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Association between post-traumatic stress disorder severity and death by suicide in US military veterans: retrospective cohort study

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Background

There is mixed evidence regarding the direction of a potential association between post-traumatic stress disorder (PTSD) and suicide mortality.

Aims

This is the first population-based study to account for both PTSD diagnosis and PTSD symptom severity simultaneously in the examination of suicide mortality.

Method

Retrospective study that included all US Department of Veterans Affairs (VA) patients with a PTSD diagnosis and at least one symptom severity assessment using the PTSD Checklist (PCL) between 1 October 1999 and 31 December 2018 ($n = 754\,197$). We performed multivariable proportional hazards regression models using exposure groups defined by level of PTSD symptom severity to estimate suicide mortality rates. For patients with multiple PCL scores, we performed additional models using exposure groups defined by level of change in PTSD symptom severity. We assessed suicide mortality using the VA/Department of Defense Mortality Data Repository.

Results

Any level of PTSD symptoms above the minimum threshold for symptomatic remission (i.e. PCL score >18) was associated with double the suicide mortality rate at 1 month after assessment. This relationship decreased over time but patients with moderate to high symptoms continued to have elevated suicide rates. Worsening PTSD symptoms were associated with a 25% higher long-term suicide mortality rate. Among patients with improved PTSD symptoms, those with symptomatic remission had a substantial and sustained reduction in the suicide rate compared with those without symptomatic remission (HR = 0.56; 95% CI 0.37–0.88).

Conclusions

Ameliorating PTSD can reduce risk of suicide mortality, but patients must achieve symptomatic remission to attain this benefit.

Keywords

Post-traumatic stress disorder; suicide; risk assessment; quantitative research; military psychiatry.

Post-traumatic stress disorder (PTSD) is a chronic and debilitating condition associated with significant morbidity and mortality, as well as disruptions in family, workplace and social contexts.[1] Extensive research has documented negative sequelae of PTSD, including other forms of psychopathology, poor physical health, poor health-related quality of life and mortality.[2] PTSD is particularly salient among US military veterans – the estimated lifetime prevalence is 11–12%.[3] In addition to high rates of PTSD, veterans have increasingly high rates of suicide.[4] Concern about increasing suicide rates among veterans has led to a proliferation of research on potential risk factors for suicide mortality.

Although there is long-standing literature on the connection between PTSD and suicidal ideation and behaviours,[5] less is known about the relationship between PTSD and suicide mortality. Patients registered with the US Department of Veterans Affairs (VA patients) with current or past diagnosis of PTSD have been found to have an unadjusted rate of 50.7 deaths by suicide per 100 000 person-years at risk,[6] compared with a rate of 13.2 in the general adult population.[7] However, meta-analyses have not demonstrated that PTSD is definitively associated with suicide mortality.[5,8] Furthermore, there is conflicting evidence regarding the direction of a potential association between PTSD and suicide mortality depending on the population and covariates used in analysis.[9]

In veteran studies, analyses without adjustment for psychiatric comorbidities such as depression or substance misuse have reported positive associations between PTSD and suicide mortality,[10–12] whereas analyses with adjustment for comorbidities have observed negative associations.[12–14] Conversely in civilian samples, there is a strong association between PTSD and suicide mortality even after adjustment for psychiatric comorbidities.[2] One explanation for the difference in adjusted findings between veteran and civilian studies may be that drivers of suicide risk are unique among veterans. Veteran-specific studies may help to clarify whether suicide mortality is elevated in the veteran population because of high-risk comorbidities[9] or whether PTSD is itself an independent risk factor. Conner et al surveyed diagnostic codes among VA patients and found that a clinical diagnosis of PTSD was associated with a lower risk of suicide mortality after accounting for psychiatric comorbidities.[12] However, this study relied solely on PTSD diagnoses reported in the medical records. Using this methodology, PTSD was considered a dichotomous variable that existed at a specific point in time rather than a continuum of severity or a condition that fluctuates over time. Therefore, it may be more informative to evaluate suicide mortality risk using self-reported PTSD symptoms.

