https://doi.org/10.5664/jcsm.9530

JCSM | Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Obstructive sleep apnea among survivors of combat-related traumatic injury: a retrospective cohort study

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Study Objectives: Obstructive sleep apnea is prevalent among military members despite fewer traditional risk factors. We sought to determine the incidence and longitudinal predictors of obstructive sleep apnea in a large population of survivors of combat-related traumatic injury and a matched control group.

Methods: Retrospective cohort study of military service members deployed to conflict zones from 2002–2016 with longitudinal follow-up in the Veterans Affairs and Military Health Systems. Two cohorts of service members were developed: (1) those who sustained combat injuries and (2) matched, uninjured participants.

Results: 17,570 service members were retrospectively analyzed for a median of 8.4 years. After adjustment, traumatic brain injury (hazard ratio [HR] 1.39, 95% confidence interval [CI] 1.20–1.60), posttraumatic stress disorder (HR 1.24, 95% CI 1.05–1.46), depression (HR 1.52, 95% CI 1.30–1.79), anxiety (HR 1.40, 95% CI 1.21–1.62), insomnia (HR 1.71, 95% CI 1.44–2.02), and obesity (HR 2.40, 95% CI 2.09–2.74) were associated with development of obstructive sleep apnea. While combat injury was associated with obstructive sleep apnea in the univariate analysis (HR 1.25, 95% CI 1.17–1.33), the direction of this association was reversed in the multivariable model (HR 0.74, 95% CI 0.65–0.84). In a nested analysis, this was determined to be due to the effect of mental health diagnoses.

Conclusions: The incidence of obstructive sleep apnea is higher among injured service members (29.1 per 1,000 person-years) compared to uninjured service members (23.9 per 1,000 person-years). This association appears to be driven by traumatic brain injury and the long-term mental health sequelae of injury.

Keywords: sleep apnea, insomnia, trauma, veterans, TBI, traumatic injury, PTSD, injury

Citation: Haynes ZA, Stewart IJ, Poltavskiy EA, et al. Obstructive sleep apnea among survivors of combat-related traumatic injury: a retrospective cohort study. *J Clin Sleep Med*. 2022;18(1):171–179.

BRIEF SUMMARY

Current Knowledge/Study Rationale: The relationship between obstructive sleep apnea and traumatic injuries is poorly defined. Traumatic brain injury has been associated with sleep disorders including obstructive sleep apnea, though studies have been limited in size and duration and there are no data examining other injury mechanisms and their relationship with obstructive sleep apnea.

Study Impact: This study bridges that gap by examining the relationship between specific types of trauma and obstructive sleep apnea while also exploring other potential risk factors for the disease within survivors of traumatic injury. This may serve to identify veterans at higher risk of developing obstructive sleep apnea who may benefit from more structured and thorough sleep medicine evaluation.

INTRODUCTION

The US military population has a high prevalence of obstructive sleep apnea (OSA) despite being a generally young, healthy, and physically fit population.[1–3] The prevalence of OSA among service members (SMs) is highest within the Army (12.15%), followed by the Air Force (9.96%) and Navy (9.06%).[4] High rates of OSA have been found following deployment, particularly among SMs with comorbid posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI).[5] SMs with OSA and PTSD have high rates of comorbid insomnia, poor adherence to continuous positive airway pressure, and reduced response to treatment.[6–8] The presence of comorbid insomnia also has a negative impact on patient outcomes.[6,7] Additionally, there is mounting evidence that patients with OSA are admitted to hospitals more frequently and have a greater utilization of health-care resources in the years preceding their diagnosis, when compared to patients without OSA.[9–11] Overall, OSA places a significant effect on the Veterans Affairs (VA) and Military Health Systems (MHS), but the factors leading to its high prevalence are incompletely understood.

SMs receive continuous care within the MHS for the duration of their active-duty service. Following separation from the service, many are eligible for continued (in some cases lifelong) care through both the MHS and VA.[12] This combined network of care allows for analysis of robust long-term outcome data that are often not available in civilian health-care systems.[13]

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OSA diagnoses in the MHS have surged by over 500% since the onset of the recent military conflicts in Iraq and Afghanistan.[14] Traumatic injuries were common in these conflicts and have previously been demonstrated to increase lifetime risk for chronic medical conditions, including diabetes, hypertension, and kidney disease, with increasing injury severity leading to further increased risk, as well as mental health disorders.[15–17] Similarly, we hypothesized that traumatic injuries could also increase the risk for developing OSA. Given the lack of data on the development of OSA among survivors of combat-related traumatic injury, we conducted a longitudinal analysis to evaluate the incidence of OSA among SMs with combat-related traumatic injuries, while also examining for associated risk factors within this population.

