K., Lee, Y., Burt, V., & Shepard, B. M. (1988). Proportionate mortality study of US Army and US Marine Corps veterans of the Vietnam War. *Journal of Occupational* and Environmental Medicine, 30, 412–419. https://doi. org/10.1097/00043764-198805000-00007
- Bullman, T., Schneiderman, A., & Gradus, J. L. (2018). Relative importance of posttraumatic stress disorder and depression in predicting risk of suicide among a cohort of Vietnam veterans. *Suicide and Life-Threatening Behavior.* 49(3), 838–845. https://doi.org/10.1111/sltb.12482
- Centers for Disease Control Vietnam Experience Study. (1987) Postservice mortality among Vietnam veterans. *JAMA*. 257(6): 790-795.
- Christensen, K., Kyvik, K. O., & Holm, N. L., Skytthe, A. (2011). Register-based research on twins Scandinavian. *Journal of Public Health*, 39(Suppl 7), 185–190. https://doi.org/10.1177/14034 94811399170
- Desai, R. A., Dausey, D., & Rosenheck, R. A. (2008). Suicide among discharged psychiatric inpatients in the Department of Veterans Affairs. *Military Medicine*, 173(8), 721–728. https:// doi.org/10.7205/MILMED.173.8.721
- Eisen, S., True, W., Goldberg, J., Henderson, W., & Robinette, C. D. (1987). The Vietnam era twin (VET) registry: method of construction. Acta Geneticae Medicae Et Gemellologiae: Twin Research, 36(1), 61–66. https://doi.org/10.1017/S000156600 0004591
- Fett, M. J., Dunn, M., Adena, M. A., O'Toole, B. I., & Forcier, L. (1984). Australian veterans health studies. Part I. A retrospective cohort study of mortality among Australian National Servicemen of the Vietnam conflict era, and an executive summary of the mortality report. Commonwealth Institute of Health in the University of Sidney.
- Fett, M. J., Nairn, J. R., Cobbin, D. M., & Adena, M. A. (1987). Mortality among Australian conscripts of the Vietnam conflict era. II. Causes of death. *American Journal of Epidemiology*, 125(5), 878–884.
- Goldberg, J., Curran, B., Vitek, M. E., Henderson, W. G., & Boyko,
 E. J. (2002). The Vietnam era twin registry. *Twin Research*, 5(5),
 476–481. https://doi.org/10.1375/136905202320906318
- Gradus, J. L. (2018). Posttraumatic stress disorder and death from suicide. *Current Psychiatry Reports*, 20(11), 98. https://doi. org/10.1007/s11920-018-0965-0
- Haney, E. M., O'Neil, M. E., Carson, S., Low, A., Peterson, K., Denneson, L. M., Oleksiewicz, C., & Kansagara, D. (2012) Suicide Risk Factors and Risk Assessment Tools: A Systematic Review. Department of Veterans Affairs (US). PMID: 22574340
- Henderson, W. G., Eisen, S., Goldberg, J., True, W. R., Barnes, J. E., & Vitek, M. E. (1990). The Vietnam Era Twin Registry: a resource for medical research. *Public Health Reports*, 105(4), 368–373.