Few studies have explored the association between PTSD symptom severity and suicide mortality. Cooper et al examined the association between veteran-reported PTSD symptoms and suicide risk using the Primary Care PTSD Screen (PC-PTSD).[15] Positive PC-PTSD results were associated with an increased suicide mortality risk, but the risk decreased over time. This study did not assess depression or other comorbidities at the time of screening, which may have inflated the suicide mortality risk. Although the study used the self-reported symptom assessment in

a large population, limitations include lack of PTSD diagnostic confirmation, a small number of assessment items that are scored dichotomously rather than continuously (5 dichotomous items on the PC-PTSD-5 screen[16] versus 20 continuous items on the PTSD Checklist-5 questionnaire[17]) and a narrow range of total assessment scores (0–5 on the PC-PTSD-5 screen[16] versus 0–80 on the PTSD Checklist-5 questionnaire[17]). Because the PC-PTSD was designed to identify respondents with probable PTSD, those screening positive require a more comprehensive assessment, preferably with the psychometrically sound PTSD Checklist (PCL[16]).

Lee et al compared both categorical (i.e. diagnostic status) and dimensional (i.e. symptom severity) approaches to measuring PTSD in predicting future suicide attempts among post-9/11 veterans.[18] Veterans whose PTSD symptoms satisfied the diagnostic criteria had a higher risk of future suicide attempts, but the risk was even higher for veterans with symptom levels above the diagnostic threshold.[18] This study underscores the importance of using diagnostic codes in conjunction with PTSD symptom severity assessments as potential indicators of suicide risk. However, the study did not use suicide mortality as a primary outcome and the sample ($n = 1649$) was too small to accurately evaluate suicide risk.

No study has examined the association between PTSD symptom severity and suicide mortality rate in a population-based cohort using both diagnostic codes and PTSD symptoms documented in the PCL. We have collected data on a complete cohort of all VA patients diagnosed with PTSD over a nearly 20-year period with at least one PCL assessment. In doing this, we have created the largest available patient-level database on PTSD symptom severity. The goal of the current study is to evaluate (a) whether PTSD symptom severity is associated with the suicide mortality rate among patients with a PTSD diagnosis and (b) whether changes in PTSD symptom severity are associated with changes in the suicide mortality rate.

Method

Sample and data sources

We conducted a retrospective cohort study that included all VA patients with a clinical diagnosis of PTSD (ICD-9: 309.81; ICD-10: F43.1x) plus at least one PCL score between the start of fiscal year 2000 (1 October 1999) and the end of calendar year 2018 (31 December 2018) in the VA Corporate Data Warehouse (CDW) ($n = 754\,197$). Patients entered the cohort in the year of their first VA use and remained in the cohort until death or 31 December 2018, whichever came first (minimum of 1 year and maximum of 20 years). We assessed suicide mortality using the VA/Department of Defense Mortality Data Repository.[19] We assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human participants/patients were approved by the Veteran's Institutional Review Board of Northern New England (USA). A waiver of consent and authorisation was granted for the study.

PTSD symptom data

We integrated two different versions of the PCL, captured from up to two data sources within the CDW. The two data sources included scores obtained from structured data produced by psychometric assessment software in the VA medical record and scores documented by clinicians in treatment notes. We used a previously published natural language processing (NLP) algorithm with 98% precision in identifying the correct score and version of the PCL to abstract scores from clinical notes.[20] Scores abstracted from structured data and from NLP of clinical notes were integrated into a single data-set, which has been described in detail elsewhere.[21] The two versions of the PCL were aligned to the DSM-IV and DSM-5, and we will call them the PCL-IV and the PCL-5.[17,22] Validation work shows a correlation of 0.87 between PCL versions in a large sample of veterans.[17] We used a validated crosswalk (ICC = 0.96) to convert all values to PCL-5 scoring.[23]

The PCL-5 has a range of 0–80 and scores of ≥31–33 are considered diagnostic for PTSD.[17] Although a threshold for remission has not been established, the largest prospective treatment study using this version of the PCL allowed early termination owing to symptomatic remission for scores of 18 or lower.[24] The mean baseline score for VA patients starting PTSD treatment in this PCL data-set is approximately 50.[25] Based on these thresholds, we created exposure groups using four PCL score ranges: minimal (0–18), low (19–30), moderate (31–49) and high (≥50).