METHODS

This was a retrospective cohort study of US military SMs deployed to Iraq or Afghanistan. The David Grant US Air Force Medical Center Institutional Review Board (IRB FDG20160014H) and the Research Review Committee of the VA Salt Lake City Health Care System (IRB 00091744) approved this study.

Cohort development

Two cohorts were derived for this study: (1) SMs who deployed to a combat zone and experienced a traumatic injury and (2) SMs who deployed and were not injured. We did not include a third nondeployed control cohort as these individuals tend to have baseline health comorbidities which prevent them from deploying overseas.[18] A random sample of 10,000 SMs who experienced traumatic injuries while deployed in Afghanistan or Iraq from February 1, 2002, to June 14, 2016, was used to build the injured cohort and these dates served as the study's start and end date. Their data were obtained from the Department of Defense Trauma Registry (DoDTR), a database used to document traumatic injuries to SMs while deployed in a combat zone severe enough to require hospital admission. All SMs enrolled in DoDTR at the time (n = 18,292) were eligible to be selected in our random sample. Randomization was done using SAS PROC SURVEYSELECT (without replacement). Selected individuals were matched 1:1 for birth year (± 1 year), military branch (Army, Navy, Marines, Air Force, and Coast Guard), and sex to create the noninjured cohort utilizing the VA/Department of Defense Identity Repository. Participants in the noninjured cohort had neither a documented traumatic injury in DoDTR, nor were they medically separated from military service for combat-related injuries.

Participants were excluded if they could not be matched, died within 90 days of index, did not have documented encounters during the study period or after their index date, had a preexisting OSA diagnosis, or were missing data on variables of interest (race/ethnicity, rank, marital status, Injury Severity Score [ISS]). Index dates for injured participants were the date of their traumatic injury and their matched, noninjured counterparts were assigned the same index date to create parallel study entry times. Participants were followed until they were diagnosed with OSA, died, or were lost to follow-up or the study period ended.

Data collection and organization

Longitudinal data to complete participants' data profiles were obtained from several sources. Birth year, military branch, rank, and sex information were obtained from DoDTR for the injured participants and VA/Department of Defense Identity Repository for the noninjured participants. Coast Guard participants in both cohorts were pooled with the Navy for analysis due to a small sample size. Rank was categorized into officer, senior enlisted, and junior enlisted to be a surrogate for socioeconomic status. Race/ethnicity information was extracted primarily from the Defense Manpower Data Center. If missing in Defense Manpower Data Center, it was derived sequentially from VA/Department of Defense Identity Repository and then the Military Health System Data Mart. Injury subtypes, mechanisms, and ISS were retrieved from DoDTR. ISS is a validated quantitative measure of injury severity with scores ranging from 1 to 75.[19] The ISS score is associated with post–trauma-related outcomes (hospitalization, morbidity, and mortality) with increasing scores indicating more severe injury and a score higher than 15 points defining major trauma.[20] Mortality data were obtained from the Joint VA-DoD Suicide Data Repository National Death Index.[21] Marital status and tobacco use data were obtained from the Military Health System Data Mart. Diagnostic codes for both cohorts were obtained from the Military Health System Data Mart and the Veterans Informatics and Computing Infrastructure.

Outcomes and covariates

Participants were identified as having the outcome of OSA if they had at least two outpatient encounters within 90 days of each other or one inpatient discharge diagnosis documenting an International Classification of Diseases 9th or 10th Revision Clinical Modification diagnosis code for OSA (327.23, 780.51, 780.53, 780.57, G47.30, G47.33, or G47.39). This was based upon the Armed Forces Health Surveillance Branch case definition for OSA and previously published case definition methods for other chronic medical conditions.[22–24]

We monitored for the development of OSA longitudinally through retrospective review of the data in relation to the presence of covariates, including age (at index date), obesity (overweight, obesity, morbid obesity), PTSD, anxiety disorders (generalized anxiety disorder, panic, phobic, and obsessive-compulsive disorders), depression (major depression, dysthymia, and other persistent mood disorders), insomnia, tobacco use, alcohol dependence/abuse, and opioid dependence/abuse, in addition to the injury subtypes of TBI, burn, and amputation. These covariates were chosen because they are either established risk factors for OSA or are prevalent among survivors of traumatic injury and could be seen as potential confounders in our analysis. The noninjured cohort did contain some participants with documented injuries (TBI, burn, and amputations) that occurred following deployment or that were not severe enough to require admission to a hospital in theater. Armed

