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Insomnia and Motor Vehicle Accident–Related Injuries, Active Component, U.S. Armed Forces, 2007–2016

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Insomnia is the most common sleep disorder in adults, and its incidence is increasing in the U.S. Armed Forces. A potential consequence of insomnia (including medications used to treat it) is increased risk of motor vehicle accidents (MVAs), which cause significant morbidity and mortality in service members. To examine the relationship between insomnia and MVA-related injuries in the U.S. Armed Forces, this retrospective cohort study compared incidence rates of MVA-related injuries from 2007 through 2016 between service members with diagnosed insomnia and an unexposed cohort. After adjustment for multiple covariates, service members with insomnia had more than double the rate of MVA-related injuries, compared to service members without insomnia (adjusted incidence rate ratio: 2.08; 95% CI: 1.95–2.22). A subanalysis of service members with insomnia during 2014–2016 found no difference in risk of MVA-related injury based on days' supply of sleep aid medications prescribed in 365 days following insomnia diagnosis. Insomnia is an important potential risk factor for MVAs in the military. Sleep health should be a component of MVA prevention efforts.

Insomnia, defined broadly by inadequate sleep duration and quality, is the most common sleep disorder among adults in the U.S.[1,2] Diagnosed insomnia cases are unlikely to represent the full extent of those experiencing inadequate sleep. Approximately one-third of adults in the U.S. report sleeping less than 7 hours per night (the lower limit of recommended sleep duration).[3] A consequence of inadequate sleep is increased risk of motor vehicle accidents (MVA).[1,4-7] Given that MVAs are the leading cause of peacetime deaths and a major cause of non-fatal injuries in U.S. military members,[8-10] it is important to understand the relationship between insomnia and MVAs in the U.S. Armed Forces.

Insomnia is defined by difficulty initiating or maintaining sleep, early awakenings, and/or non-restorative sleep.[1,11] Additional symptoms include fatigue and low energy, poor concentration, cognitive slowing, and mood disturbances.[1,11,12] Insomnia is more common in females and older adults, and is often comorbid with mental health disorders (such as anxiety, depression, and post-traumatic stress disorder [PTSD]) and substance-related disorders.[1,2,11,13,14] Occupational and environmental factors may contribute to insomnia, such as shift work, long work hours and stress—factors commonly encountered in military service.[1,2] In the U.S. military, the incidence of diagnosed insomnia increased from 7.2 to 135.8 cases per 10,000 person-years (p-yrs) between 2000 and 2009, with some evidence of increased rates of incident insomnia after deployments to Iraq or Afghanistan among Army and Marine Corps service members.[2]

Insomnia can be managed in various ways: pharmacologically with medications that induce sleep; pharmacologically by treating comorbid conditions; or non-pharmacologically with a variety of behavioral modalities.[15,16] Medications approved for treatment of insomnia include some benzodiazepines; the non-benzodiazepine hypnotics zaleplon, zolpidem, and eszopiclone (known as the Z-drugs); the melatonin receptor agonist ramelteon; the antidepressant doxepin; and the orexin receptor agonist suvorexant.[1,15,16] Insomnia treatment guidelines suggest not using these medications longer than 4–5 weeks.[15] The Z-drugs, doxepin, and suvorexant have been shown to improve insomnia symptoms.[15,16] By design, most of the sleep aid medications cause sedation, and some have additional effects that could result in daytime impairment, behavioral changes, hallucinations, and even sleep-driving.[15,17] The risks and benefits of pharmacotherapy for insomnia must be carefully considered when making treatment decisions.

Both insomnia and the use of sleep aid medications have been found to be associated with MVAs in non-military populations.[4,6,7,18,19] MVAs are the leading cause of death in Americans aged 5–24 years.[20] In the U.S. in 2012, non-fatal MVAs resulted in 2.5 million emergency department visits and estimated medical costs of $18.4 billion.[21] Injuries sustained due to MVAs may result in short- or long-term health consequences and decreased occupational performance. In the military, these consequences of MVA-related injuries decrease operational readiness. Of many studies focused on MVAs in military members, few have evaluated insomnia or use of sleep aid medications as a risk factor.[9,10,18,22-25] This report explores the relationship between insomnia diagnoses and rates of MVA-related injury in the active component of the U.S. Armed Forces over a 10-year period. Additionally, a subanalysis evaluated the potential association between the amount of sleep aid medication prescribed for insomnia and the risk of MVA-related injury.

METHODS

The surveillance period was 1 January 2007 through 31 December 2016. The surveillance population included all individuals who served at any time in the active component of the Army, Navy, Air Force, or Marine Corps. All data used to determine incident cases of insomnia, prescriptions of sleep aid medications, and MVA-related injuries were derived from the Defense Medical Surveillance System (DMSS). These records document both ambulatory encounters and hospitalizations of active component members of the U.S. Armed Forces in fixed military and civilian (if reimbursed through the Military Health System) treatment facilities.

The study design was a retrospective matched cohort study. An incident case of insomnia was defined by records of two outpatient medical encounters within 90 days of each other or one hospitalization with a diagnosis of insomnia in any diagnostic position, in a non-deployed healthcare setting. The ICD-9 or ICD-10 codes used to define a case of insomnia are listed in **Table 1.** Each individual could be an incident case only once during the surveillance period for insomnia, which ended on 31 December 2015 to allow for 365 days of follow-up post-diagnosis. An unexposed comparison cohort was selected at random (case-to-comparison ratio 1:1) from among service members in service at the same time as their matched cases (within 1 month). Matched individuals in the comparison cohort were followed for 365 days. Follow-up time was censored at time of deployment or leaving military service. Individuals with prior diagnoses of insomnia before the surveillance period were eligible for inclusion.

MVA-related injury during the 365-day follow-up period was defined as an outpatient or inpatient encounter that included any of the MVA-related ICD-9 or ICD-10 external cause of injury codes, or NATO Standardization Agreement (STANAG 2050) hospitalization cause of injury and trauma codes listed in **Table 2**. Encounters with ICD-10 codes indicating subsequent or sequelae-related visits, and codes specifically indicating injuries to passengers of motor vehicles, were not included in the case definition for MVA-related injury. Individuals could have multiple cases of MVA-related injury during the 365-day follow-up, with a requirement of 30 days without case-defining encounters between each incident case.

TABLE 1. ICD-9/ICD-10 diagnostic codes for insomnia

ICD-9	ICD-10
-	F51.0 Insomnia not due to a substance or known physiological condition
307.42 Persistent disorder of initiating or maintaining sleep	F51.01 Primary insomnia
307.41 Transient disorder of initiating or maintaining sleep	F51.02 Adjustment insomnia
307.42 (see above)	F51.03 Paradoxical insomnia
327.02 Insomnia due to mental disorder	F51.04 Psychophysiological insomnia
	F51.05 Insomnia due to other mental disorder
307.41 (see above)	F51.09 Other insomnia not due to a substance or known physiological condition
	G47.0 Insomnia
780.52 Insomnia unspecified	G47.00 Insomnia, unspecified
327.00 Organic Insomnia, unspecified	G47.01 Insomnia due to a medical condition
327.01 Insomnia due to medical condition classified elsewhere	
327.09 Other organic insomnias	G47.09 Other insomnia

Baseline demographic and clinical characteristics at the time of insomnia diagnosis or selection to the comparison cohort were analyzed. Clinical characteristics included any past history of a mental health diagnosis (limited to anxiety, depression, bipolar disorder, and PTSD) or alcohol-related disorders, per Armed Forces Health Surveillance Branch (AFHSB) standardized case definitions.[26] Pearson chi-square tests were used to compare demographic and clinical characteristics between cohorts. Incidence rates of MVA-related injuries during the 365-day follow-up periods were calculated by using the number of incident MVA-related injuries and the number of p-yrs of follow-up. Incidence rate ratios (IRRs) were used to compare rates between insomnia and comparison cohorts and between categories of demographic and clinical characteristics.

A Poisson regression model was used to generate IRRs adjusted (aIRR) for sex, age, race/ethnicity, branch of service, military rank/grade, occupational category, deployment history, history of mental health diagnosis, and history of alcohol-related disorder.

A subpopulation of those with insomnia diagnoses first recorded between 1 January 2014 and 31 December 2015 was used to analyze the association between the amount of sleep aid medications prescribed and risk for MVA-related injuries. The sleep aid medications included in this analysis are listed in **Table 3**. Three exposure categories were defined by the number of days' supply of any of the included medications prescribed during the 365 days after incident insomnia diagnosis: no medications, 1–30 days' supply, and more than 30 days' supply. MVA-related injury was considered as a dichotomous outcome (any vs. none) within 365 days following the insomnia diagnosis.

A log-linear regression model was used to generate adjusted risk ratios (aRRs) for the association between days' supply of sleep aid medications prescribed and MVA-related injury, adjusting for sex, age, race/ethnicity, branch of service, military rank/grade, occupational category, deployment history, history of mental health diagnosis, and history of alcohol-related disorder. All analyses were performed using SAS/ STAT® software, version 9.4 (2014, SAS Institute, Cary, NC).

TABLE 2. ICD-9/ICD-10/STANAG codes for motor vehicle accident (MVA)-related injury cases

ICD-9	ICD-10
E810*–E819* (5th digit ending in 0, 2, or 9 only) Motor vehicle traffic accidents	V20*–V29* (excluding codes with 4th digit 1 or 5, and 7th digit S or D) Motorcycle rider injured in transport accident
E820*–E825* (5th digit ending in 0, 2, or 9 only) Motor vehicle non-traffic accidents	V30*–V38* (excluding codes with 4th digit 1, 2, 6, or 7; and 7th digit S or D); V390*, V392*, V393*, V394*, V396*, V398*, V399* (excluding codes with 7th digit S or D) Occupant of three-wheeled motor vehicle injured in transport accident V40*–V48* (excluding codes with 4th digit 1, 2, 6, or 7, and 7th digit S or D) ; V490*, V492*, V493*, V494*, V496*, V498*, V499* (excluding codes with 7th digit S or D) Car occupant injured in transport accident V50*–V58* (excluding codes with 4th digit 1, 2, 6, or 7, and 7th digit S or D); V590*, V592*, V593*, V594*, V596*, V598*, V599* (excluding codes with 7th digit S or D) Occupant of pick-up truck or van injured in transport accident V60*–V68* (excluding codes with 4th digit 1, 2, 6, or 7, and 7th digit S or D); V690*, V692*, V693*, V694*, V696*, V598*, V699* (excluding codes with 7th digit S or D) Occupant of heavy transport vehicle injured in transport accident V70*–V78* (excluding codes with 4th digit 1, 2, 6, or 7, and 7th digit S or D); V790*, V792*, V793*, V794*, V796*, V798*, V799* (excluding codes with 7th digit S or D) Bus occupant injured in transport accident
E846 Accidents involving powered vehicles used solely within the buildings and premises of industrial or commercial establishment	V83.0XXA, V83.3XXA, V83.4XXA, V83.5XXA, V83.9XXA Driver/occupant of special industrial vehicle injured in traffic accident V86.0*XA, V86.3*XA, V86.4*XA, V86.5*XA, V86.9*XA Driver/occupant of special all-terrain or other off-road motor vehicle injured in traffic accident V87* (excluding codes with 7th digit S or D) Traffic accident of specified type but victim's mode of transport unknown V88* (excluding codes with 7th digit S or D) Non-traffic accident of specified type but victim's mode of transport unknown V89* (excluding codes with 7th digit S or D) Motor or non-motor vehicle accident, type of vehicle unspecified
E848 Accidents involving other vehicles, not elsewhere classifiable	V98.8XXA Other specified transport accidents, initial encounter V99.XXXA Unspecified transport accident, initial encounter
EXCLUDING E990*–E999* Injury resulting from operations of war	EXCLUDING Y36* Injury resulting from operations of war
EXCLUDING E979* Terrorism involving firearms	EXCLUDING Y38* Terrorism involving firearms
STANAG trauma codes	**STANAG injury codes**
5-9 or none Accidental injury	100, 102, 103, 106, 107, 109 Motor vehicle traffic accidents not involving military-owned vehicle 110, 112, 113, 116, 117, 119 Motor vehicle traffic accidents involving military-owned vehicle 120, 122, 123, 126, 127, 129 Motor vehicle non-traffic accident not involving military-owned vehicle 130, 132, 133, 136, 137, 139 Motor vehicle non-traffic accident involving military-owned vehicle
EXCLUDING 0 or 1 Battle Injury	EXCLUDING 300–499 Instrumentalities of war in wartime

*Asterisk denotes any digit/character in this and any subsequent position.

