Mental Health Outcomes Among Military Service Members After Severe Injury in Combat and TBI

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ABSTRACT

Introduction

Studies examining the mental health outcomes of military personnel deployed into combat zones have focused on the risk of developing post-traumatic stress disorder conferred by mild or moderate traumatic brain injury (TBI). However, other mental health outcomes among veterans who sustained critical combat injuries have not been described.

Materials and Methods

We examined the associations of moderate and severe TBI and combat injury with the risk for anxiety and mood disorders, adjustment reactions, schizophrenia and other psychotic disorders, cognitive disorders, and post-traumatic stress disorder. We conducted a retrospective cohort study of U.S. military service members critically injured in combat during military operations in Iraq and Afghanistan from February 1, 2002, to February 1, 2011. Health care encounters from (1) the Department of Defense (DoD) Trauma Registry (TR), (2) acute and ambulatory care in military facilities, and (3) civilian facilities are reimbursed by Tricare. Service members who sustained severe combat injury require critical care. We estimated the risk of mental health outcomes using risk-adjusted logit models for demographic and clinical factors. We explored the relationship between TBI and the total number of mental health diagnoses.

Results

Of the 4,980 subjects who met inclusion criteria, most injuries occurred among members of the Army (72%) or Marines (25%), with mean (SD) age of 25.5(6.1) years. The prevalence of moderate or severe TBI was 31.6% with explosion as the most common mechanism of injury (78%). We found 71% of the cohort was diagnosed with at least one poor mental health condition, and the adjusted risk conferred by TBI ranged from a modest increase for anxiety disorder (odds ratio, 1.27; 95% confidence interval [CI], 1.11–1.45) to a large increase for cognitive disorder (odds ratio, 3.24; 95% CI, 2.78–3.77). We found TBI was associated with an increased number of mental health diagnoses (incidence rate ratio, 1.52; 95% CI, 1.42–1.63).

Conclusions

Combat-associated TBI may have a broad effect on several mental health conditions among critically injured combat casualties. Early recognition and treatment for trauma-associated mental health are crucial to improving outcomes among service personnel as they transition to post-deployment care in the DoD, Department of Veterans Affairs, or community health systems.

INTRODUCTION

The cognitive and mental health symptoms associated with traumatic brain injury (TBI) were first described over 50 years ago as "accident neurosis."[1] Substantial progress has been made during the past 15 years toward understanding the consequences of combat exposure on mental health outcomes.[2–5] Most efforts have focused on post-traumatic stress disorder (PTSD), emphasizing treatment efficacy or risk factor identification, with less attention toward a broader recognition of multiple mental health sequelae and conditions associated with TBI. Since the earliest report of "shell shock" in 1915,[6] the medical, psychosocial, and cognitive impairments associated with TBI have been well studied in civilian[7–9] and military populations.[10–12] Several studies of military personnel deployed into combat in Afghanistan and Iraq have described mental health and neuropsychological harm.[2,13–15]

The impact of TBI on service members has come into renewed focus since the outset of U.S. military operations in Iraq and Afghanistan, beginning with Operation Enduring Freedom (OEF) on October 2001 and later including Operation Iraqi Freedom (OIF), Operation New Dawn (OND), and Operation Inherent Resolve (OIR). Since the beginning of these operations, over 2.7 million U.S. service members have been deployed into a combat theater,[16] more than 6,900 have died,[17,18] and over 52,500 have sustained severe physical injuries, including at least 7,832 who survived a severe or penetrating TBI.[17] Improvements in military technology (eg,

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improved body armor) and combat theater medical management efficacy have lowered mortality while increasing injury rates such as TBI,[18] when compared to the combat outcomes of World Wars I and II and Vietnam.[6,19]

Among Afghanistan and Iraq War veterans, the incidence of poor mental health conditions associated with mild or moderate TBI has been reported as high as 22.8%,[20] affecting up to 320,000 service members.[21] Most studies that examined the relationship between TBI and mental health outcomes in combat veterans had short post-injury follow-up periods[22,23] and focused only on PTSD[7,9] or neurocognitive disorder[24,25] in cases of mild or moderate TBI.[15,26–28] Previous studies of severe TBI have primarily been conducted in nonmilitary populations.[29] With one exception,[30] studies of military veterans have been limited by cross-sectional study design or small study populations.[31,32] Thus, little is known about the longer-term mental health diagnoses and outcomes of severely injured service members.