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Forces Health Surveillance Branch case definitions were used to define obesity, PTSD, anxiety disorders, depression, tobacco use, alcohol dependence/abuse, and opioid dependence/abuse.[24] Injury subtypes (TBI, amputation, and burn) were defined based on the presence of corresponding International Classification of Diseases 9th or 10th Revision Clinical Modification codes in the medical record. For the injured cohort, relevant International Classification of Diseases 9th or 10th Revision Clinical Modification codes were obtained from the DoDTR. For the noninjured cohort, diagnosis codes were obtained from the Military Health System Data Mart and the Veterans Informatics and Computing Infrastructure. Outcomes occurring after June 14, 2016 (the date of our IRB approval), were not collected.

Statistical analysis

Categorical variables were compared using a chi-squared test and are presented as frequencies and percentages. Continuous variables are compared through the use of Wilcoxon rank-sum tests and are displayed as medians with interquartile ranges (IQRs). Cumulative incidence functions were used to graphically represent the data. Primary analyses utilized Fine and Gray competing risk models to account for the competing risk of death for the outcome of OSA.[25] To check the linearity and proportional hazards assumptions, we used the Martingale-based supremum test for functional form and for proportional hazard assumptions. Mental health disorders, alcohol dependence/abuse, opioid dependence/abuse, obesity, and insomnia were analyzed as time-dependent covariates. Statistical analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Of the 10,000 participants randomly selected from DoDTR, 9,654 could be matched to noninjured participants. Of these matched pairs, 138 were excluded for death within 90 days, 64 for no encounter within the study period, 578 for no encounter after the index date, 60 for a preexisting diagnosis of OSA, and 29 for missing variables of interest. This left 8,785 matched pairs for a total n = 17,570.

Participants were predominantly male (98.0%) with a median age at index of 24 (IQR 22–29) years (**Table 1**). In the injured cohort, there were more non-Hispanic White participants (75.9% vs 71.8%) and fewer non-Hispanic Black participants (8.5% vs 12.8%). Junior enlisted SMs were the most widely represented rank in both cohorts, though a greater proportion was seen in the noninjured cohort (65.6% vs 58.5%). The median follow-up time after index date was 8.4 years (IQR 5.3–10.6), which was significantly different ($P < .001$) between the injured (8.8, IQR 5.7–10.8) and noninjured (7.8, IQR 4.9–10.4) cohort. Median ISS in the injured cohort was 6 (IQR 2–13), consistent with mild traumatic injury. A greater proportion of participants in the injured cohort were overweight/obese compared to the noninjured cohort (36.5% vs 32.3%, $P < .001$).

The incidence of OSA was found to be higher in injured SMs when compared to noninjured SMs (29.1 vs 23.9 per 1,000 person-years, respectively). In univariate models (**Table 2**), participants with traumatic injury (hazard ratio [HR] 1.25, 95% confidence interval [CI] 1.17–1.33, $P < .001$), TBI (HR 1.74, 95% CI 1.59–1.90, $P < .001$), burns (HR 1.50, 95% CI 1.15–1.96, $P = .003$), amputations (HR 1.78, 95% CI 1.47–2.16, $P < .001$), insomnia (HR 2.63, 95% CI 2.29–3.01, $P < .001$), obesity (HR 2.68, 95% CI 2.38–3.02, $P < .001$), PTSD (HR 2.08, 95% CI 1.88–2.30, $P < .001$), depression (HR 2.34, 95% CI 2.10–2.61, $P < .001$), anxiety (HR 2.17, 95% CI 1.94–2.42, $P < .001$), and alcohol dependence/abuse (HR 1.55, 95% CI 1.37–1.76, $P < .001$) had a significantly greater risk for OSA. Some differences in race/ethnicity were also noted with non-Hispanic Blacks (HR 1.28, 95% CI 1.12–1.46, $P < .001$) and other/multiracial participants (HR 1.84, 95% CI 1.22–2.79, $P = .004$) having a higher risk of OSA compared to non-Hispanic Whites. When compared to junior enlisted SMs, senior enlisted (HR 1.16, 95% CI 1.02–1.31, $P = .019$) had a higher risk of OSA, while officers (HR 0.77, 95% CI 0.63–0.94, $P = .009$) had a lower risk. Furthermore, married SMs (HR 1.44, 95% CI 1.30–1.61, $P < .001$) had a higher risk compared to single SMs and reserve/guard SMs (HR 0.54, 95% CI 0.48–0.61, $P < .001$) had a lower risk compared to active-duty SMs. Tobacco users (HR 1.48, 95% CI 1.31–1.67, $P < .001$) were more likely to develop OSA compared to nonusers.