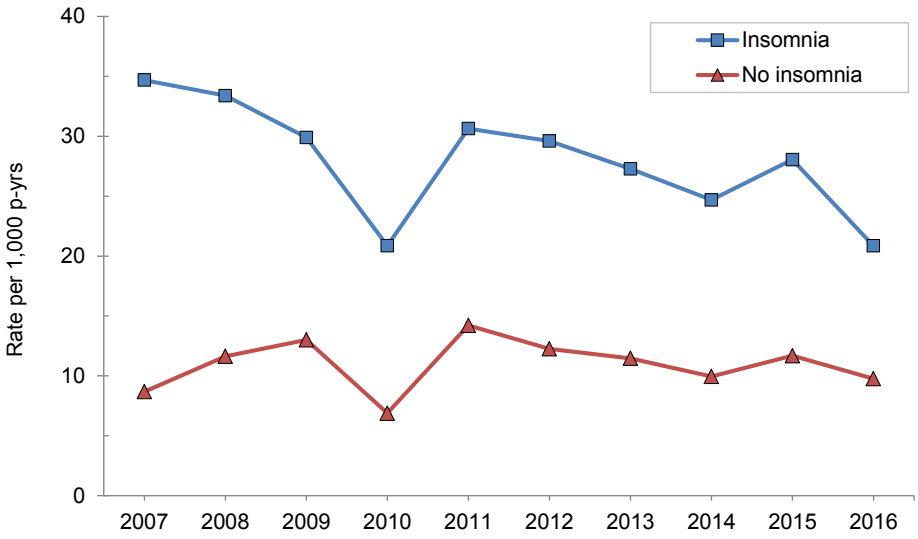
RESULTS

During the surveillance period 1 January 2007 through 31 December 2015, a total of 172,062 active component service members were diagnosed with incident insomnia. The distributions of all demographic and clinical characteristics were significantly different ($p < .001$) between cohorts **(Table 4)**. There were higher proportions of females and those aged 25 years and older in the insomnia cohort compared to the unexposed cohort. There was a higher proportion of non-Hispanic black service members in the insomnia group (20.3% vs. 15.4%). Of those with insomnia, 63.0% were in the Army while the Army accounted for just 39.8% of the unexposed cohort. The majority of those with insomnia were in the enlisted ranks (90.4%), and senior enlisted accounted for 44.8% of the insomnia cohort compared with 29.0% of the unexposed cohort. About one-third of those with insomnia had histories of mental health diagnoses (36.2%), compared to just 6.2% of the unexposed cohort. Of those with insomnia, more than two-thirds had any previous deployments (68.1%) while just one-third of the unexposed cohort had previously deployed (33.8%).

TABLE 3. Sleep aid prescription medications

Drug (generic) name	Brand name(s)
Eszopiclone	Lunesta®
Zaleplon	Sonata®
Zolpidem	Ambien®
Zolpidem, extended release	Ambien CR®
Zolpidem sublingual	Intermezzo, Edluar®
Zolpidem tartrate	Zolpimist®
Ramelteon	Rozerem®
Suvorexant	Belsomra®
Temazepam	Restoril®
Triazolam	Halcion®
Estazolam	ProSom®
Doxepin	Silenor®

FIGURE 1. Annual rates of motor vehicle accident–related injuries, active component service members with and without diagnoses of insomnia, U.S. Armed Forces, 2007–2016



There were 5,587 cases of MVA-related injuries during the surveillance period; 3,849 (68.9%) in the insomnia cohort and 1,738 (31.1%) in the unexposed cohort **(Table 5)**. The majority of individuals who experienced MVA-related injuries had just one injury during their 365-day follow-up period. The overall crude rate of MVA-related injury during the surveillance period was 27.7 cases per 1,000 p-yrs in the insomnia cohort and 11.2 per 1,000 p-yrs in the unexposed cohort. Across the surveillance period, annual rates of MVA-related injuries were higher in the insomnia cohort than the unexposed cohort **(Figure 1)**. Annual rates of MVA-related injuries were highest in the insomnia cohort in 2007 and 2008, and lowest in 2016. Among all demographic and clinical subgroups in the analysis, overall crude rates of MVA-related injuries were higher in those with insomnia than those without **(Table 5)**. The highest overall crude rates of MVA-related injuries were seen in those less than 25 years old, junior enlisted rank/grade, armor/transport occupation, those with a history of mental health diagnosis, and those with a history of alcohol-related disorders.

Multivariable Poisson regression model results revealed that, after adjusting for key background characteristics, those with insomnia had more than double the rate of MVA-related injuries, compared to those without insomnia (aRR: 2.08; 95% CI: 1.95–2.22) **(Table 6)**. Other key background characteristics associated with increased rate of MVA-related injuries included: female sex; age less than 25 years; non-Hispanic black race/ethnicity; Army branch of service; junior enlisted rank/grade; history of a mental health diagnosis; history of alcohol-related disorders; and history of one or more deployments.

There were 23,160 individuals with incident insomnia diagnoses between 1 January 2014 and 31 December 2015 included in the subanalysis **(Table 7)**. Of this subpopulation, 52.3% were not prescribed any sleep aid medications in the 365 days following their diagnosis, 15.3% were prescribed one to 30 days' supply, and 32.4% were prescribed more than 30 days' supply **(Table 7)**. Some demographic and clinical subgroups were more likely to have been prescribed more than 30 days' supply of sleep aid medications, compared with none or 1–30 days' supply: older age groups, those with senior rank/grade, healthcare occupations, those with history of a mental health or alcohol-related disorder diagnosis, and those with prior deployments **(Table 7)**. **Figure 2** shows the increasing percentage of those prescribed more than 30 days' supply of sleep aid medications within older age groups.

There were 537 cases of an MVA-related injury in the subpopulation, with an overall crude risk of 2.3% **(Table 7)**. The crude risks of MVA-related injury were similar for all exposure groups. In the log-linear model, there was no significant difference in risk of MVA-related injury between those who were prescribed one to 30 days' supply of sleep aid medications (aRR: 1.05; 95% CI: 0.83–1.33) and those who were prescribed more than 30 days' supply (aRR: 1.04; 95% CI: 0.86–1.26), compared to those not prescribed sleep aid medications, after adjusting for covariates **(data not shown)**.

EDITORIAL COMMENT

This report documents that insomnia was associated with an increased rate of MVA-related injuries in active component U.S. military members between 2007 and 2016. This finding is consistent with prior studies in civilian populations,[6,7] and adds to the knowledge base about MVA risk factors in the U.S. Armed Forces. A subanalysis of those with insomnia diagnosed in 2014 and 2015 found no association between the days' supply of sleep aid medications prescribed in the 365 days following diagnosis and risk of MVA-related injury.

The distribution of characteristics of those diagnosed with insomnia in this analysis was generally consistent with risk factors identified in the general population, with those diagnosed with insomnia

TABLE 4. Characteristics of study population,[a] active component, U.S. Armed Forces, 2007–2016

	Insomnia		No insomnia		Overall		
	N	%	N	%	N	%	p-value
Total	172,062	50.0	172,062	50.0	344,124	100.0	
Sex							
Male	138,897	80.7	147,398	85.7	286,295	83.2	<.001
Female	33,165	19.3	24,664	14.3	57,829	16.8	
Age group							
<20	5,790	3.4	24,638	14.3	30,428	8.8	<.001
20–24	49,727	28.9	63,504	36.9	113,231	32.9	
25–29	41,268	24.0	37,038	21.5	78,306	22.8	
30–34	25,862	15.0	20,917	12.2	46,779	13.6	
35–39	22,946	13.3	13,895	8.1	36,841	10.7	
40+	26,469	15.4	12,070	7.0	38,539	11.2	
Race/ethnicity							
Non-Hispanic white	102,857	59.8	105,463	61.3	208,320	60.5	<.001
Non-Hispanic black	35,004	20.3	26,512	15.4	61,516	17.9	
Hispanic	19,749	11.5	22,282	13.0	42,031	12.2	
Other/unknown	14,452	8.4	17,805	10.4	32,257	9.4	
Service							
Army	108,367	63.0	68,546	39.8	176,913	51.4	<.001
Air Force	17,487	10.2	37,695	21.9	55,182	16.0	
Navy	30,176	17.5	34,244	19.9	64,420	18.7	
Marine Corps	16,032	9.3	31,577	18.4	47,609	13.8	
Military rank/grade							
E1–E4	78,397	45.6	94,062	54.7	172,459	50.1	<.001
E5–E9	77,044	44.8	49,812	29.0	126,856	36.9	
O1–O3	6,981	4.1	17,729	10.3	24,710	7.2	
O4–O10	6,986	4.1	8,233	4.8	15,219	4.4	
WO1–WO5	2,654	1.5	2,226	1.3	4,880	1.4	
Primary occupational category							
Infantry/artillery/combat	32,788	19.1	26,753	15.6	59,541	17.3	<.001
Armor/motor transport	7,164	4.2	5,400	3.1	12,564	3.7	
Pilot/air crew	1,625	0.9	5,965	3.5	7,590	2.2	
Repair/engineer	40,945	23.8	44,823	26.1	85,768	24.9	
Communications/intelligence	41,599	24.2	34,009	19.8	75,608	22.0	
Health care	20,348	11.8	12,116	7.0	32,464	9.4	
Other/unknown	27,593	16.0	42,996	25.0	70,589	20.5	
History of mental health diagnosis[b]							
No	109,794	63.8	161,399	93.8	271,193	78.8	<.001
Yes	62,268	36.2	10,663	6.2	72,931	21.2	
History of alcohol-related disorder							
No	153,377	89.1	166,253	96.6	319,630	92.9	<.001
Yes	18,685	10.9	5,809	3.4	24,494	7.1	
Deployment history							
None	54,889	31.9	113,844	66.2	168,733	49.0	<.001
One	56,713	33.0	27,983	16.3	84,696	24.6	
Two or more	60,460	35.1	30,235	17.6	90,695	26.4	
Prior insomnia diagnosis[c]							
No	168,938	98.2	171,782	99.8	340,720	99.0	<.001
Yes	3,124	1.8	280	0.2	3,404	1.0	
One or more more motor vehicle accident–related injury							
No	168,294	97.8	170,378	99.0	338,672	98.4	<.001
Yes	3,768	2.2	1,684	1.0	5,452	1.6	

[a] Time-varying covariates are the values at time of insomnia diagnosis or assignment to unexposed cohort.
[b] Pre-existing anxiety, depression, bipolar, or post-traumatic stress disorder
[c] Any diagnosis of insomnia prior to the study period

TABLE 5. Crude incidence rates and incidence rate ratios (IRRs) of motor vehicle accident (MVA)-related injury in those with and without insomnia diagnoses, by subgroup, active component, U.S. Armed Forces, 2007–2016