We sought to characterize the incidence of mental health outcomes in a cohort of critically injured U.S. military personnel. Given prior work in other populations,[8,9,29] we hypothesized that service members who sustained a TBI during combat would be associated with a greater risk of being diagnosed with several mental health conditions—anxiety and mood disorders, adjustment reactions, schizophrenia and other psychotic disorders, cognitive disorders, and PTSD—when compared to severely injured patients without TBI.

METHODS

Study Design and Participants

We conducted a retrospective cohort study of U.S. military service members who sustained critical injuries from February 1, 2002 to January 31, 2011, during combat operations in Iraq and Afghanistan. The analytic data set was constructed using several Department of Defense (DoD) assets: the DoD Trauma Registry (DoDTR), Armed Forces Medical Examiner System (AFMES), and other data sets maintained by the Defense Health Agency (DHA) as described previously.[33] Social security numbers were used to link unique subjects across data sets and multiple clinical encounters. Using the DoDTR, we included service members if they were injured in combat, received critical care in theater, and survived at least 90 days from the injury date. Service members who sustained more than one critical injury episode (during multiple combat deployments) were excluded from the analyses. Patients with a mental health diagnosis that preceded the injury date were excluded from the corresponding analysis.

Exposures and Outcomes

Demographic variables (age, sex, military service, and active duty status), military operation (OIF, OND, OEF), and injury characteristics (mechanism, type, mean arterial pressure [MAP], and heart rate at presentation to the emergency room in the combat theater) were obtained from the DoDTR. MAP was collapsed into three clinically relevant categories: "high" (>106 mm Hg), "normal" (65–106 mm Hg), and "low" (<65 mm Hg), based on prior studies of this patient population.[33] We used two instruments to quantify trauma, one to represent the magnitude (Injury Severity Score [ISS])[34] and the other to determine if a TBI had occurred (Barell Injury Matrix).[35] Moderate (ISS, 15–25) and severe (ISS >25) TBI were collapsed into a binary indicator. Death records were obtained from AFMES. Patients' post-injury clinical characteristics were determined using electronic health records obtained from DoD-operated ambulatory and acute care hospital facilities and encounters occurring at civilian facilities reimbursed by Tricare (the U.S. military health benefit program) from the DHA. Mental health diagnoses were determined using the International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) diagnostic codes. Six clinically meaningful categories were derived using ICD-9-CM diagnostic codes reported in previous studies[25,36,37] with minor modifications: anxiety disorders, mood disorders, adjustment reactions, schizophrenia and other psychotic disorders, cognitive disorders, and PTSD (Supplementary Material, Appendix Table 1). The dichotomous outcome was defined as one or more diagnosis and was determined independently for each mutually exclusive category.

Statistical Analyses

We calculated descriptive statistics for demographics, military operational characteristics, clinical characteristics for acute and post-injury episodes, and the post-injury duration. We calculated the Kendall tau correlation coefficients (corr procedure in SAS 9.4) for each outcome category combination. Patients were excluded from all model analyses if a predictor variable was missing or if they were lost to follow-up within 90 days.

In our primary analyses, we estimated the risk of being diagnosed with a mental health condition for each category separately using unadjusted and adjusted fixed-effects logit models (logistic procedure in Stata). The adjusted models included predictor variables for patient characteristics (age, sex, military service branch, active duty status) and clinical risk factors (heart rate, ISS, mode of injury, and MAP). In our secondary analyses, we explored the relationship between TBI and the number of mental health conditions using negative binomial (nbreg procedure in Stata) and Poisson models (Poisson procedure in Stata), accounting for the subject-specific follow-up period; we retained the covariates used in the primary analysis models. All analyses were performed using Stata 14.0 (College Station, Texas).

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were used to prepare this manuscript. The U.S. Army Medical Research and