A clinically meaningful change in PCL score is approximately 15 points.[26] Because this change criterion was calculated using the Jacobson and Truax Reliable Change Index (1.96 times the standard error of the difference in change, which is the 'distribution of change scores that would be expected if no actual change had occurred'[27]), we used a corollary that changes of 7 points or less could be due to measurement error. Based on these thresholds, we created exposure groups using three PCL score ranges, each delineating a change in PTSD symptom severity: worse (increase of 15 points or more), no change (change within 7 points) and improved (decrease of 15 points or more). For patients with more than two PCL scores, we defined the change category based on the last two consecutive PCL scores that were documented between 8 weeks and 1 year apart, prioritising the shorter period. Additionally, we performed subgroup analysis based on whether patients who improved achieved symptomatic remission, which we defined as a follow-up PCL score ≤18.

Covariates

We measured patient characteristics at the time of their last PCL score, including age, gender, ethnicity, marital status, service-connected disability, and burden of mental and physical illness. In addition to PTSD diagnosis, we summarised physical and mental diagnoses in the preceding two calendar years (supplementary Appendix available at https://doi.org/10.1192/bjp.2022.110) using counts of diagnostic categories developed in prior research using VA electronic medical record (EMR) data.[28] Specifically, we used ICD codes in patients' medical records to create a modified Elixhauser Comorbidity Index for physical health,[29] which was orthogonal to a mental health index based on the DSM-5 diagnostic groups.[1] Patients were categorised as having a low, medium or high burden of physical or mental illness if they had diagnoses from 0, 1–2 or 3+ relevant groups. We also specifically assessed whether patients had comorbid depressive or substance use disorder diagnoses.

Study outcomes

We measured suicide mortality from 1 day after the last PCL administration date through to 31 December 2018 using ICD-10 codes U03, X60–X84 and Y87.0.

Statistical analysis

For descriptive analyses, we calculated frequencies, both overall and by suicide mortality status, for all variables among patients in the cohort with at least one PCL score. We calculated suicide rates per 100 000 person-years at the patient level by multiplying the

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Table 1 Characteristics of Department of Veterans Affairs patients with a post-traumatic stress disorder (PTSD) diagnosis and at least one PTSD Clinician Checklist (PCL) score[a]