	Insomnia	Cases of MVA-related injury	Incidence rate per 1,000 p-yr	IRR
Total				
	No	1,738	11.2	ref
	Yes	3,849	27.7	2.47
Sex				
Male	No	1,339	10.1	ref
	Yes	2,943	26.4	2.61
Female	No	399	18.0	ref
	Yes	906	33.0	1.84
Age group				
<20	No	284	12.5	ref
	Yes	179	41.8	3.36
20–24	No	752	13.3	ref
	Yes	1,484	38.6	2.90
25–29	No	341	10.3	ref
	Yes	986	29.6	2.87
30–34	No	182	9.6	ref
	Yes	498	22.8	2.38
35–39	No	100	7.9	ref
	Yes	374	18.8	2.38
40+	No	79	7.4	ref
	Yes	328	15.6	2.09
Race/ethnicity				
Non-Hispanic white	No	958	10.1	ref
	Yes	2,283	27.7	2.73
Non-Hispanic black	No	384	16.1	ref
	Yes	820	28.7	1.78
Hispanic	No	241	11.9	ref
	Yes	439	27.2	2.30
Other/unknown	No	155	9.6	ref
	Yes	307	26.1	2.72
Service				
Army	No	830	13.8	ref
	Yes	2,599	29.8	2.16
Navy	No	353	10.4	ref
	Yes	381	27.3	2.63
Air Force	No	302	9.6	ref
	Yes	538	21.5	2.24
Marine Corps	No	253	8.8	ref
	Yes	331	26.4	3.02
Military rank/grade				
E01–E04	No	1,107	13.2	ref
	Yes	2,176	36.2	2.74
E05–E09	No	497	11.1	ref
	Yes	1,483	23.0	2.06
O01–O03	No	82	4.9	ref
	Yes	90	14.8	3.00
O04–O10	No	37	4.9	ref
	Yes	65	11.2	2.30
W01–W05	No	15	7.6	ref
	Yes	35	15.6	2.07
Primary occupational category				
Infantry/artillery/combat	No	252	10.8	ref
	Yes	734	28.5	2.64
Armor/motor transport	No	69	14.6	ref
	Yes	194	34.1	2.33
Pilot/air crew	No	18	3.3	ref
	Yes	25	19.9	5.98
Repair/engineer	No	474	11.8	ref
	Yes	908	27.7	2.34
Communications/intelligence	No	389	12.8	ref
	Yes	877	25.8	2.02
Health care	No	146	13.0	ref
	Yes	488	28.2	2.16
Other/unknown	No	390	9.8	ref
	Yes	623	28.2	2.87
History of mental health diagnosis[a]				
No	No	1,574	10.8	ref
	Yes	2,205	24.7	2.29
Yes	No	164	18.6	ref
	Yes	1,644	33.2	1.79
History of alcohol-related disorder				
No	No	1,661	11.1	ref
	Yes	3,340	26.8	2.42
Yes	No	77	16.6	ref
	Yes	509	36.0	2.17
Deployment history				
None	No	1,010	9.7	ref
	Yes	1,372	31.9	3.28
One	No	411	17.0	ref
	Yes	1,340	29.4	1.73
Two or more	No	317	11.9	ref
	Yes	1137	22.6	1.90

[a]Pre-existing anxiety, depression, bipolar, or post-traumatic stress disorder

more likely to be older and female.[1] The distribution of characteristics was also consistent with risk factors previously identified in the U.S. Armed Forces, with those diagnosed with insomnia more likely to be in the Army and have a history of deployment.[2] This analysis found that a disproportionate number of those with insomnia were of enlisted rank/grade, especially senior enlisted, which has not previously been evaluated as a potential insomnia risk factor. It is possible that enlisted service members are more likely to experience shift work or stressors that can cause insomnia, or perhaps are more likely to seek care for insomnia than officers and warrant officers. Further consideration of enlisted rank as an insomnia risk factor is warranted.

There was an increased rate of MVA-related injuries in women overall, which was unexpected because men are typically at higher risk for MVAs.[9,22,23,27] However, this analysis only considered non-fatal MVA-related injuries for which persons sought medical care. Prior studies that have focused on specific types of MVAs or specific clinical outcomes (e.g., requiring hospitalization, fatal vs. non-fatal) have had inconsistent findings with respect to gender. Males tend to be at higher risk for higher-impact crashes, more severe clinical outcomes and death,[22,27,28] but results of some studies suggest that females have higher rates of crashes per miles driven.[27,29,30] In this analysis, it is possible that females experienced more MVAs of lower severity, and also may have been more likely to seek medical care for injuries. Given the known increased risk of insomnia in females, it is also possible that there were more females with undiagnosed insomnia in the unexposed cohort compared to males, which could have contributed to the overall increased rate of MVA-related injuries in females.

This report has several limitations that should be considered when interpreting the results. Insomnia, as captured by clinical diagnostic codes, was likely underdiagnosed and not representative of the true amount of inadequate sleep within the population. Individuals with mental health conditions often have concurrent sleep problems that may not receive a separate diagnostic code. The potential for exposure

TABLE 6. Adjusted incidence rate ratios (IRRs) of motor vehicle accident–related injury, active component service members, U.S. Armed Forces, 2007–2016

	Adjusted IRR[a]	95% CI
Insomnia		
No	ref	-
Yes	2.08	1.95–2.22
Sex		
Male	ref	-
Female	1.37	1.28–1.46
Age group		
<20	ref	-
20–24	0.97	0.87–1.08
25–29	0.75	0.66–0.84
30–34	0.61	0.53–0.70
35–39	0.51	0.44–0.60
40+	0.46	0.39–0.54
Race/ethnicity		
Non-Hispanic white	ref	-
Non-Hispanic black	1.17	1.10–1.26
Hispanic	1.00	0.92–1.09
Other	0.98	0.89–1.09
Service		
Army	ref	-
Navy	0.87	0.80–0.95
Air Force	0.76	0.70–0.83
Marine Corps	0.74	0.67–0.81
Military rank/grade		
E01–E04	ref	-
E05–E09	0.89	0.82–0.96
O01–O03	0.51	0.43–0.59
O04–O10	0.59	0.48–0.74
W01–W05	0.71	0.53–0.95
Primary occupational category		
Infantry/artillery/combat	ref	-
Armor/motor transport	0.85	0.74–0.98
Pilot/aircrew	0.75	0.54–1.05
Repair/engineer	0.92	0.80–1.05
Communications/intelligence	0.85	0.75–0.98
Health care	0.93	0.81–1.08
Other/unknown	0.87	0.75–0.99
History of mental health diagnosis[b]		
No	ref	-
Yes	1.39	1.31–1.48
History of alcohol-related disorder		
No	ref	-
Yes	1.25	1.14–1.36
Deployment history		
None	ref	-
One	1.25	1.16–1.34
Two or more	1.16	1.06–1.26

[a]Adjusted for all covariates in this table
[b]Pre-existing anxiety, depression, bipolar, or post-traumatic stress disorder

misclassification could impact the difference in rates of MVA-related injuries between cohorts.

There are potential insomnia treatments that were not considered in this analysis. The primary analysis did not include any treatment information, and the subanalysis did not include treatments other than prescribed sleep aid medications, such as behavioral therapies, over-the-counter medications, and off-label use of other medications. Treatments could have improved insomnia symptoms and thereby decreased MVA risk, or increased MVA risk due to medication side effects. This potential for confounding by treatment effect may have contributed to the lack of a significant difference in MVA-related injury risk between medication groups in the subanalysis of those with insomnia.

The MVA-related injury outcome was based on ICD-9/ICD-10/STANAG codes reflecting cause of injury within medical encounters. Cause of injury coding is recognized to be incomplete,[21,31] so the rates of MVA-related injuries may be underestimated. The transition from ICD-9 to ICD-10 in late 2015 may have contributed to the decreased rate of MVA-related injuries seen in 2016. ICD-10 includes hundreds more MVA-related cause of injury codes than ICD-9, which may have affected coding practices and decreased the assignment or accuracy of cause of injury codes. Although care was taken to exclude cause of injury codes that specifically indicated injury to a passenger, other included codes were non-specific and it is possible that some injuries included in the analysis were sustained when individuals were not drivers of the vehicle. Because only cause of injury codes were used to define cases, the types and severity of the injuries were not included. This analysis cannot estimate the actual impact of the MVA-related injuries on health and military readiness.

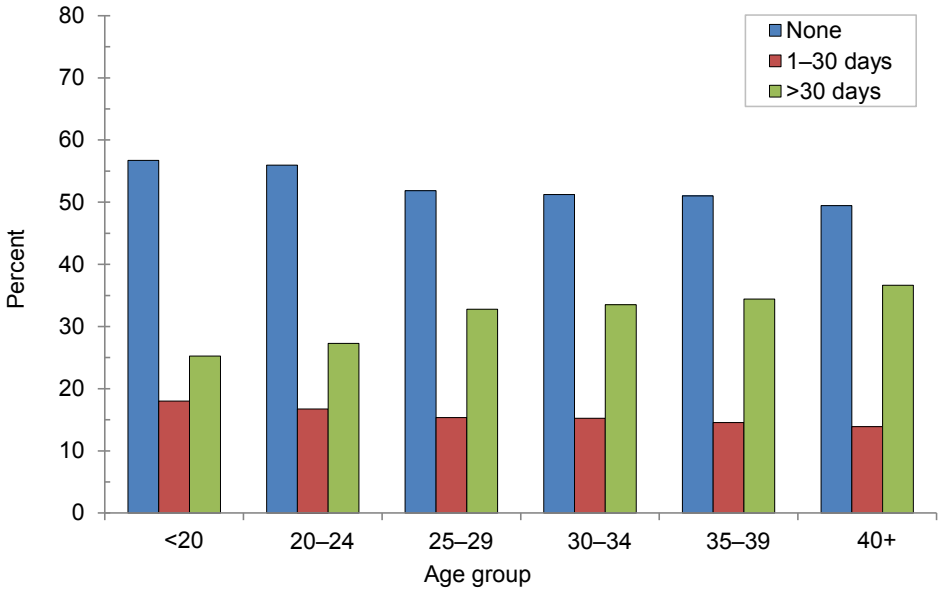
In summary, the findings of this report highlight insomnia as a potential risk factor for MVA-related injuries, a high-priority public health issue for the U.S. Armed Forces.[32] MVA prevention efforts should address sleep with the same level of intensity applied to other recognized MVA risk factors. Inadequate sleep, whether accompanied by a clinical diagnosis of insomnia

TABLE 7. Characteristics of subpopulation[a] of service members with insomnia diagnoses, active component, U.S. Armed Forces, 2014–2015

	No meds		1–30 days' supply		>30 days' supply		Total	
	N	%	N	%	N	%	N	%
Total	12,110	52.3	3,555	15.4	7,495	32.4	23,160	100.0
Sex								
Male	9,562	79.0	2,708	76.2	5,740	76.6	18,010	77.8
Female	2,548	21.0	847	23.8	1,755	23.4	5,150	22.2
Age group[a]								
<20	375	3.1	119	3.4	167	2.2	661	2.9
20–24	3,013	24.9	902	25.4	1,469	19.6	5,384	23.3
25–29	2,603	21.5	770	21.7	1,646	22.0	5,019	21.7
30–34	2,158	17.8	643	18.1	1,412	18.8	4,213	18.2
35–39	2,036	16.8	580	16.3	1,374	18.3	3,990	17.2
40+	1,925	15.9	541	15.2	1,427	19.0	3,893	16.8
Race/ethnicity								
Non-Hispanic white	6,317	52.2	1,829	51.5	4,035	53.8	12,181	52.6
Non-Hispanic black	2,989	24.7	905	25.5	1,767	23.6	5,661	24.4
Hispanic	1,679	13.9	487	13.7	993	13.3	3,159	13.6
Other	1,125	9.3	334	9.4	700	9.3	2,159	9.3
Service								
Army	7,333	60.6	2,051	57.7	4,534	60.5	13,918	60.1
Navy	1,437	11.9	432	12.2	861	11.5	2,730	11.8
Air Force	2,168	17.9	791	22.3	1,344	17.9	4,303	18.6
Marine Corps	1,172	9.7	281	7.9	756	10.1	2,209	9.5
Military rank/grade								
E01–E04	4,462	36.9	1,339	37.7	2,373	31.7	8,174	35.3
E05–E09	6,260	51.7	1,740	49.0	4,046	54.0	12,046	52.0
O01–O03	568	4.7	207	5.8	454	6.1	1,229	5.3
O04–O10	535	4.4	196	5.5	439	5.9	1,170	5.1
W01–W05	285	2.4	73	2.1	183	2.4	541	2.3
Primary occupational category								
Infantry/artillery/combat	1,860	15.4	475	13.4	1,100	14.7	3,435	14.8
Armor/motor transport	455	3.8	97	2.7	287	3.8	839	3.6
Pilot/aircrew	99	0.8	42	1.2	70	0.9	211	0.9
Repair/engineer	2,968	24.5	831	23.4	1,632	21.8	5,431	23.5
Communications/intelligence	3,344	27.6	1,031	29.0	2,015	26.9	6,390	27.6
Health care	1,485	12.3	528	14.9	1,257	16.8	3,270	14.1
Other/unknown	1,899	15.7	551	15.5	1,134	15.1	3,584	15.5
History of mental health diagnosis[b]								
No	7,973	65.8	2,437	68.6	4,250	56.7	14,660	63.3
Yes	4,137	34.2	1,118	31.5	3,245	43.3	8,500	36.7
History of alcohol-related disorder								
No	11,008	90.9	3,279	92.2	6,760	90.2	21,047	90.9
Yes	1,102	9.1	276	7.8	735	9.8	2,113	9.1
Deployment history								
None	4,023	33.2	1,278	36.0	2,259	30.1	7,560	32.6
One	2,985	24.7	876	24.6	1,909	25.5	5,770	24.9
Two or more	5,102	42.1	1,401	39.4	3,327	44.4	9,830	42.4
Motor vehicle accident–related injury								
No	11,831	97.7	3,471	97.6	7,321	97.7	22,623	97.7
Yes	279	2.3	84	2.4	174	2.3	537	2.3