The results of the multivariable analysis are presented in **Table 2**. In this model, marital status (HR 1.16, 95% CI 1.02–1.33, $P = .026$ for married compared to single SMs), military status (HR 0.67, 95% CI 0.57–0.77, $P < .001$ for reserve/guard compared to active-duty SMs), obesity (HR 2.40, 95% CI 2.09–2.74, $P < .001$), insomnia (HR 1.71, 95% CI 1.44–2.02, $P < .001$), PTSD (HR 1.24, 95% CI 1.05–1.46, $P = .010$), depression (HR 1.52, 95% CI 1.30–1.79, $P < .001$), anxiety (HR 1.40, 95% CI 1.21–1.62, $P < .001$), and TBI (HR 1.39, 95% CI 1.20–1.60, $P < .001$) remained significant for the subsequent development of OSA after adjustment. With respect to rank, officers (HR 1.04, 95% CI 0.81–1.34, $P = .75$) were not more likely to develop OSA compared to junior enlisted, after adjustment. However, senior enlisted SMs continued to be at higher risk in the multivariable model (HR 1.20, 95% CI 1.03–1.40, $P = .02$). Tobacco users (HR 1.27, 95% CI 1.09–1.47, $P = .002$) were more likely to develop OSA compared to nontobacco users, after adjustment. Race/ethnicity, alcohol dependence/abuse, amputation, and burn injury lost significance in the multivariable model.

While combat injury was associated with the development of OSA in the univariate analysis, SMs with combat injury were less likely to develop OSA in the multivariable model (HR 0.74, 95% CI 0.65–0.84, $P < .001$). Similar results were seen for opioid dependence/abuse, which was not significant in the univariate model (HR 1.15, 95% CI 0.89–1.48, $P = .300$) but was in the multivariable model (HR 0.62, 95% CI 0.45–0.85, $P = .003$). To further elucidate this relationship, we performed post hoc nested models (**Table S1** in the supplemental material). These models demonstrated that the associations between injury and opioid dependence with OSA reversed when mental health outcomes (PTSD, anxiety disorders, and depression) were introduced into the models.

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Table 1—Demographic, injury, and health characteristics of participants.

	Total (n = 17,570)	Injured Cohort (n = 8,785)	Noninjured Cohort (n = 8,785)	*P*
Male	17,222 (98.0%)	8,611 (98.0%)	8,611 (98.0%)	1.000
Age,* median (IQR), y	24 (22–29)	24 (22–29)	24 (22–29)	.446
Race/ethnicity				<.001
NH White	12,979 (73.9%)	6,668 (75.9%)	6,311 (71.8%)	
NH Black	1,876 (10.7%)	749 (8.5%)	1,127 (12.8%)	
Hispanic	1,840 (10.5%)	932 (10.6%)	908 (10.3%)	
Asian/PI	577 (3.3%)	288 (3.3%)	289 (3.3%)	
Other/multi	298 (1.7%)	148 (1.7%)	150 (1.7%)	
Rank				<.001
Junior enlisted	10,906 (62.1%)	5,143 (58.5%)	5,763 (65.6%)	
Senior enlisted	5,406 (30.8%)	3,062 (34.9%)	2,344 (26.7%)	
Officer	1,258 (7.2%)	580 (6.6%)	678 (7.7%)	
Married	8,372 (47.7%)	4,317 (49.1%)	4,055 (46.2%)	<.001
Military branch				1.000
Army	12,904 (73.4%)	6,452 (73.4%)	6,452 (73.4%)	
Navy	492 (2.8%)	246 (2.8%)	246 (2.8%)	
Air Force	312 (1.8%)	156 (1.8%)	156 (1.8%)	
Marine Corps	3,862 (22.0%)	1,931 (22.0%)	1,931 (22.0%)	
Burn	939 (5.3%)	929 (10.6%)	10 (0.1%)†	<.001
Amputation	1,141 (6.5%)	1,128 (12.8%)	10 (0.1%)†	<.001
TBI	8,529 (49.5%)	6,577 (74.9%)	1,952 (22.2%)†	<.001
Insomnia	4,631 (26.4%)	3,238 (36.9%)	1,393 (15.9%)	<.001
OSA	3,558 (20.3%)	2,014 (22.9%)	1,544 (17.6%)	<.001
Tobacco use				<.001
Yes	5,397 (30.7%)	3,003 (34.2%)	2,394 (27.3%)	
No	5,682 (32.3%)	2,695 (30.7%)	2,987 (34.0%)	
Unknown	6,491 (36.9%)	3,087 (35.1%)	3,404 (38.8%)	
PTSD	9,755 (55.5%)	6,123 (69.8%)	3,623 (41.2%)	<.001
Anxiety disorders	7,900 (45.0%)	4,706 (53.6%)	3,194 (36.4%)	<.001
Depression	8,447 (48.1%)	4,888 (55.6%)	3,559 (40.5%)	<.001
Opioid dependence	966 (5.5%)	682 (7.8%)	284 (3.2%)	<.001
Alcohol dependence	4,681 (26.6%)	2,550 (29.0%)	2,131 (24.3%)	<.001
Encounters per year, mean (SD)	18.3 (25.4)	27.3 (29.9)	9.3 (15.3)	<.001