TABLE I. Descriptive Statistics for the Cohort

	Full Cohort $n = 4{,}980$ 100%	TBI $n = 1{,}574$ 31.6%	No TBI $n = 3{,}406$ 68.4%	P
Age (years)	25.5 ± 6.1	25.4 ± 6	25.5 ± 6.2	0.62
Male sex	98.2	98.6	98.0	0.16
Service branch				0.009
Army	71.7	74.0	70.6	
Air Force	1.1	1.5	0.9	
Marines	24.7	22.5	25.7	
Navy	2.6	2.0	2.8	
Duty status				<0.001
Active duty	87.3	90.7	85.7	
Reserves	12.8	9.3	14.3	
Military operation				<0.001
OEF	19.7	32.1	13.9	
OIF	80.2	67.9	86.0	
OND	0.1	0.1	0.1	
Mechanism of injury				<0.001
Explosive	78.4	86.5	74.7	
GSW	18.6	9.3	22.9	
Other	3.0	4.3	2.4	
Injury type				<0.001
Penetrating	43.5	48.0	41.4	
Blunt	54.4	50.4	56.3	
Burn	2.1	1.5	2.3	
MAP				0.002
High (>106 mm Hg)	13.7	15.1	13.1	
Normal (65–106 mm Hg)	77.9	74.9	79.2	
Low (<65 mm Hg)	8.4	10.0	7.7	
Heart rate	95 ± 24	97 ± 26	94 ± 23	0.002
Injury Severity Score	13 (8–22)	20 (14–27)	10 (5–17)	<0.001

Values for categorical variables are expressed as percentages; values for continuous variables are presented as means (± standard deviation) or median (interquartile range) as appropriate. GSW, gunshot wound.

Material Command Institutional Review Board reviewed and approved the study protocol.

RESULTS

Demographics and Injury Characteristics

From records of 6,004 unique individual patients surviving to be evacuated out of theater, 4,980 of these were included in the analysis. Patients were excluded for any of the following reasons: (1) missing data for MAP ($n = 438$) or heart rate ($n = 32$), (2) died within 90 days of injury (n = 123) or follow-up less than 90 days after injury ($n = 46$), and (3) previous diagnosis of one of the outcomes of interest ($n = 385$). The characteristics of the patient cohort are described in Table I.

Most injuries occurred during OIF (80.2%) and were among members of the Army (71.7%) or Marines (24.7%). The cohort was predominantly young men (mean age 25.5 ± 6.1 years; males, 98.2%). Blunt force trauma (54.4%) and penetrating (43.5%) injuries were the predominant primary injury mechanisms, most often resulting from an explosion (78.4%). Patients with a TBI were more severely injured as demonstrated by higher ISS (median 20, interquartile range [IQR], 14–27) compared to patients without TBI (median 10, IQR, 5–17). Differences in duty status, military operation, mechanism of injury, and presenting vital signs (MAP and heart rate) were also noted.

Mental Health Risk

The incidence for any disorder was 70.6% when considered as a composite outcome (at least one diagnosis in any category), while diagnosis categories were low-to-modestly correlated (Kendall tau correlation range, −0.09–0.24) (Fig. 1 and Supplementary Material, Appendix Table 2). Post-traumatic stress (46.1%), adjustment (40.9%), and anxiety (37.0%) disorders were the most incident mental health diagnoses (Fig. 1 and Supplementary Material, Appendix Table 3). Cognitive, mood, and schizophrenia/psychotic disorders were diagnosed in 22.1, 33.0, and 2.3% of the cohort, respectively; schizophrenia and psychotic outcomes were rare ($n = 116$).

For most patients, the first mental health diagnosis was documented within the first post-injury year (median months, 3.6; IQR, 1.2–10.6). However, 22.5% of patients received an initial diagnosis beyond 1 year following their injury. The post-injury follow-up period differed when comparing between strata. Patients who sustained a TBI had longer follow-up periods than patients without a TBI (median [IQR], 5.6 [3.0–7.4] vs. 4.3 [2.0–6.9] years; $P < 0.001$). Patients diagnosed with at least one mental health disorder had longer follow-up