[a]Time-varying covariates are the values at time of insomnia diagnosis.
[b]Pre-existing anxiety, depression, bipolar, or post-traumatic stress disorder

FIGURE 2. Distribution of days' supply of sleep aid medications prescribed by age group, subpopulation of service member with insomnia, active component, U.S. Armed Forces, 2014–2015



or not, is common in service members and may be related to an array of social, cultural, behavioral, medical, and occupational factors.[33-35] Inadequate sleep may impact the health and performance of individuals, as well as military readiness.[36-39] A comprehensive public health approach is needed to more clearly assess sleep health in the military, better understand sleep impacts on health and readiness, support sleep-related behavioral change in individuals, and recommend policies that support sleep health.

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Seizures Among Active Component Service Members, U.S. Armed Forces, 2007–2016

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Traumatic brain injury (TBI) is a known risk factor for seizures. Evidence also shows that post-traumatic stress disorder (PTSD) is associated with seizures, but the relationship in the absence of TBI remains unclear. This retrospective study spanning 2007–2016 separately quantifies the rates of seizures diagnosed among deployed and non-deployed active component military service members to understand the factors associated with seizures and whether they differ in deployed settings. Higher rates of seizures were associated with service members who were in the Army or Marine Corps; female; black; younger; lower enlisted; in a combat-specific, armor/motor transport, or healthcare occupation; and who had no more than one previous deployment. These associations were similar among both deployed and non-deployed service members. Either a TBI or recent PTSD diagnosis was associated with a 3- to 4-fold increased seizure rate. For service members who had received both diagnoses, seizure rates among the deployed and the non-deployed were two and three times the rates among those with only one of those diagnoses, respectively. If the current results are supported by future investigations, there may be implications for both clinical care and military policy.

Seizures have been defined as paroxysmal neurologic episodes caused by abnormal neuronal activity in the brain.[1] Epilepsy is a condition that can cause seizures from abnormal brain activity. However, not all seizures are due to epilepsy. Some seizures may instead be triggered by reversible insults to the brain (e.g., fever or trauma). Known risk factors for epilepsy include central nervous system disease or infections, head injury, and family history. These factors can differ from transient or temporary triggers for individual seizures such as traumatic events, exposure to chemicals, and some medical conditions.[2-5]

Seizures may also have psychological origins as in the case of psychogenic non-epileptic seizures (PNES). There is evidence that former psychological trauma and post-traumatic stress disorder (PTSD) may be associated with PNES.[6-9] It is often difficult to determine the causes of seizures and therefore to diagnose epilepsy, which is usually treated with antiepileptic medications. It is common for a PNES patient to receive years of inappropriate treatment prior to receiving an accurate diagnosis.[1,10,11] It can be difficult to clarify the etiologic nature and the diagnosis of a seizure disorder because epileptic seizures are also related to behavioral health concerns such as PTSD, depression, and anxiety.[1,7,11]

Approximately one in 10 individuals will experience a seizure in their lifetime.[2] The risk of recurrence following an initial unprovoked seizure has been estimated at 40%–52%; the risk increases to 73% after two unprovoked seizures.[12] The age-adjusted prevalence of epilepsy among Iraq and Afghanistan War veterans is 6.1 cases per 1,000 persons; this rate is lower than the rate among the general U.S. population of 10 cases per 1,000.[11,13,14] The incidence rate among active component military members in 2012 was approximately 4.7 cases per 10,000 person-years (p-yrs), which represented a decline from a high of 7.5 cases per 10,000 p-yrs in 2010.[15] In 2007, the incidence rate of epilepsy in the general U.S. population was estimated to be 4.8 cases per 10,000 p-yrs.[5]

Traumatic brain injury (TBI) is recognized as one of the contributing causes of epilepsy.[1,5,14,15] The Centers for Disease Control and Prevention estimated the rate of TBI in the U.S. population as 82.4 incidents per 10,000 p-yrs.[16] Before the wars in Iraq and Afghanistan, the TBI rate among U.S. military personnel was similar to the civilian rate but it has since more than doubled to 181.1 cases per 10,000 p-yrs, with the largest increases occurring among active component soldiers and Marines.[17] An estimated one-third of those in the military diagnosed with TBI also had PTSD, but that estimate doubled among Iraq and Afghanistan war veterans.[11,17] Studies have shown that PTSD may have affected 8.6%–14% of veterans of Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF).[18,19] In contrast, it is estimated that only 3.5% of the adult U.S. population has PTSD.[20]

Seizures of all etiologies among military service members are an important concern, as evidenced by Congress establishing the Veterans Health Administration Epilepsy Centers of Excellence in 2008. Department of Defense induction standards mandate that individuals must be seizure free without medications for 5 years and have normal EEG and neurologic exams before they are eligible for military service.[21] Retention standards are more lenient in that service members can continue to serve provided they remain seizure free with medication. However, seizure disorders are considered

deployment-limiting conditions. For example, in the Army, soldiers must remain seizure free for a minimum of 1 year before they are eligible to deploy.[22]

Although TBI has received increased levels of scrutiny in the military and the association between seizures, TBI, and PTSD has been acknowledged, the extent to which other potential risk factors, such as PTSD alone, may be associated with seizures remains to be thoroughly evaluated. This report attempts to bridge that knowledge gap by determining the incidence rates and correlates of seizures among active component military service members. Deployed service members are exposed to different environmental and occupational factors and must maintain a higher standard of medical readiness. Separate analyses were performed on deployed service members and on non-deployed service members to determine whether there are differences between the two groups in the factors that may be associated with the occurrence of seizures.

TABLE 1. ICD-9/ICD-10 diagnostic codes for post-traumatic stress disorder (PTSD), seizures, and traumatic brain injury (TBI)

	ICD-9	ICD-10
PTSD	309.81	F43.1, F43.10, F43.11, F43.12
Epileptic seizures	345.*, 649.4*,	G40.*
Non-epileptic seizures	780.33, 780.39	F44.5, R56.1, R56.9
TBI	310.2, 800.0*804.*, 850.0–850.9, 850.11, 850.12, 851.*–854.*, 905.0, 907.0, 950.1–950.3, 950.01, 959.01, V15.5, V15.52, V15.59, V80.01	F07.81, S04.02–S04.04, S04.06, S04.02X, S04.02XA, S04.031, S04.031A, S04.032, S04.032A, S04.039, S04.039A, S04.041, S04.041A, S04.042, S04.042A, S04.049, S04.049A, S06.0X0–S06.0X9, S06.0X0A–S06.0X9A, S06.1X–S06.2X, S06.1X0–S06.2X0, S06.1X0A–S06.2X9A, S06.30–S06.38, S06.300–S389, S06.300A–S06.389A, S06.4X–S06.6X, S06.4X0–S06.6X9, S06.4X0A–S06.4X9A, S06.89, S06.890–S06.899, S06.890A–S06.899A, S06.9X, S06.9X0–S06.9X9, S06.9X0A–S06.9X9A, S06.9X9S, S02.0–S02.11, S02.19, S02.111–S02.113, S02.119, S02.0XXA, S02.0XXB, S02.10XA, S02.10XB, S02.110A–S02.113A, S02.110B–S02.113B, S02.118A, S02.118B, S02.119A, S02.119B, S02.19XA, S02.19XB, S02.8, S02.9, S02.8XXA, S02.8XXB, S02.91, S02.91XA, S02.91XB, S07.1, S07.1XXA, Z87.820

*Asterisk denotes any digit/character in this and any subsequent position.

METHODS

This retrospective cohort study spanned a surveillance period from 1 January 2007 through 31 December 2016. The study population included all individuals who served in active components of the Army, Navy, Air Force, or Marine Corps at any time during the surveillance period. Data were retrieved from the Defense Medical Surveillance System (DMSS) from records of both ambulatory encounters and hospitalizations of active component members of the U.S. Armed Forces in fixed military treatment facilities and civilian sources of purchased care. The secondary analysis included members of the study population during periods of deployment to OEF, OIF, or Operation New Dawn (OND). Due to incomplete medical encounter data during deployments in 2007, the secondary analysis utilized data from 1 January 2008 through 31 December 2016.

The outcome variable was diagnoses of seizure events documented in the first or second diagnostic position of healthcare records **(Table 1)**. Both epileptic and non-epileptic seizure events were included. For the primary analysis, the diagnosis must have been documented in the record of a hospitalization or an encounter in an urgent or emergency care facility within the military healthcare system (as defined by the Medical Expense and Performance Reporting System [MEPRS] codes BIA or BHI). Limiting the case definition to hospitalizations and emergency settings was intended to minimize the inclusion of encounters for routine or follow-up seizure care. This primary analysis used outcomes and person-time derived from periods not spent on OEF, OIF, or OND deployments. Incidence rates were calculated as the number of cases per 10,000 p-yrs.

Febrile seizures (ICD-9: 780.31, 780.32; ICD-10: R56.00, R56.01) were excluded from consideration as such seizures are primarily diagnosed in young children and at a very low rate (0.65 cases per 10,000 p-yrs) in the active component.[23] The secondary analysis allowed seizure diagnoses to be made during any type of deployed medical encounter as documented in the records of the Theater Medical Data Store (TMDS). During deployment, individuals were eligible to be counted as a seizure case only once every 30 days. This restriction was applied to reduce the likelihood of counting follow-up care because in-theater records did not have MEPRS codes available to determine emergency care.

In addition to demographic and military factors, the primary covariates of interest were the diagnoses of PTSD and/or TBI. For the purpose of this analysis, an incident PTSD case was defined by a record of an ICD-9 or ICD-10 code for PTSD in the first or second diagnostic position of a record of any one of the following: 1) one hospitalization, or 2) two outpatient medical encounters (or deployment medical encounters) within 180 days of each other, or 3) one outpatient medical encounter in a psychiatric or mental healthcare facility **(Table 1)**. The at-risk period for a seizure event following a diagnosis of PTSD was restricted to 365 days following the incident PTSD diagnosis, as well as 365 days following any medical encounter with PTSD listed in any diagnostic position, as long as the individual was previously diagnosed as an incident case. TBI was defined as either: 1) one hospitalization, or 2) one outpatient

medical encounter, or 3) one deployment medical encounter with a qualifying TBI ICD-9 or ICD-10 diagnosis in any diagnostic position **(Table 1)**. The at-risk period for a seizure event following a TBI diagnosis extended through the surveillance period. Additional covariates included sex, race, age, rank, service branch, and number of previous deployments.