Values are n (%) unless otherwise indicated. *At index date. †Participants in the noninjured cohort could not have been injured severely enough to require admission to a theater hospital, but less severe wartime injuries or injuries incurred during longitudinal follow-up were observed. IQR = interquartile range, NH = non-Hispanic, OSA = obstructive sleep apnea, PI = Pacific Islander, PTSD = posttraumatic stress disorder, SD = standard deviation, TBI = traumatic brain injury.

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The variables in our analysis did not strictly adhere to the assumption of proportionality when examined with the Martingale-based supremum tests. On visual inspection of cumulative incidence functions, it is clear that OSA incidence increased at a greater rate over time for individuals with any mental health diagnosis (**Figure 1**), TBI (**Figure 2**), and insomnia (**Figure 3**), compared to individuals without mental health diagnosis, TBI, and insomnia, respectively. Thus, the reported HRs represent a conservative estimate of the mean risk differential between comparison groups over the observation period since the risk difference exceeds the overall HR after 8 years of follow-up.

DISCUSSION

We present the first longitudinal study of OSA incidence and associated risk factors within a large cohort of combat-related

Table 2—Univariate and multivariable models for obstructive sleep apnea.

	Univariate		Multivariable	
	Hazard Ratio (95% CI)	*P*	Hazard Ratio (95% CI)	*P*
Age*	1.03 (0.96–1.12)	.409	1.11 (1.00–1.23)	.053
Injured cohort†	1.25 (1.17–1.33)	<.001	0.74 (0.65–0.84)	<.001
Race/ethnicity				
NH White	Reference	—	Reference	—
NH Black	1.28 (1.12–1.46)	<.001	1.19 (1.00–1.41)	.055
Hispanic	1.12 (0.96–1.31)	.148	0.94 (0.77–1.14)	.504
Asian/PI	1.04 (0.81–1.35)	.751	1.00 (0.73–1.39)	.982
Other/multi	1.84 (1.22–2.79)	.004	1.71 (1.00–2.94)	.051
Rank				
Junior enlisted	Reference	—	Reference	—
Senior enlisted	1.16 (1.02–1.31)	.019	1.20 (1.03–1.40)	.023
Officer	0.77 (0.63–0.94)	.009	1.04 (0.81–1.34)	.755
Marital status				
Single	Reference	—	Reference	—
Married	1.44 (1.30–1.61)	<.001	1.16 (1.02–1.33)	.026
Military status				
Active	Reference	—	Reference	—
Reserve/Guard	0.54 (0.48–0.61)	<.001	0.67 (0.57–0.77)	<.001
Tobacco use				
No	Reference	—	Reference	—
Yes	1.48 (1.31–1.67)	<.001	1.27 (1.09–1.47)	.002
Unknown	0.85 (0.75–0.95)	.006	0.78 (0.67–0.91)	.001
Obesity**	2.68 (2.38–3.02)	<.001	2.40 (2.09–2.74)	<.001
Insomnia**	2.63 (2.29–3.01)	<.001	1.71 (1.44–2.02)	<.001
PTSD**	2.08 (1.88–2.30)	<.001	1.24 (1.05–1.46)	.010
Depression**	2.34 (2.10–2.61)	<.001	1.52 (1.30–1.79)	<.001
Anxiety**	2.17 (1.94–2.42)	<.001	1.40 (1.21–1.62)	<.001
Opioid abuse/dependence**	1.15 (0.89–1.48)	.300	0.62 (0.45–0.85)	.003
Alcohol Abuse/ dependence**	1.55 (1.37–1.76)	<.001	1.09 (0.93–1.29)	.297
TBI (yes vs no)	1.74 (1.59–1.90)	<.001	1.39 (1.20–1.60)	<.001
Amputation (yes vs no)	1.78 (1.47–2.16)	<.001	1.26 (0.99–1.62)	.061
Burn injury				
No burn	Reference	—	Reference	—
Burn only	1.50 (1.15–1.96)	.003	1.08 (0.77–1.52)	.667
Burn + IH	1.07 (0.64–1.79)	.793	0.68 (0.34–1.34)	.264