Characteristic	Total	PTSD symptom severity by last PCL score[b]			
		Minimal	Low	Moderate	High
Patients, *n* (%)	754 197 (100)	71 513 (9.5)	94 698 (12.6)	251 813 (33.4)	336 173 (44.6)
Suicide mortality					
Died, *n* (%)	2097 (0.3)	179 (0.25)	238 (0.25)	708 (0.28)	972 (0.29)
Rate per 100 000 person-years	77.6	62.3	67.6	78.5	83.8
Gender, *n* (%)					
Male	658 261 (87.3)	61 993 (86.7)	83 133 (87.8)	221 746 (88.1)	291 389 (86.7)
Female	95 936 (12.7)	9520 (13.3)	11 565 (12.2)	30 067 (11.9)	44 784 (13.3)
Age, years: *n* (%)					
18–34	211 535 (28.1)	20 986 (29.4)	28 122 (29.7)	72 244 (28.7)	90 183 (26.8)
35–54	272 900 (36.2)	22 846 (32.0)	31 266 (33.0)	87 113 (34.6)	121 675 (39.2)
55–74	256 953 (34.1)	25 502 (35.7)	32 968 (34.8)	87 875 (34.9)	110 608 (32.9)
≥75	12 809 (1.7)	22 179 (3.1)	2342 (2.5)	4581 (1.8)	3707 (1.1)
Marital status, *n* (%)					
Divorced	174 725 (23.2)	16 183 (22.6)	20 712 (21.9)	56 792 (22.6)	81 038 (24.1)
Married	395 304 (52.4)	36 800 (51.5)	50 655 (53.5)	134 395 (53.4)	173 454 (51.6)
Single	128 389 (17.0)	13 467 (18.8)	16 513 (17.4)	42 303 (16.8)	56 106 (16.7)
Separated	35 475 (4.7)	2881 (4.0)	4016 (4.2)	11 365 (4.5)	17 213 (5.1)
Widowed	14 280 (1.9)	1675 (2.3)	1974 (2.1)	4854 (1.9)	5777 (1.7)
Unknown	6024 (0.8)	507 (0.7)	828 (0.9)	2104 (0.8)	2585 (0.8)
Ethnicity, *n* (%)					
White (non-Hispanic)	467 979 (62.1)	48 292 (67.5)	63 999 (67.6)	163 585 (65.0)	192 103 (57.1)
Black (non-Hispanic)	164 512 (21.8)	12 644 (17.7)	16 512 (17.4)	49 814 (19.8)	85 542 (25.5)
Hispanic	76 373 (10.1)	6597 (9.2)	8702 (9.2)	23 885 (9.5)	37 189 (11.1)
Pacific Islander	20 877 (2.8)	1841 (2.6)	2458 (2.6)	6387 (2.5)	10 191 (3.0)
American Indian	11 267 (1.5)	953 (1.3)	1359 (1.4)	3749 (1.5)	5206 (1.6)
Unknown	13 189 (1.8)	1186 (1.7)	1668 (1.8)	4393 (1.7)	5942 (1.8)
Service era, *n* (%)					
Vietnam	126 917 (16.8)	12 143 (17.0)	16 690 (17.6)	44 546 (17.7)	53 538 (15.9)
OEF/OIF/OND[c]	349 995 (46.4)	32 644 (45.7)	45 831 (48.4)	119 806 (47.6)	151 714 (45.1)
Service-connected disability, *n* (%)					
None	403 328 (53.4)	38 619 (54.0)	49 991 (52.8)	133 243 (52.9)	181 475 (54.0)
0–60%	103 941 (13.7)	12 994 (18.2)	15 906 (16.8)	37 045 (14.7)	37 996 (11.3)
70–100%	246 928 (32.7)	19 900 (27.8)	28 801 (30.4)	81 525 (32.4)	116 702 (34.7)
Burden of physical illness, *n* (%)[d]					
Low: 0 conditions	314 200 (41.7)	29 388 (41.1)	40 181 (42.4)	106 085 (42.1)	138 546 (41.2)
Medium: 1–2 conditions	298 122 (39.5)	27 625 (38.6)	36 399 (38.4)	99 073 (39.3)	135 025 (40.2)
High: 3+ conditions	141 875 (18.8)	14 500 (20.3)	18 118 (19.1)	46 655 (18.5)	62 602 (18.6)
Burden of mental illness, *n* (%)[d]					
Low: 0 conditions	14 528 (1.9)	3347 (4.7)	2451 (2.6)	4604 (1.8)	4126 (1.2)
Medium: 1–2 conditions	297 390 (39.4)	33 662 (47.1)	42 698 (45.1)	104 678 (41.6)	116 352 (34.6)
High: 3+ conditions	442 279 (58.6)	34 504 (48.3)	49 549 (52.3)	142 531 (56.6)	215 695 (64.2)
Mental health comorbidities, *n* (%)[d]					
Depression only	312 352 (41.4)	25 198 (35.2)	36 374 (38.4)	103 169 (41.0)	147 611 (43.9)
Substance use only	58 668 (7.8)	6093 (8.5)	7665 (8.1)	19 732 (7.8)	25 178 (7.5)
Depression and substance use	158 967 (21.1)	11 786 (16.5)	16 019 (16.9)	48 936 (19.4)	82 226 (24.5)
Neither	224 210 (29.7)	28 436 (39.8)	34 640 (36.6)	79 976 (31.8)	81 158 (24.1)
Time since last PCL	Median 3.1 years (interquartile range 4.5 years)				

a. Patients with at least one documented PTSD Clinician Checklist (PCL) score.
b. PTSD symptom severity is categorised by four PCL score ranges: minimal symptoms, PCL score ≤18; low symptoms, PCL score 19–30; moderate symptoms, PCL score 31–49; high symptoms, PCL score ≥50.
c. OEF/OIF/OND, Operations Enduring Freedom, Iraqi Freedom and New Dawn.
d. Burden of mental and physical illness and mental health comorbidities in the 2 years prior to the last PCL.

number of observed suicides by 100 000, then dividing that value by the number of person-years at risk from the day after each patient's last PCL until death or 31 December 2018, whichever occurred first.

For proportional hazards regression analyses examining the effect of PTSD symptom category or change in PTSD symptom category on suicide mortality rate, we used each patient's last PCL score or change in PCL score as the unit of analysis. The patient's time at risk began the day after the last PCL was administered and ended at death or on 31 December 2018, whichever occurred first. We used partially conditional proportional hazards regression models; by treating each PCL as the unit of analysis, the models were conditioned on the baseline covariates (age, gender, ethnicity, marital status, service-connected disability, and mental and physical health diagnoses) but not on the time-varying covariates (PCL responses). We conducted a set of stratified analyses for patients with and without comorbid depressive or substance use disorders for the PTSD symptom severity analysis but not the change in severity analyses, because of limitations in sample size.