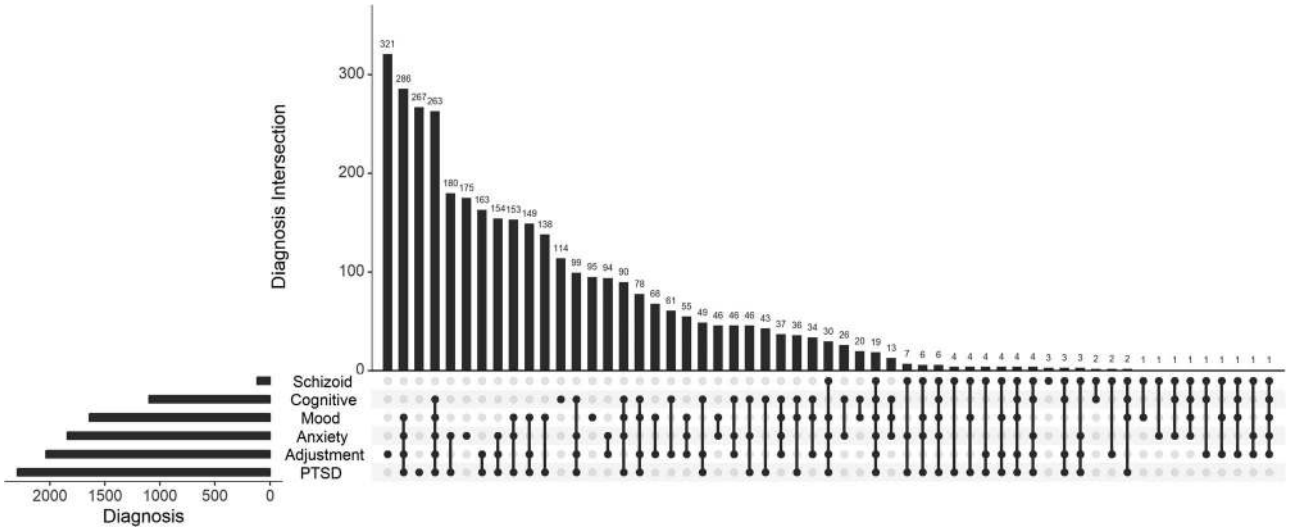

FIGURE 1. Correlation between mental health condition categories.

periods (median [IQR] 5.3 [2.8–7.2], vs. 4.0 [1.5–6.9] years; $P < 0.001$). However, the follow-up period was similar when comparing active duty to reserve members (median [IQR], 5.0 [2.5–7.1] vs. 5.3 [2.2–7.3] years; $P = 0.670$) (Supplementary Material, Appendix Table 4). Incidence of mental health diagnoses was consistently higher (range percent difference 1–24) among patients with TBI exposure when compared to those without TBI (Figure 2).

Generalized Linear Models

In the adjusted logit models, sex was significantly associated with a twofold decreased risk among men (odds ratio [OR] mood disorder 0.48, 95% confidence interval [95% CI, 0.31, 0.73]; anxiety 0.54 [95% CI, 0.35, 0.82]; Supplementary Material, Appendix Table 5). However, no statistically significant association was found for cognitive disorder (OR 0.76 [95% CI 0.45, 1.29]). Similarly, high ISS was associated with a 1.4-fold elevated risk for mood disorder (OR, 1.43 [95% CI, 1.20–1.70]), but was not a significant risk factor for PTSD (OR, 1.02 [95% CI, 0.86–1.20]; Supplementary Material, Appendix Table 5).

Traumatic Brain Injury

The unadjusted risk associated with TBI ranged from an OR of 1.34 (95% CI, 1.19–1.51) for PTSD to an OR of 3.71 (95% CI, 3.23–4.26) for cognitive disorder. The adjusted model estimates were similar but modestly attenuated and ranged from 1.27 OR (95% CI, 1.11–1.45) for anxiety disorder to a 3.24 OR (95% CI, 2.78–3.77) for cognitive disorder (Table II). When considering the Poisson and negative binomial models, TBI was associated with greater frequency of poor mental health outcomes (Poisson incident risk ratio, 1.48 [95% CI, 1.41–1.63]; negative binomial incident risk ratio, 1.52 [95% CI, 1.42–1.63]).

TABLE II. Adjusted Odds Ratio for Mental Health Outcome-Associated Categories, TBI vs. No TBI

	TBI			
	OR	95% CI	p	*P* (BH Corrected)
PTSD	1.35	1.18–1.54	<0.001	<0.001
Adjustment	1.39	1.21–1.58	<0.001	<0.001
Anxiety	1.27	1.11–1.45	0.001	0.0012
Cognitive	3.24	2.78–3.77	<0.001	<0.001
Mood	1.40	1.22–1.60	<0.001	<0.001
Schizophrenia and psychotic	1.07	0.71–1.61	0.74	0.74

BH, Benjamini-Hochberg.

DISCUSSION

Primary Findings

Our study examines the largest cohort of patients who have sustained severe physical injury in combat ($n = 4{,}980$) to determine the onset of their long-term mental health conditions for several years following injury, across the arc of clinical care delivered in hospitals, emergency departments, psychiatric and rehabilitation facilities, and outpatient settings. It also includes membership from the four service branches—Army, Navy, Marines Corps, and Air Force—who sustained moderate or severe TBI in combat. In our cohort of military personnel who were severely injured in combat, we found that most patients (70.6%) were diagnosed with at least one mental health disorder during the multi-year follow-up period (median years, 4.1). The unique risk—as represented by odds ratios and incidence rate ratios—for five mental health diagnosis categories was consistently greater among patients who sustained a TBI.