*At index date. **Time-dependent covariates. †Compared to noninjured participants. IH = inhalation injury, NH = non-Hispanic, OSA = obstructive sleep apnea, PI = Pacific Islander, PTSD = posttraumatic stress disorder, TBI = traumatic brain injury.

traumatic injury survivors. Although the incidence rates of OSA among SMs who experienced traumatic injury were higher than those that did not (29.1 vs 23.9 per 1,000 person-years, respectively), our data suggest that the risk of OSA is primarily driven by comorbid medical and psychiatric sequelae following traumatic injury rather than the injury itself. When we evaluated specific types of injury, TBI predicted development of OSA, similar to other military and civilian populations.[5,26–28] The incidence rate of OSA with TBI was 33.6 per 1,000 person-years, compared to 19.8 per 1,000 person-years for those without TBI. No other type of injury (amputation or burn) was significantly associated with developing OSA after adjustment, though the risk of OSA was significantly increased within SMs with mental health disorders.

The relationship between trauma and OSA is complex. When examining the relationship between injury and OSA in

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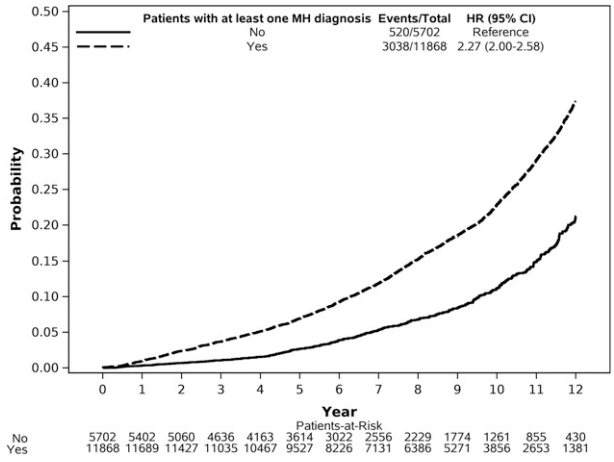
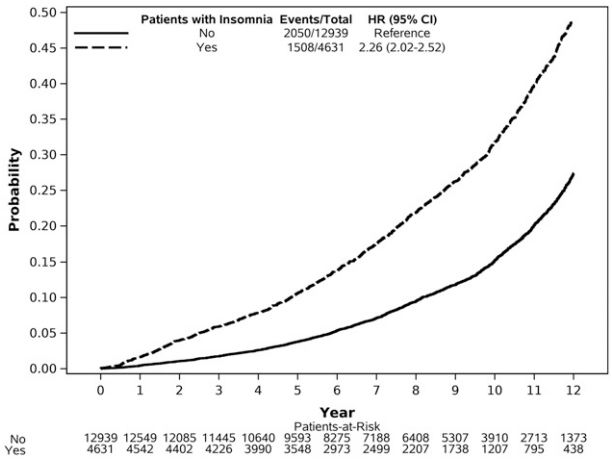
Figure 1—Cumulative incidence function for the development of obstructive sleep apnea stratified by the presence of any mental health diagnosis (PTSD, anxiety, or depression).



CI = confidence interval, HR = hazard ratio, MH = mental health, PTSD = posttraumatic stress disorder.

Figure 3—Cumulative incidence function for the development of obstructive sleep apnea stratified by insomnia status.