Covariates were included in the models to adjust for potential confounding variables in the association between PCL responses and suicide mortality. We adjusted for covariates using a stepped process to better understand the associations between the covariates, the exposure groups and the outcome. Data collection and analyses were conducted from 1 May 2021 to 9 September 2021. Data analyses were performed using SAS software (Windows), version 9.4 and the SAS Enterprise Guide, version 7.1 (SAS Institute Inc.).

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Table 2 Unadjusted and adjusted proportional hazards models for suicide mortality by post-traumatic stress disorder (PTSD) symptom severity

Risk of suicide by last PTSD Clinician Checklist (PCL) score (n = 754 197)

	1 month		All time[a]	
Comparisons based on PTSD symptom severity[b]	HR	95% CI	HR	95% CI
Model 1: Unadjusted				
Low *v.* minimal	2.27	(0.83–6.24)	1.07	(0.88–1.30)
Moderate *v.* minimal	**2.68***	(1.07–6.73)	**1.23***	(1.05–1.45)
High *v.* minimal	**2.57***	(1.03–6.39)	**1.31****	(1.11–1.53)
Model 2: Adjusted for age, gender, ethnicity				
Low *v.* minimal	2.22	(0.81–6.10)	1.05	(0.87–1.28)
Moderate *v.* minimal	**2.70***	(1.07–6.79)	**1.25****	(1.06–1.48)
High *v.* minimal	**2.83***	(1.12–7.04)	**1.44*****	(1.23–1.69)
Model 3: Adjusted for age, gender, ethnicity, marital status, service-connected disability				
Low *v.* minimal	2.21	(0.80–6.07)	1.05	(0.87–1.28)
Moderate *v.* minimal	**2.70***	(1.07–6.79)	**1.25****	(1.06–1.47)
High *v.* minimal	**2.84***	(1.14–7.10)	**1.43*****	(1.22–1.68)
Model 4: Adjusted for age, gender, ethnicity, marital status, service-connected disability, burden of mental and physical illness				
Low *v.* minimal	2.13	(0.77–5.86)	1.02	(0.84–1.24)
Moderate *v.* minimal	**2.52***	(1.00–6.35)	1.18	(0.99–1.39)
High *v.* minimal	**2.56***	(1.03–6.41)	**1.29****	(1.10–1.52)

*P < 0.05, **P < 0.01, ***P < 0.001; bold indicates statistical significance.
a. Length of follow-up after last PCL: median 3.1 years, IQR = 4.5 years.
b. PTSD symptom severity is categorised by four PCL score ranges: minimal symptoms, PCL score ≤18; low symptoms, PCL score 19–30; moderate symptoms, PCL score 31–49; high symptoms, PCL score ≥50.

Results

Across our 20-year period of examination, 754 197 VA patients with a PTSD diagnosis had at least one PCL score recorded (Table 1). The distribution of patients by number of PCL scores is as follows: 347 111 individuals had only one PCL score; 407 145 had two or more PCL scores (249 687 of these patients had at least two usable PCL scores); 267 244 had three or more PCL scores. For patients with two or more PCL scores (n = 190 822), we defined usable pre–post score pairs as those documented at least 8 weeks apart and we disregarded pairs documented less than 8 weeks apart. Among patients with at least one PCL score, 62.1% were White, 52.4% were married, 87.3% were male, 36.2% were 35–54 years old and 46.4% served in post-9/11 conflicts. Patients were followed for a median of 3.1 years (interquartile range 4.5 years) after the last PCL assessment.

Among patients with at least one PCL score, a total of 2097 (0.3%) died by suicide within the follow-up period. The unadjusted suicide mortality rate was 77.6 deaths per 100 000 person-years. The unadjusted suicide mortality rate was highest in patients with high PTSD symptoms (PCL score ≥50). Patients with high PTSD symptoms were more commonly male, 35–54 years old, married, White, post-9/11 veterans and had greater numbers of mental health comorbidities, especially depression. The unadjusted suicide mortality rate was lowest in patients with minimal PTSD symptoms (PCL score ≤18). Patients with minimal PTSD symptoms were more common in the 55–74 age group and had fewer mental health comorbidities.