Crude incidence rates were calculated for seizures diagnosed among currently non-deployed and among currently deployed service members. Because the etiology of seizures is complex and multifactorial, crude incidence rates were initially stratified by type of seizure. However, results for this stratified analysis failed to yield new information or patterns and were therefore not presented in this report. To better understand the relationship between having been recently diagnosed with PTSD without TBI and subsequent seizures, crude incidence rates of seizures were also calculated among a population of service members without any history of TBI. A multivariable Poisson regression model was used with a 5% random sample of service members to calculate the incidence rate ratios for seizure events diagnosed during OIF, OEF, and OND deployments after adjusting for service branch, race, age group, military occupation, previous deployments, TBI diagnosis, and recent PTSD diagnosis. As part of a sensitivity analysis, the model was also run on a non-deployed population who had no prior history of seizure. All statistical analyses were conducted using SAS 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

A total of 16,257 seizure events of all types were identified among non-deployed service members during the 10-year surveillance period, which accumulated 12,589,995 p-yrs **(Table 2)**. The overall incidence rate during this period was 12.9 seizures per 10,000 p-yrs. The overall rates were highest among service members in the Army or Marine Corps; females; blacks; those younger than age 30; junior enlisted; those in combat-specific, armor/motor

TABLE 2. Crude incidence rate of seizures by military and demographic characteristics among non-deployed active component U.S. service members, total cohort and subcohort of service members without a history of traumatic brain injury (TBI), U.S. Armed Forces, 2007–2016

	Total			No history of TBI		
	Cases	Rate[a]	IRR	Cases	Rate[a]	IRR
Overall	16,257	12.9	ref	10,819	9.3	ref
Sex						
Male	12,712	11.9	ref	8,215	8.3	ref
Female	3,545	18.6	1.6	2,604	14.5	1.7
Race						
White	11,442	13.2	ref	7,394	9.2	ref
Black	3,261	15.2	1.2	2,335	11.7	1.3
Other/unknown	1,554	8.8	0.7	1,090	6.6	0.7
Age group						
<20	2,918	18.5	ref	2,321	15.0	ref
20–24	5,190	15.9	0.9	3,633	11.8	0.8
25–29	3,912	13.1	0.7	2,428	8.9	0.6
30–34	1,847	9.5	0.5	1,035	5.9	0.4
35–39	1,272	8.7	0.5	749	5.7	0.4
40+	1,118	8.2	0.4	653	5.3	0.4
Service						
Army	9,830	21.6	ref	6,059	15.0	ref
Navy	2,571	8.1	0.4	1,845	6.1	0.4
Air Force	1,645	5.4	0.2	1,316	4.5	0.3
Marines	2,211	12.4	0.6	1,599	9.5	0.6
Rank						
E1–E4	10,650	19.5	ref	7,522	14.5	ref
E5–E9	4,648	9.3	0.5	2,679	6.0	0.4
O1–O4	693	4.3	0.2	442	2.9	0.2
O5–O10	152	3.9	0.2	116	3.1	0.2
W1–W5	114	6.8	0.4	60	4.0	0.3
Military occupation						
Combat-specific[b]	3,381	19.4	ref	1,953	12.7	ref
Armor/motor transport	754	20.6	1.1	478	14.2	1.1
Pilot/air crew	138	2.9	0.1	101	2.2	0.2
Repair/engineering	3,808	10.3	0.5	2,603	7.5	0.6
Communications/intelligence	3,491	12.6	0.6	2,370	9.2	0.7
Health care	1,697	15.2	0.8	1,198	11.5	0.9
Other/unknown	2,988	12.3	0.6	2,116	9.2	0.7
History of deployment						
None	9,270	13.2	ref	7,008	10.4	ref
1	4,274	14.3	1.1	2,425	8.9	0.9
2+	2,713	10.6	0.8	1,386	6.3	0.6
PTSD + TBI						
Yes	1,401	185.8	15.7	687	60.3	6.9
No	14,856	11.9	ref	10,132	8.8	ref
TBI only						
Yes	4,037	48.4	4.7	4,667	2,864.0	543.0
No	12,220	10.4	ref	6,152	5.3	ref
PTSD only						
Yes	687	60.3	4.8	679	59.6	7.0
No	15,570	12.5	ref	9,846	8.5	ref
History of prior seizure						
Yes	7,840	3,247.3	484.8	4,511	2,834.9	549.8
No	8,417	6.7	ref	6,014	5.2	ref

IRR, incidence rate ratio; PTSD, post-traumatic stress disorder
[a]Rate per 10,000 person-years
[b]Infantry/artillery/combat engineering

transport, or healthcare occupations; and those with a history of only one deployment. During the surveillance period, the annual rates increased from 13.9 seizures per 10,000 p-yrs in 2007 to a peak of 15.1 seizures per 10,000 p-yrs in 2011. Rates reached their lowest point in 2015 (9.0 seizures per 10,000 p-yrs) **(Figure 1)**. Annual rates were markedly higher among service members with recent PTSD and TBI diagnoses, and among those with prior seizure diagnoses **(Table 2, Figure 2)**. Approximately half (55%) of individuals experienced only one seizure during the surveillance period, 19% experienced two, and 26% experienced three or more **(data not shown).** When seizure rates were stratified by epileptic versus non-epileptic seizures, the same overall demographic patterns were observed **(data not shown)**. The rate of non-epileptic seizures was higher (7.8 seizures per 10,000 p-yrs) than epileptic (5.1 seizures per 10,000 p-yrs) among the non-deployed. However, among those diagnosed with a seizure during deployment, the epileptic rate was higher (5.4 seizures per 10,000 p-yrs) than the non-epileptic rate (3.7 seizures per 10,000 p-yrs) **(Table 3)**.

The results of the multivariable Poisson model indicated that history of PTSD, TBI, and both, as well as military branch, sex, and deployment history were significantly positively associated with seizures of all types after controlling for all other factors **(Table 4)**. The adjusted incidence rate ratio (aIRR) for those with a previous TBI diagnosis (without a recent PTSD diagnosis) was 4.9, and the aIRR ratio for those with a recent PTSD diagnosis (without any history of TBI) was 5.9. However, for those with a diagnosis of both PTSD and TBI, the aIRR was 15.6.

A total of 814 cases of seizures were identified during deployment among military service members deployed to Iraq and Afghanistan during the 9-year surveillance period (2008–2016), which accumulated 897,768 p-yrs **(Table 5)**. For deployed service members, the overall incidence rate was 9.1 seizures per 10,000 p-yrs. Overall incidence rates among deployed service members were highest for those in the Army; females; those younger than age 25; junior enlisted; and in healthcare occupations. The annual rates of seizures among

FIGURE 1. Annual crude incidence rates of seizures among non-deployed active component service members, U.S. Armed Forces, 2007–2016

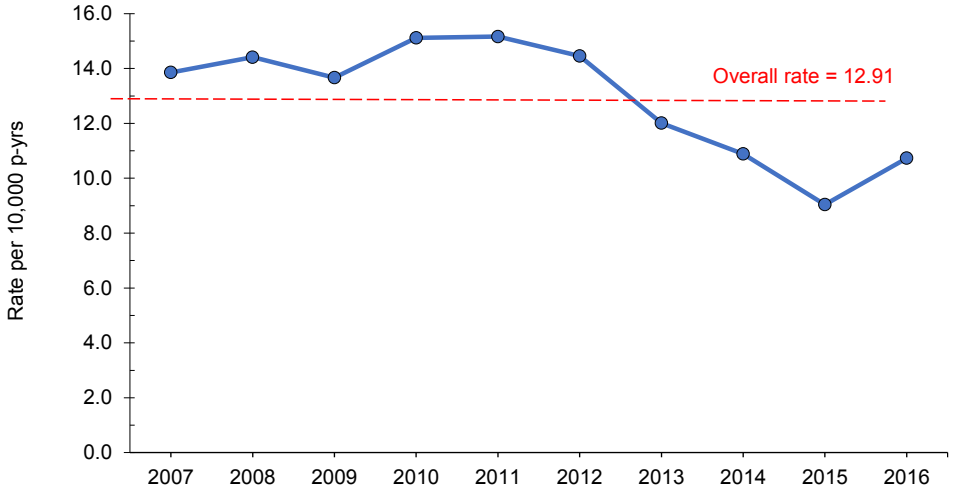


FIGURE 2. Annual crude incidence rates of seizures by traumatic brain injury (TBI) and recent post-traumatic stress disorder (PTSD) diagnosis among non-deployed active component service members, U.S. Armed Forces, 2007–2016

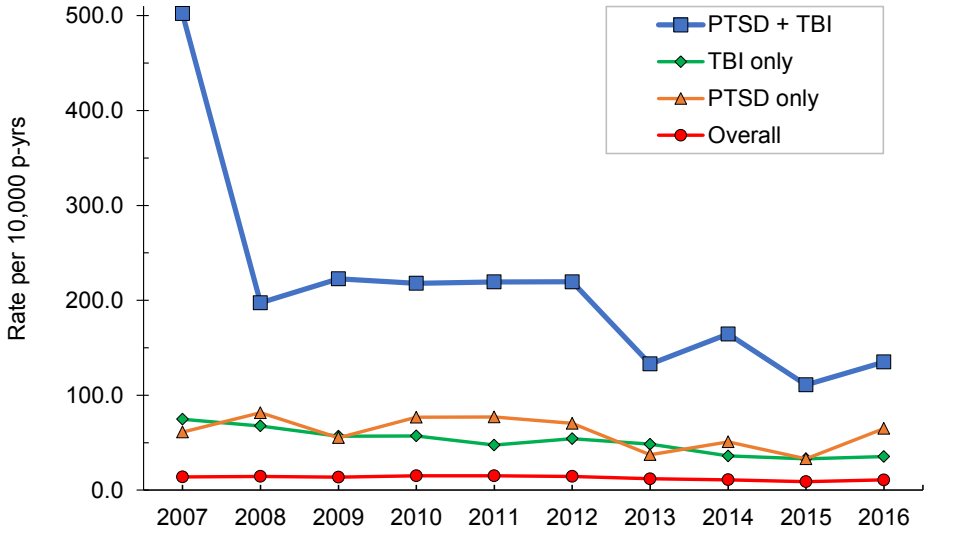


TABLE 3. Distribution of seizures by type and crude incidence rate stratified by seizure types of two active active component U.S. military populations

	Epileptic seizures			Non-epileptic seizures		
	Cases	%	Rate[a]	Cases	%	Rate[a]
Non-deployed service members	6,433	40	5.1	9,824	60	7.8
Service members deployed to Iraq or Afghanistan	482	59	5.4	332	41	3.7

[a]Rate per 10,000 person-years

TABLE 4. Adjusted incidence rate ratios (aIRRs) of seizures by military and demographic characteristics among non-deployed active component U.S. service members, U.S. Armed Forces, 2007–2016

	Total			
	aIRR	95% CI		p-value
Sex				
Male	ref	-	-	-
Female	1.66	1.18	2.34	.004
Race				
White	ref	-	-	-
Black	1.10	0.73	1.66	.655
Other	0.86	0.48	1.53	.610
Age group				
<20	ref	-	-	-
20–24	0.62	0.41	0.93	.020
25–29	0.59	0.35	0.99	.046
30–34	0.32	0.19	0.56	<.0001
35–39	0.38	0.19	0.75	.005
40+	0.26	0.15	0.47	<.0001
Service				
Army	ref	-	-	-
Navy	0.44	0.26	0.73	.002
Air Force	0.31	0.20	0.47	<.0001
Marines	0.75	0.50	1.11	.148
Military occupation				
Combat-specific[a]	ref	-	-	-
Health care	1.16	0.65	2.05	.619
Other/unknown	0.76	0.51	1.15	.199
History of deployment				
None	ref	-	-	-
1	0.89	0.60	1.33	.578
2+	0.55	0.36	0.85	.007
PTSD + TBI				
Yes	15.65	8.79	27.86	<.0001
No	ref	-	-	-
TBI only				
Yes	4.91	3.28	7.34	<.0001
No	ref	-	-	-
PTSD only				
Yes	5.90	3.14	11.08	<.0001
No	ref	-	-	-

PTSD, post-traumatic stress disorder; TBI, traumatic brain injury
[a]Infantry/artillery/combat engineering

deployed service members remained fairly stable from 2008 (9.8 seizures per 10,000 p-yrs) through 2011 (9.9 seizures per 10,000 p-yrs) and then declined to their lowest value in 2016 (4.0 seizures per 10,000 p-yrs) **(Figure 3)**. The annual rates of seizures stratified by other demographic and military characteristics followed a similar pattern **(data not shown)**. As with the non-deployed cohort, seizure rates were elevated in deployed service members with a TBI diagnosis, recent PTSD diagnosis, and prior seizures **(Table 5)**.