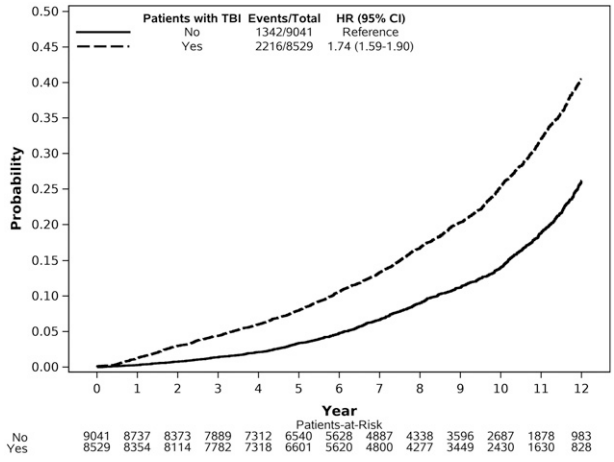


CI = confidence interval, HR = hazard ratio.

our nested multivariable models, the relationship reversed with the introduction of mental health disorders (**Table S1**). Similar findings were seen with opioid dependence/abuse. This implies that these variables serve more as a proxy for patients at greater risk for mental health diagnoses, and thus the subsequent development of OSA. This can be inferred as the relationships shifted after the impact of mental health diagnoses was added to the multivariable model and was maintained in the final, fully adjusted model.

The long-term effects of combat-related traumatic injuries continue to be discovered, but many survivors have developed

Figure 2—Cumulative incidence function for the development of obstructive sleep apnea stratified by TBI status.



CI = confidence interval, HR = hazard ratio, TBI = traumatic brain injury.

psychiatric diagnoses, including PTSD.[18] Previous evidence on mental health outcomes within our cohort have corroborated this, showing that traumatic injuries significantly increase the risk of developing a mental health disorder.[29] Similarly, we identified a high prevalence of all comorbid psychiatric disorders examined in our injured cohort. Our analysis suggests that these disorders are the underlying driving force for the development of OSA in participants with traumatic injuries, as they attenuated the relationship between injury and OSA when they were introduced into our nested models (**Table S1**). Although our data do not suggest that all traumatic injuries are a direct precipitating factor for OSA, they do highlight these downstream effects from injuries and their potential for impacting long-term outcomes. Psychiatric comorbidities commonly develop after traumatic injuries, with up to 26% of survivors developing PTSD and 15% being diagnosed with major depressive disorder in prior studies.[30,31] Our injured cohort saw an even greater proportion of participants with mental health disorders, with 69.8% developing PTSD and 55.6% experiencing depressive disorders, in addition to 53.6% being diagnosed with an anxiety disorder. The increased prevalence may also be due, in part, to the high proportion of TBI in our study, as the odds of developing a psychiatric diagnosis in this population have been previously shown to double after injury.[32] The increased prevalence is particularly concerning when considering the possibility of the coexistence of TBI and a mental health disorder. Our population displayed a 39% increased risk of OSA attributed to TBI independent of a psychiatric diagnosis and all psychiatric diagnoses examined were independently associated with OSA as well.

During the time when our study population served, 53,119 US SMs experienced life-threatening traumatic injuries.[33] Many were due to high-energy explosive munitions and complicated by TBI, burns, and amputations.[34] As we examined

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specific injury mechanisms in our analysis, we identified that TBI is an independent risk factor for developing OSA after adjusting for mental health disorders, obesity, and participant demographics. This may be due to the high-energy mechanisms of TBIs, which can lead to direct neuronal damage via focal compression, concussion forces, and high-pressure shock waves.[35] This damage may interfere with the mechanisms of respiration and arousal and promote disease development; however, animal models of TBI have not identified these specific abnormalities.[28] Further research into the specific neurophysiological mechanisms of OSA after TBI is warranted to optimize medical management decisions and to guide the development of future advanced therapies for this subset of patients.

We also found that the presence of an insomnia diagnosis significantly increased a participant's risk of developing OSA in our cohorts, demonstrating an HR = 1.71 after controlling for confounding variables. Prior research has demonstrated similar relationships.[7] The incidence of OSA in SMs with insomnia was 42.9 per 1,000 person-years, compared to 20.8 per 1,000 person-years in SMs without insomnia. Median time from insomnia to OSA diagnosis was 927 (IQR 318–2057) days (**Table S2** in the supplemental material). This relationship highlights the importance of insomnia in our population and suggests that the presence of insomnia promotes the development of OSA. The effect of insomnia on OSA development is likely multifactorial. Sleep deprivation and fragmentation, as seen in insomnia, can destabilize nocturnal breathing and promote OSA, likely through the induction of upper airway collapse.[36] It is also possible that sleep difficulties related to insomnia increase the likelihood of referral to a sleep clinic, which in turn affects the likelihood of a patient undergoing polysomnography and being given an OSA diagnosis.