In proportional hazards models for suicide mortality by PTSD symptom severity (Table 2), any level of PTSD symptoms (low, medium or high) compared with minimal levels of PTSD symptoms was associated with over double the suicide mortality rate at 1 month after assessment. As symptom category increased from low to high, there was a pattern of increasing rates compared with the minimal symptom group, but the confidence intervals overlapped. Covariate adjustment did not change these general patterns of associations at 1 month. In models including all available follow-up time, the strength of the association between PTSD symptoms and suicide rate was diminished but still indicated a pattern of 20–40% increase in the long-term rate for those with moderate or high symptoms compared with those with minimal symptoms across models. In stratified analyses, patients with comorbid depression or substance misuse who had any PTSD symptoms at 1 month had a two- to threefold elevated rate of suicide at 1 month compared with those with minimal PTSD symptoms, but the relationship was attenuated in models including all available follow-up time (Table 3). However, among patients without comorbid depression

Table 3 Proportional hazards models for suicide mortality adjusted for age, gender and ethnicity by post-traumatic stress disorder (PTSD) symptom severity

Risk of suicide by last PTSD Clinician Checklist (PCL) score

	1 month		All time	
Comparisons based on PTSD symptom severity[a]	HR	95% CI	HR	95% CI
Patients with PTSD with either depressive disorders and/or substance use disorders (n = 529 987)				
Low *v.* minimal	2.32	(0.64–8.42)	0.98	(0.79–1.21)
Moderate *v.* minimal	2.90	(0.89–9.41)	1.05	(0.88–1.27)
High *v.* minimal	2.96	(0.92–9.50)	1.15	(0.96–1.38)
Patients with PTSD without either depressive disorders or substance use disorders (n = 224 210)				
Low *v.* minimal	2.01	(0.39–10.38)	1.21	(0.79–1.86)
Moderate *v.* minimal	2.19	(0.49–9.78)	**1.74****	(1.21–2.51)
High *v.* minimal	2.19	(0.48–9.87)	**2.01*****	(1.39–2.89)

**P < 0.01, ***P < 0.001; bold indicates statistical significance.
a. PTSD symptom severity is categorised by four PCL score ranges: minimal symptoms, PCL score ≤18; low symptoms, PCL score 19–30; moderate symptoms, PCL score 31–49; high symptoms, PCL score ≥50.

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Table 4 Unadjusted and adjusted proportional hazards models for suicide mortality by change in post-traumatic stress disorder (PTSD) symptom severity

Risk of suicide by change in PTSD Clinician Checklist (PCL) score (n = 190 822)				
	1 month		All time	
Change in PTSD symptom severity[a]	HR	95% CI	HR	95% CI
Model 1: Unadjusted				
Worse *v.* no change	1.04	(0.46–2.34)	1.26	(0.99–1.60)
Improved *v.* no change	0.94	(0.48–1.85)	1.10	(0.90–1.35)
Model 2: Adjusted for age, gender, ethnicity				
Worse *v.* no change	1.01	(0.45–2.28)	1.24	(0.98–1.58)
Improved *v.* no change	0.91	(0.46–1.79)	1.08	(0.88–1.33)
Model 3: Adjusted for age, gender, ethnicity, marital status, service-connected disability				
Worse *v.* no change	1.05	(0.47–2.38)	1.28	(1.01–1.62)
Improved *v.* no change	0.95	(0.48–1.87)	1.11	(0.91–1.36)
Model 4: Adjusted for age, gender, ethnicity, marital status, service-connected disability, burden of mental and physical illness				
Worse *v.* no change	1.04	(0.46–2.34)	1.25	(0.98–1.59)
Improved *v.* no change	0.94	(0.47–1.84)	1.09	(0.89–1.34)

a. Change in PTSD symptom severity is categorised by three PCL score ranges: symptoms worse, 15 points or more increase; no change, 7 or fewer points in either direction; symptoms improved, 15 points or more reduction.

or substance misuse, the relationships persisted: patients with moderate PTSD symptoms (HR = 1.74, 95% CI 1.21–2.51) and high PTSD symptoms (HR = 2.01, 95% CI 1.39–2.89) had a meaningfully higher long-term suicide rate compared with those with minimal PTSD symptoms.