Several sensitivity analyses were carried out to assess the robustness of the results **(data not shown)**. A 30-day incidence rule for the ascertainment of seizures was used in the analysis of the non-deployed population. The resulting seizure rates were predictably lower, but the patterns were similar to those obtained from the previous analyses. When a Poisson model was used with the non-deployed population without a prior history of seizures or TBI, a history of PTSD remained positively associated with incident seizure events (aIRR=6.3, p<.001) **(data not shown)**.

EDITORIAL COMMENT

This report documents a decrease in the rate of seizures diagnosed in the active component of the military during a 10-year period. The decrease was evident in populations whose seizures were diagnosed during periods of non-deployment as well as in service members deployed to Iraq or Afghanistan. The initially stable annual seizure rates in both populations began a gradual decrease after 2011 to current rates. The declines in rates accompanied the changing size and missions of the military in both Iraq and Afghanistan.

The highest rates of seizures were found among soldiers and Marines, who share similar military combat missions. The rate was also significantly higher among females. This finding may be due to the higher rate of idiopathic generalized epilepsy and PNES among females.[24,25] The demographic and temporal patterns of seizure incidence were similar in non-deployed service members and in a deployed population.

One pronounced difference between the two populations was the increased risk of seizures diagnosed during deployment among healthcare workers. Prior studies have indicated that healthcare workers are at higher risk for developing PTSD in a deployed environment.[26,27] Medical personnel had the same level of risk as service members in other occupations who leave

TABLE 5. Crude incidence rates of seizures diagnosed during deployment, by military and demographic characteristics, among service members deployed to Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn: total cohort and subcohort of service members without a history of traumatic brain injury (TBI), U.S. Armed Forces, 2008–2016

	All			No history of TBI		
	Cases	Rate[a]	IRR	Cases	Rate[a]	IRR
Overall	814	9.1	ref	657	7.8	ref
Sex						
Male	683	8.5	ref	544	7.2	ref
Female	131	14.4	1.7	113	13.1	1.8
Race						
White	601	9.3	ref	483	8.0	ref
Black	145	9.8	1.1	113	8.1	1.0
Other	68	6.4	0.7	61	6.1	0.8
Age group						
<20	88	10.6	ref	81	10.0	ref
20–24	295	10.8	1.0	245	9.4	0.9
25–29	222	9.3	0.9	168	7.6	0.8
30–34	114	8.5	0.8	89	7.2	0.7
35–39	58	6.1	0.6	45	5.1	0.5
40+	37	5.0	0.5	29	4.3	0.4
Service						
Army	696	11.9	ref	555	10.3	ref
Navy	21	4.3	0.4	18	3.8	0.4
Air Force	46	3.1	0.3	44	3.1	0.3
Marines	51	4.4	0.4	40	3.6	0.3
Rank						
E1–E4	478	11.4	ref	399	9.9	ref
E5–E9	275	8.2	0.7	206	6.7	0.7
O1–O4	47	4.4	0.4	42	4.2	0.4
O5–O10	7	4.2	0.4	4	2.5	0.3
W1–W5	7	3.7	0.3	6	3.4	0.3
Military occupation						
Combat-specific[b]	229	10.1	ref	184	8.9	ref
Armor/motor transport	40	10.9	1.1	33	9.7	1.1
Pilot/air crew	3	0.9	0.1	3	0.9	0.1
Repair/engineering	155	7.1	0.7	123	5.9	0.7
Communications/intelligence	182	9.0	0.9	144	7.6	0.9
Health care	106	19.3	1.9	89	17.2	1.9
Other/unknown	99	7.9	0.8	81	6.8	0.8
PTSD and TBI						
Yes	9	55.3	6.2	-	-	-
No	805	9.0	ref	-	-	-
TBI only						
Yes	148	27.6	3.5	-	-	-
No	666	7.9	ref	-	-	-
PTSD only						
Yes	10	26.1	2.9	10	26.1	3.4
No	804	9.0	ref	647	7.7	ref
History of prior seizure						
Yes	167	1,356.4	188.0	121	1,290.9	202.7
No	647	7.2	ref	536	6.4	ref

IRR, incidence rate ratio; PTSD, post-traumatic stress disorder
[a]Rate per 10,000 person-years
[b]Infantry/artillery/combat engineering

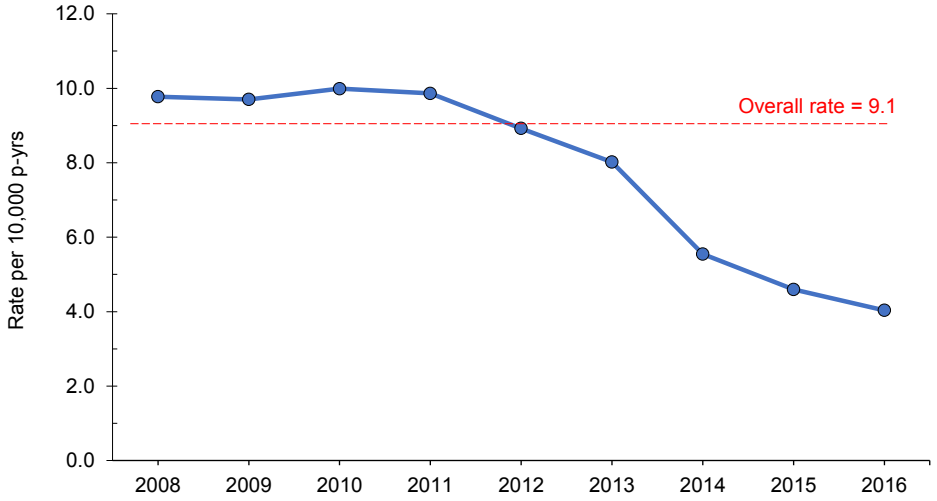
the relative safety of the forward operating bases. It should be noted that healthcare workers were often uniquely exposed to multiple traumas and deaths while working in medical facilities during a combat deployment. They also had higher access to medical care resulting in a greater chance of receiving a diagnosis.

Having either a TBI or recent PTSD diagnosis alone was associated with a 3- to 4-fold increase in the rate of seizures. Compared to service members with TBI or PTSD alone, among service members who had been previously diagnosed with both TBI and PTSD, the seizure rate doubled among the deployed population and more than tripled among those not currently deployed. There appeared to be a greater than additive association between TBI and recent diagnoses of PTSD on subsequent seizure occurrence, at least among the non-deployed service members. The effects of recent PTSD and TBI were attenuated in the deployed population. The apparent reduced level of interaction between the two exposures during deployment may be due in part to the small number of cases identified. Only 19 cases of seizures were diagnosed among deployed individuals with a recent PTSD diagnosis during the 9-year surveillance period.

This study was limited by the use of administrative data. Seizure events identified here may not have represented unique incidents of seizures but may have included follow-up care. Specifying only emergency clinic encounters and hospitalizations was designed to minimize this limitation. Preliminary analysis stratifying by seizure type did not yield differences in the patterns of seizure rates in this study. Medical providers may misdiagnose as seizures the pseudoseizures of PNES. The resultant administrative records of such diagnoses may reflect the misclassification of seizure type, introducing a greater degree of uncertainty into the results of stratified analyses. Stratified results were therefore not presented. Administrative records also may not capture all seizures because some individuals who suffer from multiple seizures often do not seek treatment for each episode.

Some selection bias may be introduced because only direct care encounters

FIGURE 3. Annual crude incidence rates of seizures diagnosed among service members deployed to Operation Enduring Freedom, Operation Iraqi Freedom, or Operation New Dawn, U.S. Armed Forces, 2008–2016



at military treatment facilities were considered for this analysis. This methodology may have underestimated seizure rates due to missing data from civilian emergency care facilities. Because individuals who had seizures prior to the surveillance period were not excluded, no conclusions can be drawn regarding causality.

Ascertainment of exposures may have changed during the surveillance period as increased attention was given to both PTSD and TBI. There also exists the possibility of differential misclassification of exposures. There is evidence that both PTSD and TBI, especially mild TBI, are underreported, despite increased attention, in the military for reasons such as stigmatization and incomplete documentation.[28,29] These factors have the potential of biasing the association between PTSD and seizures towards the null.

Another limitation is the slightly different rules for case determination used in the analysis of the deployed and nondeployed populations. Because MEPRS codes are not utilized in the TMDS system, seizure rates among service members during deployment may be underestimated. Patterns remain similar between the two populations despite this limitation.

In summary, having a history of TBI is a recognized risk factor for seizures and was also indicated as a risk factor in this study. In addition, this analysis found that recently diagnosed PTSD (within 365 days) was independently associated with subsequent seizure events in a military population. Prior diagnoses of both TBI and PTSD were associated with a much higher rate of seizures. In light of these findings, it is important to develop future studies to further evaluate the interaction between PTSD and TBI on seizure risk. PTSD appears to be associated with both epileptic and non-epileptic seizures, but how this association varies between types of seizure remains unclear. It is important to try to evaluate these associations as the treatments for seizure types differ significantly.

If the results reported here are replicated in future investigations, there may be implications for both clinical care and military policy. For example, providers may want to consider patients with a history of TBI and PTSD to have a potentially increased risk for seizures. Currently, the Joint Trauma System, representing all services, has a list of Clinical Practice Guidelines.[30] Given the prevalence of TBI and PTSD in the military as well as the potential impact of seizures, formal evidence-based Clinical Practice Guidelines may standardize care and improve outcomes. Also, results from this study may provide justification to eventually reevaluate military profiling and retention standards to include a more conservative standard for patients with co-occurring TBI and PTSD diagnoses.

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Brief Report

Prevalence of Hepatitis B and C Virus Infections in U.S. Air Force Basic Military Trainees Who Donated Blood, 2013–2016

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Hepatitis B virus (HBV) and hepatitis C virus (HCV) can cause significant morbidity in military service members. Prevalences of HBV and HCV infections among military recruits accessioning into the U.S. Air Force have not previously been described. The Joint Base San Antonio-Lackland Blood Donor Center was queried for the results of HBV and HCV screening tests among all basic military trainees who donated blood between 25 November 2013 and 16 April 2016. Other active and reserve component members were excluded. The estimated prevalences of HBV and HCV infections among recruit blood donors were 0.0098% and 0.007%, respectively. This study suggests that the overall estimated prevalence of HBV and HCV infection is much lower among U.S. Air Force basic trainees, compared to other active and reserve component members and U.S. civilian populations. HBV and HCV viral infections can have a negative impact on mission readiness and individual deployment status, and have significant costs for the military. Additional studies are needed to determine cost effectiveness of screening for viral hepatitis among military populations.

Chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections can cause significant morbidity in military service members due to prolonged inflammatory damage to the liver and potential complications including cirrhosis, hepatocellular carcinoma, and fulminant liver failure, which may necessitate liver transplantation.[1,2] The estimated prevalence of chronic HBV infection in the U.S. civilian population is 0.4%; however, it is possible that the prevalence in the civilian population is underestimated because prior studies assessing hepatitis B prevalence excluded groups of people at higher risk of infection such as Asians, Pacific Islanders, and homeless populations.[3] The prevalence of chronic HBV infections among residents of group quarters, such as military barracks, college dormitories, nursing homes, and long-term care facilities in the U.S., has been estimated as approximately 0.5%.[3] The overall prevalence of chronic HCV infection in the U.S. has been found to be 0.48%, 5.4% and 1.6% for active duty, veteran, and civilian populations respectively.[4-6] Risk factors for acquisition of HBV include high-risk sexual behavior, intravenous (IV) drug use, and vertical transmission through childbirth in developing countries. Risk factors for acquiring HCV include IV drug use, receiving blood transfusions before 1992, and engaging in high-risk sexual behavior.[7]

Although the overall prevalence and incidence rates of chronic HBV and HCV infections have been previously estimated in active component service members, the prevalence among military recruits accessioning into the U.S. Air Force has not been described. Incoming trainees are not routinely screened for acute or chronic HBV and HCV infection. They are screened for immunity for hepatitis B, and they are given the hepatitis B vaccination series if they test negative for the hepatitis B surface antibody. Screening for hepatitis B immunity involves screening only for the surface antibody, with a positive test indicating immunity from either prior vaccination or resolved acute HBV infection. Serologic test results for acute and chronic HBV infections, along with the different phases of infection are summarized in the **Table**.