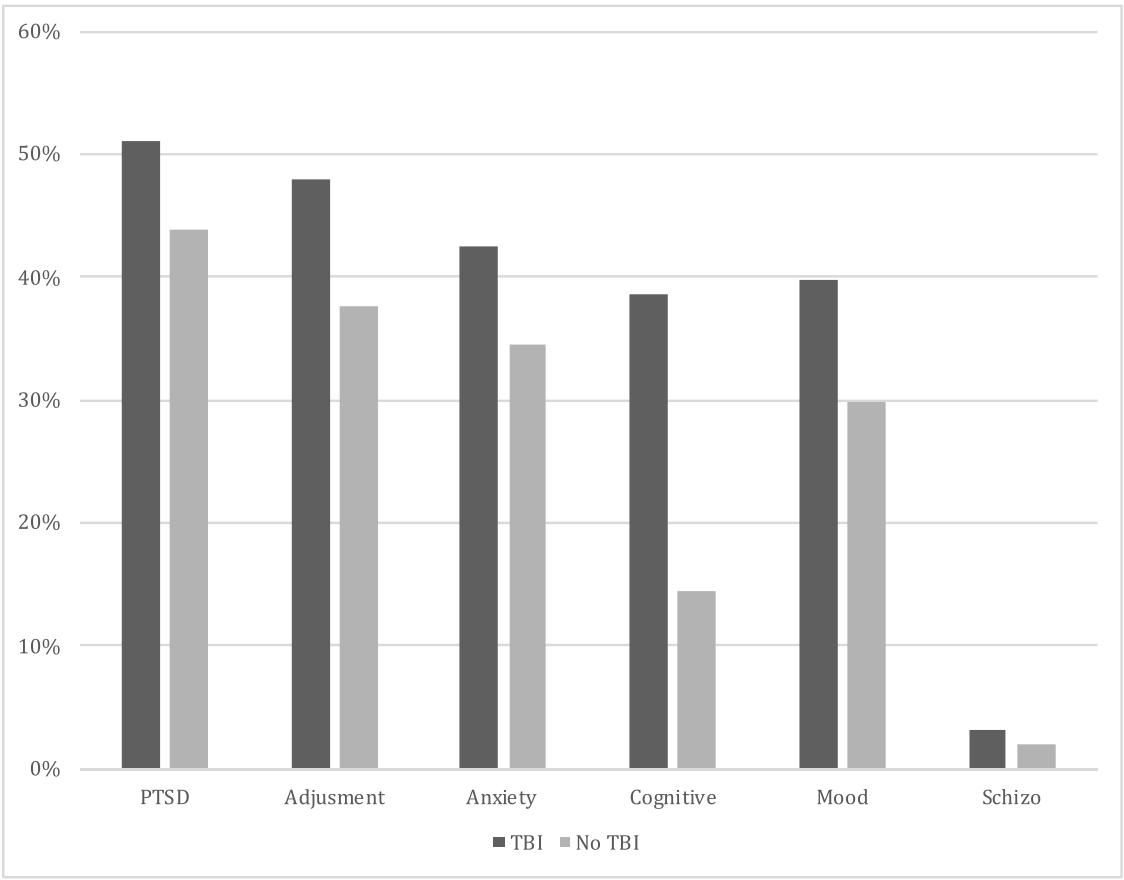

FIGURE 2. Incident mental health diagnosis category stratified by TBI exposure.

Our study focused on the incidence of mental health conditions in service personnel who sustained severe physical trauma in combat for several reasons. First, little is known about the effect of severe physical injury, particularly moderate to severe TBI on mental health diagnoses among combat-injured service members. Second, most studies of mental health among military personnel have captured outcomes occurring only within the first post-exposure year,[2,14,15] with little evidence on the incidence of conditions diagnosed after longer intervals. Third, most studies of the mental health outcomes among military members only included one service branch.[5,38–40] In contrast, our study is the largest longitudinal cohort of military service members from four services branches who sustained severe injuries in combat.