Among patients with usable repeated PCL measurements (n = 190 822), those with worsening PTSD symptoms compared with patients with no change in PTSD symptoms had an approximately 25% higher suicide rate in models including all available follow-up time (Table 4), although there was no association in models truncated at 1 month. There did not appear to be a corresponding decrease in long-term suicide rate when PTSD symptoms improved. However, when we added a requirement for symptomatic remission, the rate reduction became apparent (Table 5): among patients with improvements in PTSD symptoms, those whose final PCL score was ≤18 had a substantially diminished rate of suicide in the model including all available risk time compared with those with a final PCL score >18 (HR = 0.56; 95% CI 0.37–0.88).

Discussion

This study was the first to examine suicide mortality rates in a national sample of veterans with PTSD using both diagnostic codes and symptom severity. Compared with having negligible PTSD symptoms, having PTSD symptoms increases the rate of suicide mortality, even after adjusting for mental and physical health comorbidities. We observed a modest gradient effect whereby higher levels of PTSD symptoms increase the long-term rate. Although comorbid depression or substance misuse increase the suicide mortality rate in veterans with PTSD, veterans without these comorbidities and moderate to severe PTSD symptoms continue to have high suicide rates. PTSD symptom severity alone may be an independent risk factor for suicide mortality. Compared with not having a clinically meaningful change in PTSD symptoms, worsening PTSD symptoms increase the suicide rate. Although improved PTSD symptoms alone cannot predict suicide rates, improving to the point of symptomatic remission does seem to lower the suicide rate. These findings have critical implications in treatment planning and clinical assessment for patients with PTSD: we must do more to treat patients to remission and develop better treatments for those whose symptoms do not remit with available treatments. For practitioners who work directly with veterans with PTSD, associating higher PTSD symptom severity with higher suicide risk may help guide clinical decisions and identify priorities for prevention.

The finding that veterans with PTSD are at elevated risk for suicide mortality is consistent with several studies.[6] However, the unadjusted suicide rate was higher, at 77.6 deaths per 100 000 person-years at risk compared with the unadjusted 50.7 deaths per 10 000 person-years at risk previously reported.[6] Compared with studies that analysed PTSD symptom severity, the results of this study are consistent with those of both Cooper et al, who found that positive PC-PTSD screening results were associated with an increased suicide mortality risk,[15] and Lee et al, who found that the risk of suicide attempts was higher for veterans with PTSD symptom levels above the diagnostic threshold.[18]

Unlike Conner et al, who found that PTSD was associated with a lower suicide mortality risk after accounting for psychiatric comorbidities,[12] this study found that PTSD may serve as an independent risk factor for suicide mortality. Conner et al found that depression had the largest influence on the association between PTSD and suicide. However, without longitudinal measurements of psychiatric comorbidities, it is difficult to establish the temporal ordering of variables and avoid collider bias. Collider bias would

Table 5 Proportional hazards models for suicide mortality adjusted for age, gender and ethnicity by change in post-traumatic stress disorder (PTSD) symptom severity and final PTSD symptom severity

Risk of suicide by change in PTSD Clinician Checklist (PCL) score and final PCL score (n = 190 822)				
	1 month		All time	
	HR	95% CI	HR	95% CI
Patients with PCL scores that improved by ≥15 points (n = 41 652)				
Final PCL score ≤18 *v.* final PCL score >18	0.28	(0.04–2.17)	**0.56***	(0.37–0.88)

*P < 0.05; bold indicates statistical significance.

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occur through inappropriate adjustment for a psychiatric comorbidity, such as adjustment for variables that are affected by PTSD and share common causes with suicide. Adjustment for depression may have introduced collider bias in the association between PTSD and suicide, thus potentially biasing the strength and direction of the association.

Limitations

This study has several limitations, primarily related to sample selection. First, the approach did not account for potentially relevant confounders, including patient-level treatment characteristics. Additional multiyear longitudinal cohorts are required to assess whether implementation of evidence-based treatment for PTSD or other mental health conditions influenced suicide mortality outcomes for VA patients with PTSD.

Second, our cohort only included veterans with a PTSD diagnosis. We did not compare veterans with PTSD with veterans with just depression or substance misuse. Although comorbidities were assessed in the 2 years prior to the last PCL score, it may be difficult to establish a temporal relationship between PTSD and depression or substance misuse. Depression or substance misuse may act as a mediator between PTSD and suicide mortality, and adjustment for these variables may diminish the impact of PTSD symptom severity alone.