- Janes, G. R., Goldberg, J., Eisen, S. A., & True, W. R. (1991). Reliability and validity of a combat exposure index for Vietnam-era veterans. *Journal of Clinical Psychology*, *47*(1), 80–86.
- Kang, H. K., Bullman, T. A., Smolenski, D. J., Skopp, N. A., Gahm, G. A., & Reger, M. A. (2015). Suicide risk among 1.3 million veterans who were on active duty during the Iraq and Afghanistan wars. *Annals of Epidemiology*, 25(2), 96–100. https://doi. org/10.1016/j.annepidem.2014.11.020
- Kessler, R. C., & Ustun, T. B. (2004). The World Mental Health (WMH) survey initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). International Journal of Methods in Psychiatric Research, 13, 93–121. https://doi.org/10.1002/mpr.168
- Knapik, J. J., Marin, R. E., Grier, T. L., & Jones, B. H. (2009). A systematic review of post-deployment injury-related mortality among military personnel deployed to conflict zones. *BMC Public Health*, 9(1), 231. https://doi.org/10.1186/1471-2458-9-231
- Magruder, K., Yeager, D., Goldberg, J., Forsberg, C., Litz, B., Vaccarino, V., Friedman, M., Gleason, T., Huang, G., & Smith, N. (2015). Diagnostic performance of the PTSD checklist and the Vietnam Era Twin Registry PTSD scale. *Epidemiology and Psychiatric Sciences*, 25(5), 415–422. https://doi.org/10.1017/ S2045796014000365
- Marmar, C. R., Schlenger, W., Henn-Haase, C., Qian, M., Purchia, E., Li, M., Corry, N., Williams, C. S., Ho, C.-L., Horesh, D., Karstoft, K.-I., Shalev, A., & Kulka, R. A. (2015). Course of posttraumatic stress disorder 40 years after the Vietnam War: Findings from the national Vietnam veterans longitudinal study. *JAMA Psychiatry*, 72(9), 875–881. https://doi.org/10.1001/jamapsychi atry.2015.0803
- McGue, M., Osler, M., & Christensen, K. (2010). Causal inference and observational research: The utility of twins. *Perspectives on Psychological Science*, 5(5), 546–556. https://doi. org/10.1177/1745691610383511
- O'Toole, B. I., & Cantor, C. (1995). Suicide risk factors among Australian Vietnam era draftees. Suicide and Life-Threatening Behavior, 25(4), 475–488.
- Pompili, M., Sher, L., Serafini, G., Forte, A., Innamorati, M., Dominici, G., Lester, D., Amore, M., & Girardi, P. (2013). Posttraumatic stress disorder and suicide risk among veterans: a literature review. *The Journal of Nervous and Mental Disease*, 201(9), 802– 812. https://doi.org/10.1097/NMD.0b013e3182a21458

- Roy-Byrne, P., Arguelles, L., Vitek, M. E., Goldberg, J., Keane, T. M., True, W. R., & Pitman, R. K. (2004). Persistence and change of PTSD symptomatology. *Social Psychiatry and Psychiatric Epidemiology*, *39*(9), 681–685. https://doi.org/10.1007/s0012 7-004-0810-0
- Rozanov, V., & Carli, V. (2012). Suicide among war veterans. International Journal of Environmental Research and Public Health, 9(7), 2504–2519. https://doi.org/10.3390/ijerph9072504
- Thomas, T. L., Kang, H. K., & Dalager, N. A. (1991). Mortality among women Vietnam Veterans, 1973–1987. *American Journal of Epidemiology*, *134*, 973–980. https://doi.org/10.1093/oxfordjour nals.aje.a116182
- Tsai, M., Mori, A. M., Forsberg, C. W., Waiss, N., Sporleder, J. L., Smith, N. L., & Goldberg, J. (2013). The Vietnam Era Twin Registry: a quarter century of progress. *Twin Research and Human Genetics*, 16(1), 429–436. https://doi.org/10.1017/ thg.2012.122
- Watanabe, K. K., & Kang, H. K. (1996). Mortality patterns among Vietnam veterans: a 24-year retrospective analysis. Journal of Occupational and Environmental Medicine, 38(3), 272–278. https://doi.org/10.1097/00043764-199603000-00012
- Zivin, K., Kim, H. M., McCarthy, J. F., Austin, K. L., Hoggatt, K. J., Walters, H., Valenstein, M. (2007). Suicide mortality among individuals receiving treatment for depression in the Veterans Affairs health system: associations with patient and treatment setting characteristics. *American Journal of Public Health*, 97(12), 2193–2198. https://doi.org/10.2105/AJPH.2007.115477

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Forsberg, C. W., Estrada, S. A., Baraff, A., Magruder, K. M., Vaccarino, V., Litz, B. T., Friedman, M. J., Goldberg, J., & Smith, N. L. (2022). Risk factors for suicide in the Vietnam-era twin registry. *Suicide and Life-Threatening Behavior*, *52*, 631–641. <u>https://doi.org/10.1111/sltb.12848</u>