Our findings hold value for providers beyond the MHS. The introduction of the Veteran's Choice Program in 2014 allowed for veterans living a long distance from a VA medical center to be seen by civilian providers, subsequently increasing the number of US veterans being seen within civilian centers.[37] There is also added relevance for understanding sleep disorders among civilian trauma survivors, a group often challenged by an inability to achieve adequate statistical power longitudinally due to loss to follow-up and fragmented health care.[38] Finally, psychiatric disease and insomnia are prevalent in civilian populations, and our findings suggest that clinicians should consider testing for OSA in the presence of these diagnoses.

Limitations

Our study has some limitations, predominantly due to its retrospective, observational design. Although we present data collected over 14 years, adequate time for thorough diagnostic evaluation and clinical follow-up, it may be inadequate to give an accurate portrayal of how rates of a chronic disease like OSA increase with advancing age. As rates of OSA rise in prevalence with age, more participants in both cohorts would likely be diagnosed, which might impact our findings. Given our reliance on coded diagnostic data from the electronic medical record, we did not have results of polysomnography or continuous positive airway pressure adherence and therefore we were unable to assess the impact of OSA severity and treatment adherence. OSA studies in other military populations have revealed a high prevalence of mild disease generated by elevated polysomnography referral rates, but this continues to be of uncertain clinical significance.[39,40] Additionally, the study population was nearly all young males with consistent access to health care, which may limit these data's generalizability and may have facilitated an increase in the number of diagnoses. This is particularly true for wounded SMs who commonly undergo broad multispecialty evaluations, including for behavioral health and sleep disorders. An increase in diagnoses among wounded SMs may be due to the bias of diagnostic momentum (once a patient has a diagnosis in the record, there is a tendency for future providers to add additional diagnoses to the record that they might have otherwise considered only possibilities). We also saw a relatively high prevalence of TBI within our noninjured cohort (22.2%) and we are unable to differentiate the underlying mechanism behind their injuries (ie, sports concussion, blast, or penetrating), which could have provided greater granularity to our findings. Finally, although we had data on opioid and alcohol dependence/abuse, we did not have quantitative data on opioid medication prescriptions or alcohol use across our population, and both are likely to be high in the presence of traumatic injuries, PTSD, and other psychiatric diagnoses.

CONCLUSIONS

Among survivors of combat-related trauma there is a heightened risk for developing OSA. Although TBI increased the risk of OSA, as has been demonstrated in prior populations, other types of injury did not increase the risk of OSA. Instead, the rise in OSA among combat trauma survivors was primarily driven by the mental health sequelae following injury. Clinicians should remain vigilant for OSA among survivors of traumatic injury, particularly those who have comorbid psychiatric disease or insomnia or have experienced TBI. The relationship between OSA, psychiatric disease, and insomnia deserves further study to elucidate the mediators of these associations so that screening and treatment may be optimized.

ABBREVIATIONS

CI, confidence interval
DoDTR, Department of Defense Trauma Registry
HR, hazard ratio
IQR, interquartile range
ISS, Injury Severity Score
MHS, Military Health System
OSA, obstructive sleep apnea
PTSD, posttraumatic stress disorder
SM, service member
TBI, traumatic brain injury
VA, Veterans Affairs Healthcare System

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ACKNOWLEDGMENTS

The authors thank the Department of Defense Trauma Registry, the Defense Health Agency, the Defense Suicide Prevention Office, the VA Informatics and Computing Infrastructure, the VA/DoD Identity Repository, and the Department of Veterans Affairs for providing data for this study. Kevin Chung introduced the authors' respective research groups, assisted in study design, and provided administrative research support. The data underlying this article are available in the article and in its supplemental material.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication March 24, 2021
Submitted in final revised form June 29, 2021
Accepted for publication June 29, 2021
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DISCLOSURE STATEMENT

All authors have seen and approved the final version of this manuscript. This study was funded by the US Air Force Headquarters, Office of the Surgeon General and supported by VA Center of Innovation Award I50HX001240 from the Office of Research and Development of the US Department of Veterans Affairs. E.M.W.'s institution has received prior research support from the AASM Foundation, Department of Defense, Merck, and ResMed. E.M.W. has served as a scientific consultant for DayZz, Eisai, Merck, and Purdue and is an equity shareholder in WellTap. The views expressed in this manuscript are those of the authors and do not reflect the official policy or position of the Uniformed Services University, the Department of Veterans Affairs, the Department of Defense, the Department of the Army/Navy/Air Force, or the US government. The authors report no other conflicts of interest.

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