Finally, the study population was limited to VA patients. The veteran population has demonstrated characteristics that make it different from other PTSD populations.[30] Notably, veterans are predominantly older and male.[30] Veterans who access the VA healthcare system are more likely to have poorer health, lower socioeconomic status and more medical conditions than the general population.[30] Therefore, these findings may not be generalisable to civilians with PTSD. It will be important that other studies replicate these results in non-veteran populations and adjust for relevant confounders.

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Supplementary material

Supplementary material is available online at https://doi.org/10.1192/bjp.2022.110.

Data availability

The Department of Veterans Affairs Corporate Data Warehouse (CDW) contains electronic medical record data compiled from individual VA facilities and is described at http://www.hsrd.research.va.gov/for_researchers/vinci/cdw.cfm. Researchers with VA network access can obtain descriptions of CDW data at http://vaww.virec.research.va.gov/.

Author contributions

The study concept and design were completed by J.A.F., B.S. and J.L.G. Material preparation and primary authorship of the manuscript were performed by J.A.F. Data collection and analysis were conducted by V.D., T.J. and J.A.F. Additional writing, editing and formatting for submission were provided by B.S., J.L.G. and B.V.W. Subject matter expertise and editing were provided by S.M. and N.H. All authors read and approved the final manuscript.

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Declaration of interest

None.

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EXTRA CONTENT ONLINE

Psychiatry in History

Dr Manfred J. Sakel: discoverer of insulin shock therapy

Alexander Wellington

Dr Manfred Sakel was an Austrian American neuropsychologist and psychiatrist credited for introducing insulin shock (or coma) therapy (IST) as a treatment for psychoses, especially schizophrenia (1927). He conceived the idea shortly after graduating in medicine at the University of Vienna (1925) while working as an internist at the Lichterfelde Sanatorium in Berlin. Sakel allegedly induced prolonged convulsions and superficial coma in a morphine addict from an accidental overdose of insulin after which the patient woke with enriched mental clarity and a diminution of withdrawal symptoms (i.e. tremors, vomiting and opiate craving). Later Sakel coined the method 'Sakel's technique'. He theorised that insulin antagonised the neuronal effects of the products of the adrenal cortex which (he quoted) 'will force [the nerve cell] to conserve functional energy and store it to be available for the reinforcement of the cell'. He experimented with animals, supposedly from his private kitchen to ensure that hypoglycaemia can be reversed safely, permitting deeper induced comas without harm. His findings were first published under the title, 'New treatment of morphine addiction' in the *Deutsche Medizinische Wochenschrift* (1930).

Sakel returned to Vienna as a research associate at the University's neuropsychiatric clinic (1933). Despite initial opposition from his supervisor, Sakel successfully persuaded them and patients were induced to 5–6 comas per week until amassing 50–60 comas or a normal psychiatric response was achieved. According to his reports, 70% of patients had a full remission, 18% had a 'social remission' and a total of 68% were discharged whereas 2 years prior to his arrival 20% were discharged. His experiences were reported in the Vienna Medical Society (1933) and in 13 publications (1934–1935) wherein he further claimed an over 88% improvement rate.

He earned international attention as documented in his obituary: 'psychiatrists from all over the world went there to learn from [him]'; among them was Dr Isabel Wilson, Commissioner of the Board of Control for England and Wales, who visited Vienna to confirm the efficacy of IST (1936) and who later published a 61-page report entitled *A Study of Hypoglycaemic Shock Treatment in Schizophrenia*. IST was positively reviewed in esteemed medical journals and by 1938, there were 31 psychiatric hospitals with insulin coma units in England and Wales.

Sakel emigrated to the USA (1937) with the help of Joseph Wortis who translated his 1938 book *The Pharmacological Shock Treatment of Schizophrenia*. Sakel resumed study at the Harlem Valley State Hospital which became the first hospital in the USA to adopt IST. However, this saw a decline due to the integration of electroconvulsive therapy (ECT) into psychiatric practice; as depicted in 1956 at Severalls Hospital in Essex, wherein 39 patients received IST and an overwhelming 432 patients received ECT.

Sakel persistently defended the use of IST and continued treating patients privately at the Murray Hill Hotel on Park Avenue and the Slocum Clinic in Beacon, New York, affording him a reputation of being arrogant and driven by greed. He remained single until his death of a myocardial infarction at age 57.

His contribution to psychiatry remains historically significant even though IST is no longer in use.

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