Screening for HCV infection is initially performed with serum antibody testing. If the HCV antibody test is positive, then assessment for active infection is performed by testing for the presence of HCV RNA. A positive HCV RNA result indicates active infection, whereas a negative RNA test in the presence of HCV antibody indicates cleared infection, or, rarely, a false-positive test.

Identification of the prevalence of acute and chronic HBV and HCV infections is important because of not only the possible health consequences of these infections, but also the high cost of clinical evaluation and treatment. Identification of recruits with acute and chronic HBV or HCV infections would likely benefit the military from a mission readiness standpoint because these individuals do not meet the standards for entry into active military service and disease management costs would be avoided.

METHODS

The Joint Base San Antonio-Lackland Blood Donor Center was queried for the results of HBV and HCV screening for all

TABLE. Typical results of laboratory tests relevant to hepatitis B virus (HBV) infection and immunity

HBV status	HBV surface antigen	HBV IgM core	HBV IgG core	HABV e-antigen	HBV e-antibody	HBV surface antibody	HBV DNA copies per ml
Acute infection	+	+	+	+			>20,000
Resolved acute infection			+		+	+	
Vaccination only						+	
Chronic infection							
Replicative phase	+		+	+			>20,000
Nonreplicative phase	+		+		+		±
Flare of chronic HBV	+	+	+	±			>2,000

IgM, immunoglobulin M; IgG, immunoglobulin G

basic military trainees who donated blood between 25 November 2013 and 16 April 2016. Other active duty or reserve personnel were excluded. Demographic data including age, race, sex, and state or country of origin were collected for donors whose screening tests were positive. Blood from trainee donors was screened for HBV and HCV infection as described earlier. Estimated HBV and HCV prevalences among basic trainees who donated blood were calculated by using the 30,660 trainees who donated blood as the denominator to determine prevalences. This cross-sectional study was approved by the Wilford Hall Ambulatory and Surgical Center Institutional Review Board.

RESULTS

An estimated 30,660 of 76,732 basic trainees donated blood during the study period. Approximately 140 basic trainees donated blood each week. A total of 44 basic trainees who donated blood had a positive screening test result for either HBV or HCV infection during the study period. Five of the trainee donors were positive for HBV surface antigen, and three of them subsequently tested positive for HBV core antibody and HBV DNA. Of the 39 trainee donors who tested positive for HCV antibody, two subsequently tested positive for HCV RNA. Cases were predominantly male (one female with HCV) and the age range was 18–33 years.

The three trainees with confirmed HBV infection were of Asian descent; of these, two were born in Hawaii and one was born in Vietnam. The two trainees with confirmed HCV infection were both white and were born in Missouri and California. Based on the number of basic trainees who donated blood during the study period, the estimated prevalences of HBV and HCV infections among donors were 0.0098% and 0.007%, respectively.

EDITORIAL COMMENT

This study suggests that the overall estimated prevalences of HBV and HCV infection are much lower among U.S. Air Force basic trainees, compared to other active duty and U.S. civilian populations. The lower prevalence may be secondary to a reduction in risk factors for HBV and/or HCV infection because most of the trainees who donated blood likely did not have blood transfusions before 1992 (many were born after 1992) and may have had relatively low levels of prior high-risk sexual behaviors or IV drug use.

The small number of cases found in this study limits the ability to make comparisons of the prevalence of HCV among different race/ethnicity groups. Of the patients who were positive for HBV, all were of either Asian or Pacific Islander descent, a finding that is consistent with the higher prevalence noted in civilian Asians and Pacific Islanders in the U.S.[3]

Screening for HBV immunity occurs at the start of basic training.[8] However, HBV screening for immunity involves only screening for the HBV surface antibody and does not include screening for other markers that suggest acute or chronic infection such as the HBV surface antigen, HBV core antibody, HBV e-antigen, HBV e-antibody, and HBV DNA. Some trainees could potentially harbor HBV during the subclinical phase of acute hepatitis B or during an inactive carrier state. If the virus later becomes active, then the risks of cirrhosis and hepatocellular carcinoma (HCC) are higher in HBV infection than in HCV infection. Screening for HBV infection includes a test for HBV surface antigen, but the test cost of $99 per person may not be cost effective due to low prevalence in the population. However, it may be reasonable to consider targeting testing of populations that are at higher risk for HBV such as foreign-born Asians, Pacific islanders, and Africans.[9]

A prior study by Brett-Major et al. evaluating the active duty population suggested a cost benefit to HCV screening.[10] Although the cost of HCV treatment varies based on viral genotype, most new drug regimens targeted at genotype 1 cost approximately $100,000. A limitation to the current study is that only 40% of the

total number of recruits during the study time period donated blood, so this study could not assess the proportion of all basic trainees that may have tested positive for viral hepatitis. Although this study estimated a prevalence of HCV infection of 0.0065%, the Brett-Major study estimated a prevalence of 0.043%. It is likely that, if all recruits were screened rather than only those who donated blood, there would be more positive tests for HBV and HCV infection, but this approach would greatly increase the cost of screening. Based on these data, it is not possible to demonstrate a cost benefit for HCV screening in basic military trainees as was demonstrated in the Brett-Major study because a significant portion of the trainee population was not tested. However, this analysis does not factor in the potential long-term costs to the U.S. military health system of managing patients with liver complications due to HCV, such as HCC and/or cirrhosis, that may be associated with delayed diagnosis and treatment.

A significant limitation of the study is that it failed to include infected basic trainees who chose not to donate blood, leading to possible selection bias due to the healthy donor effect. Recruit trainee donors, when compared to the general population, tend to be younger, healthier, and likely exposed to fewer risk factors for acquisition of viral hepatitis. All of these factors may have potentially lowered the prevalence rates of HBV and HCV infection within the study population.

HBV and HCV infections can have a negative impact on mission readiness and individual deployment status, and have significant costs for the military. Currently, it is unclear whether routine screening for HBV and HCV infections would result in a cost benefit for the military healthcare system. Additional studies are needed to determine cost effectiveness of screening for viral hepatitis among military populations.

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Fatigue and Related Comorbidities, Active Component, U.S. Armed Forces, 2007–2016

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Fatigue is a common complaint in the civilian population and may be a presenting symptom of more serious physical and mental disorders. Data from the Defense Medical Surveillance System (DMSS) were utilized to characterize the incidence and burden of fatigue in active component military members from 1 January 2007 through 31 December 2016. A subanalysis of 3 years within this surveillance period (2012–2014) was also conducted to assess the burden of comorbidities related to incident fatigue and the strength of the association between fatigue and selected comorbidities. The study identified 211,213 incident cases of fatigue with an overall incidence rate of 18.1 per 1,000 person-years between 2007 and 2016. Mental disorders and musculoskeletal disease accounted for about 35% of all medical encounters and about 40% of all hospital days within a year for those diagnosed with fatigue in 2013. The adjusted odds ratio for fatigue was highest in those with male hypogonadism, thyroid disorder, and sleep problems. These results show that fatigue is a common diagnosis with high incidence and burden among active component U.S. military. By focusing on the conditions that frequently occur and are highly associated with fatigue, more rapid diagnosis and treatment of the underlying cause of service member fatigue is possible.

Fatigue is a term that describes exhaustion, tiredness, or a lack of energy to complete tasks, and can be the presenting symptom for underlying medical or psychological illnesses, such as depression, hypothyroidism, or anemia.[1] Fatigue is a common complaint at medical visits. In the U.S., 21%–33% of adult patients report a history of significant fatigue to their primary care physicians,[2-8] utilizing 7 million office visits per year.[9] The 2-week self-reported prevalence of fatigue among the U.S. workforce is 38%, costing employers more than $136 billion in lost productive work time annually.[10] Large burdens of fatigue in the U.S. military would likely equate to significant numbers of medical encounters and productivity loss as well.

Population-based surveys in the U.S. and U.K. have estimated a prevalence of fatigue between 6.0% and 7.5%.[1-5,11] The prevalence in women is generally higher than in men, and women comprise 75% of patients with Chronic Fatigue Syndrome (CFS).[1-5] Fatigue has also been reported to increase with age.[12]

With regard to both acute and persistent or chronic fatigue, one study found that acute fatigue (fatigue of less than 1 month duration) was more likely to be associated with a physical problem, most commonly a prolonged viral illness, while persistent fatigue (fatigue of 1–6 months duration) and chronic fatigue (fatigue of greater than 6 months duration) were more likely to be associated with psychological problems.[8] In a study of an adult primary care population, among patients who presented with a new diagnosis of fatigue, the most common diagnoses identified during follow-up were musculoskeletal disorders, followed by psychological or social causes (including depression and anxiety).[6, 13] Other relatively common diagnoses associated with fatigue were digestive symptoms (including irritable bowel syndrome), asthma or chronic obstructive pulmonary disease, sleep problems (including somnolence and insomnia), headache/dizziness, anemia, cough, hypothyroidism and diabetes. No medical or psychiatric explanation is found for fatigue in 8.5%–34% of patients who present with fatigue.[1-5]

The incidences of many of the fatigue-associated diagnoses noted above have been reported for service members in the active component of the U.S. military. Among these diagnoses, musculoskeletal disease and mental health disorders occur most frequently, followed by headache, obstructive sleep apnea, thyroid disease, asthma, insomnia, iron-deficient anemia, and diabetes.[14-15] Malignancy and HIV or hepatitis infections were reported less frequently as potential causes of fatigue.[16-30] At the time of this report, no recent studies of the prevalence or incidence of fatigue in the U.S. military were available in the published literature.

Quantification of the incidence and burden of fatigue in U.S. military service members will inform efforts to prevent and investigate causes of fatigue. Furthermore, classification of the diseases most commonly associated with fatigue in the military would assist in more rapid diagnosis and treatment of underlying causes, which could improve readiness of service members.

METHODS

All data used to determine incident cases of fatigue, the morbidity burden of fatigue, and associated comorbidities and their burdens were derived from the Defense Medical Surveillance System (DMSS). DMSS records document both ambulatory encounters and hospitalizations of active component members of the U.S. Armed Forces in fixed military and civilian (if reimbursed through the Military Health System) treatment facilities. The surveillance population included all individuals who served at any time during the surveillance period in the active component of the Army, Navy, Air Force, or Marine Corps.

For determining the incidence of fatigue and the burden of fatigue, the surveillance period was 1 January 2007 through 31 December 2016. The study design used to determine incidence of fatigue was a retrospective cohort study. An incident case of fatigue was defined by a record of one ambulatory visit or one hospitalization with a diagnosis of fatigue in any diagnostic position. The ICD-9/ICD-10 codes used to define a case of fatigue were 780.7 and R53 (malaise and fatigue); 780.79 and R53.8 (other malaise and fatigue); R53.81 (other malaise); R53.82 (chronic fatigue unspecified); and R53.83 (other fatigue). An individual could be an incident case only once during his or her lifetime. Diagnoses of fatigue that were recorded in a theater of operations were not included. Follow-up time was censored during periods of deployment and at the time of service members' incident fatigue diagnoses or departures from military service, whichever came first.

The morbidity burden attributable to fatigue was based on the number of medical encounters attributable to fatigue (i.e., encounters in which fatigue was listed in the primary diagnostic position). The measures of burden included total encounters (both hospital and ambulatory encounters) for fatigue with a limit of one encounter per individual with a diagnosis of fatigue per day; number of service members affected by fatigue (i.e., individuals with at least one medical encounter for fatigue during the year); and total bed days during hospitalizations for fatigue.