Context and Comparability

The definition of incident mental health conditions varied widely among prior studies that examined the association between mental health and moderate and severe TBI in U.S. veterans who served in OEF/OIF/OND.[38,41] Several studies focused primarily on the effect of combat deployment on PTSD[42,43] or suicide risk,[5] without examining the risk contributed by physical trauma.[5,42] Only one reported the health-related quality of life—a complex composite outcome measure that incorporates physical, mental, emotional, and social functioning—as the primary outcome measure.[31] None have reported comparable outcome measures. In contrast, several investigators have examined the impact of mild TBI,[15,23,25,28,44] but these studies vary widely in design, population, and result. For example, one study that was underpowered did not detect an effect of mild TBI on PTSD or cognitive outcome measures.[44] Earlier investigators have posited PTSD could not develop following TBI because of impaired consciousness at the time of trauma;[45] this may have precluded encoding of the traumatic experience and prevented trauma memories that are necessary for PTSD development.[45] Our findings, which illustrate a relationship between moderate and severe TBI and greater risk for PTSD, extend previous studies of comorbidities associated with mild TBI exposures.[15,23]

Our PTSD incidence estimate (46.1%) was similar to one previous investigation (43.9%),[15] but was notably higher when compared to several previous studies (22%–29.4%)[46,47] and a large meta-analysis (23%),[48] and substantially higher than previously reported among veterans of the wars in Afghanistan (7.1%) and Iraq (12.9%).[49] Our finding that service personnel received at least one mental health diagnosis (70.6%) was also considerably higher than previously reported (42%)[47] even though our mental health diagnoses

were defined more narrowly and substantially higher when compared to a study of TBI-associated psychiatric disorders occurring 3 months after deployment (12.9%).[50] Similarly, we found the incidence of anxiety (37.0%) was higher than previous reports (11%).[47] Consistent with previous studies,[51] the relationship between TBI and schizophrenia or other psychotic conditions was not significant.

However, several important differences should be considered when comparing our results to those of previous studies. Our work examined critically injured patients and had longer follow-up times. Clinical outcomes have been reported for hypertension and diabetes for this cohort, but this study emphasizes new mental and cognitive health diagnoses following injury; our findings suggest that critically injured combat casualties have particularly high rates of mental health disorders. Furthermore, these diagnoses may be delayed, which suggests that surveillance should continue well after the injury.

Our findings that women are at greater risk for a diagnosis of post-traumatic stress (OR 1.51; 95% CI 0.99–2.31), adjustment (OR 1.63; 95% CI 1.07–2.49), and mood disorders (OR 2.02; 95% CI 1.33–3.07) are consistent with several previous studies[41,52,53] and a meta-analysis which found women had greater PTSD risk (OR 1.63).[54] However, this effect may be attributable to differences in the prevalence of sexual abuse[55] or lower cohesion within military units.[56] While a recent study from the Millennium Cohort found no significant gender differences after propensity score adjustment, our findings suggest that gender differences may persist in service members that were severely injured in combat.[43]

Limitations

We could not obtain information on military personnel who were deployed into combat but not injured or for non-deployed personnel; thus, we could not separate the contribution to mental health risk attributable to non-injury or combat deployment. Demographic data were not available for social determinants of health such as economics, family or community support, service member rank, and educational attainment, which may contribute to mental health risk directly or through an indirect pathway. Health records were only available for clinical encounters that occurred within a DoD health care facility or were reimbursed by Tricare; encounters with other health care providers were not included in our analyses. Examining a longer follow-up period (median 4.1 years) to capture late mental health diagnoses may also increase the potential for effects from non-injury or nonmilitary exposures occurring after discharge from active duty status. It is also important to acknowledge that between demographic groups, comparisons (eg, gender, ethnicity minorities) have reported experiential differences[57] that we could not examine.

Implications

Our finding of the high incidence of mental health conditions in critically injured combat casualties, particularly those with TBI, may have implications for many stakeholders. Policymakers may consider the potential for undetected long-term mental health disability, particularly among patients receiving late diagnoses. Clinicians and health system administrators may consider opportunities to augment long-term follow-up, monitoring of mental health status, and patient education. Patients who have sustained a combat injury and their family members may be prepared to recognize mental health sequelae and anticipate future behavioral health care needs while considering potential stigma associated with mental health diagnosis and treatment in the military[57]. Previous studies that described the importance of military culture when caring for service members[58] may be extended to interpret these research findings. Future investigations are needed to partition the risk components attributable to physical injury vs. the psychological experience of the injury event through convalescence.

SUPPLEMENTARY DATA

Supplementary data are available at *MilMed* online.

AUTHORS CONTRIBUTIONS

D.L.C. and J.E.Z. provided substantial contributions to the design, acquisition, analysis, or interpretation of the work, revised it critically for important intellectual content, and approved the final version.

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