To determine which comorbid diagnoses may be associated with fatigue, a burden of comorbidities analysis was conducted among those with incident fatigue in 2013. The diseases with the highest burdens, as well as those that appeared to be more common in those with fatigue compared to prior *MSMR* reports for the entire active component,[14] were then used as exposure variables for a case-control study of fatigue cases versus non-fatigue cases. For both the burden analysis and the case-control study, a narrower surveillance period (1 January 2012 through 31 December 2014) was used, as this period was assumed to be fairly representative of the entire study period and allowed for simpler summarization of comorbidities using ICD-9 codes only. Diagnoses from all inpatient and outpatient medical encounters up to 365 days before or after incident fatigue cases occurring in 2013 were summarized according to the primary (first-listed non-V or non-E code) diagnosis (if reported with an ICD-9 code between 001 and 999 excluding the ICD-9 codes used to define fatigue). Numbers of service members affected and numbers of bed days were also summarized for each primary diagnosis. All diagnostic comorbidities were summarized using ICD-9 codes at the four-digit level, and were additionally grouped according to the categories of disease used in prior burden issues of the *MSMR*.[14] The 365-day before-and-after window was selected because it was deemed wide enough to capture many comorbidities but narrow enough to exclude comorbidities that are less likely to be connected with the diagnosis of fatigue. The window also allowed for the possibility of a patient presenting with fatigue and being diagnosed with a potential cause of the fatigue at a follow-up encounter, as well as the possibility of a diagnosed disease being associated with a fatigue diagnosis at a later time. The authors also investigated the burden of comorbidities stratified by those diagnosed before, after, or on the day of fatigue diagnoses, but there was little variation among these groups and so those results are not reported here.

The case-control subanalysis was conducted on the subset of incident fatigue cases that occurred during 2013. Fatigue cases were matched 1:1 to controls based on age and sex. All inpatient and outpatient medical encounters up to 365 days before or after incident diagnoses of fatigue (for both cases and matched controls) were included in the analysis. Cases or controls who were deployed within 365 days of the date of the case's incident fatigue diagnosis were excluded. Pearson chi-square tests were used to compare demographic characteristics between cases and controls. In addition, a multivariable logistic regression analysis was used to determine the odds ratios (ORs) and confidence intervals (CIs) for the relationships between investigator-selected comorbid diagnoses (in any diagnostic position), which were the exposures of interest **(Table 1)**, and fatigue, the outcome of interest. Potential confounding factors, including race/ethnicity, branch of military service, rank/grade, and occupation, were adjusted for in the analysis. All analyses were performed using SAS/STAT© software, version 9.4 (2014, SAS Institute, Cary, NC).

RESULTS

During the surveillance period 1 January 2007 through 31 December 2016, a total of 211,213 active component service members were diagnosed with incident fatigue. The surveillance period consisted of 11,642,948 person-years, and the overall incidence rate during the surveillance period was 18.1 cases (according to the case definition) of fatigue per 1,000 person-years (p-yrs) **(Table 2).**

During 2007–2012, rates of fatigue increased by about 50% (2007: rate = 13.8 cases per 1,000 p-yrs; 2012: rate = 21.0 cases per 1,000 p-yrs) before leveling off for a few years and then declining during 2015–2016. The rate in 2016 was approximately 30% higher than in 2007 (2016: rate = 17.7 cases per 1,000 p-yrs) **(Figure 1)**. Similar patterns of time trends were observed for the annual incidence rates according to service branch and history of deployments **(Figures 2 and 3).**

The overall incidence rate during the surveillance period was highest among

TABLE 1. Selected diagnoses and diagnosis groups used as exposures in logistic regression model to determine odds of fatigue versus no fatigue in a case-control study of those with incident fatigue in 2013 (cases) and age/sex-matched controls who did not have fatigue through the end of the study period, active component, U.S. Armed Forces, 2012–2014

Diagnoses	ICD-9 codes
Musculoskeletal diseases	719.4, 724.2, 723.1, 729.5, 724.5, 728.8, 724.1, 722.5, 722.1
Mental health disorders	309.8, 300.0, 309.2, 311, 296.3, 296.2, 309.0, 309.9
Organic sleep apnea	327.2
Abdominal/digestive symptoms	789.0, 787.0, 558.9, 530.8, 564.0, 564.1
Headache or dizziness	784.0, 346.9, 339.8, 780.4, 346.0, 346.1, 339.1
Cardiovascular sysmptoms	786.5, 780.2, 785.1, 796.2
Hypertension	401.9
Sleep disturbance	780.5, 307.4
Alcohol dependence	303.9
Tobacco use disorder	305.1
Asthma	493.9
Respiratory symptoms	786.0, 786.2
Overweight/obese	278
Hyperlipidemia	272.4
Malignancy	186.9, 204.0, 174.9, 239.2, 201.9, 193, 202.8, 205.0
Male hypogonadism	257.2
Thyroid disease	244.9, 242.9
Diabetes	250
Anemia	285.9, 280.9

women, who had more than double the rates of fatigue compared to men (women: rate = 35.5 cases per 1,000 p-yrs; men: rate = 15.3 cases per 1,000 p-yrs) **(Table 2, Figure 1)**. The incidence rates increased with age and higher rank, with service members in the oldest age category having a rate of fatigue more than three times that of service members in the youngest age category (less than 20 years old: 11.0 cases per 1,000 p-yrs; 40 years or older: 35.2 cases per 1,000 p-yrs). Senior enlisted service members had a 59% higher rate of fatigue than junior enlisted service members over the surveillance period (junior enlisted: 14.1 cases per 1,000 p-yrs; senior enlisted: 22.4 cases per 1,000 p-yrs), while senior officers had a 40% higher rate of fatigue than junior officers (junior officer: 17.5 cases per 1,000 p-yrs; senior officer: 24.6 cases per 1,000 p-yrs) **(Table 2).** The rates of fatigue among Army and Air Force members were roughly double the rates among Navy and Marine Corps service members; non-Hispanic blacks had higher rates of fatigue than those in other race/ethnicity groups, and healthcare workers had the highest rates of fatigue among the occupations considered, while pilots/air crew and combat personnel had the lowest rates **(Table 2)**. During the early years of the surveillance period (up to 2009), annual incidence rates were similar for service members with different deployment histories. However, by 2016, those with two or more deployments had approximately double the rate of fatigue compared to those with no prior deployments (no deployments: 12.9 cases per 1,000 p-yrs; two or more deployments: 26.3 cases per 1,000 p-yrs) **(Figure 3)**.

Burden of fatigue, 2007–2016

From 1 January 2007 through 31 December 2016, a total of 112,014 service members received medical care for fatigue **(Table 3)** over 11,642,948 p-yrs **(data not shown)**. The care of these service members entailed 162,796 medical encounters for which a fatigue diagnosis was recorded in the first diagnostic position of the associated records, and included a total of 708 bed days among hospitalized patients **(Table 3).** Broadly similar to the trend for the incidence of fatigue, the number of medical encounters and individuals affected increased until 2013, then decreased during 2014–2016 **(Figure 4).**

Comorbidity burden, 2012–2014

From 1 January 2012 through 31 December 2014, among service members diagnosed with fatigue during 2013, the most medical encounters within 365 days before or after the incident diagnosis were for pain in a joint (n=97,058; 8.9% of all encounters), followed by other ill-defined conditions (n=69,970, 6.4% of all encounters), lumbago (n=51,995, 4.7% of all encounters), other specified adjustment reactions (n=42,815, 3.9% of all encounters) and organic sleep apnea (n = 41,894, 3.8% of all encounters) **(Table 4)**. Pain in a joint also accounted for the most individuals affected (n=12,585, 3.5% of all individuals affected). Other specified adjustment reactions accounted for the most bed days (n=5,179, 9% of all hospital bed days) **(Table 4)**. The distribution of burden indicators for all categories of diseases (which combines related conditions) can be seen in **Figure 5.** Together, mental disorders and musculoskeletal diseases accounted for about 35% of all medical encounters and about 44% of all hospital days **(Figures 5 and 6).**

In the case-control analysis, there was a sample size of roughly 34,000 matched cases and controls. The distribution of demographic characteristics was broadly similar between cases and controls **(Table 5)**. However, the differences that emerged warranted inclusion of these characteristics in the multivariable model used to calculate adjusted ORs (AORs) **(Table 6)**.

The adjusted odds of fatigue were greater for males with hypogonadism, compared to those without hypogonadism (AOR: 6.79: CI: 5.24–8.82), followed by service members with thyroid disorders (AOR=2.68; 95% CI: 2.24–3.20) or sleep problems (AOR=2.15; 95% CI: 2.00–2.32), compared to those without these respective

TABLE 2. Incident diagnoses and incidence rates of fatigue, active component, U.S. Armed Forces, 2007–2016

	2007–2016	
	No	Rate[a]
Total	211,213	18.1
Sex		
Male	153,587	15.3
Female	57,626	35.5
Race/ethnicity		
Non-Hispanic white	126,922	17.9
Non-Hispanic black	40,636	22.1
Hispanic	23,750	16.3
Other/unknown	19,905	16.0
Age		
<20	16,991	11.0
20–24	39,580	12.7
25–29	46,849	16.8
30–34	34,534	19.7
35–39	32,538	25.3
40+	40,721	35.2
Service		
Army	92,602	21.8
Navy	37,099	12.9
Air Force	63,828	22.8
Marine Corps	17,684	10.2
Military rank/grade		
Junior enlisted (E1–E4)	73,876	14.1
Senior enlisted (E5–E9)	99,583	22.4
Junior officer (O1–O4)	25,680	17.5
Senior officer (O5–O10)	8,443	24.6
Warrant officer (W01–W05)	3,631	24.3
Military occupation		
Combat-specific[b]	23,763	14.3
Motor transport	5,472	15.9
Pilot/air crew	5,159	11.6
Repair/engineering	53,763	15.7
Communications/ intelligence	55,659	22.2
Health care	27,706	28.0
Other/unknown	39,691	17.5
Previous deployments		
0	85,489	15.1
1	54,945	19.0
2+	70,779	22.9

[a]Rate per 1,000 person-years
[b]Infantry/artillery/combat engineering

FIGURE 1. Annual incidence rates of fatigue, by sex, active component, U.S. Armed Forces, 2007–2016

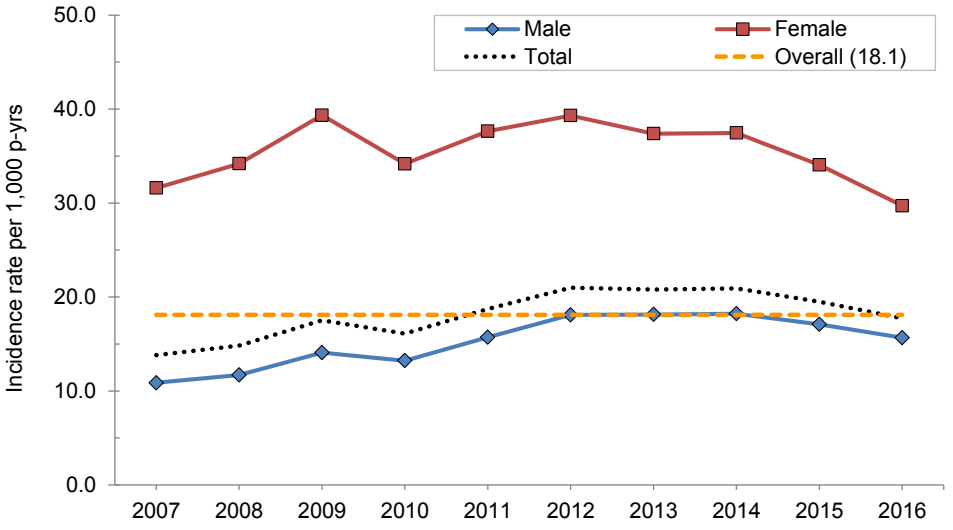
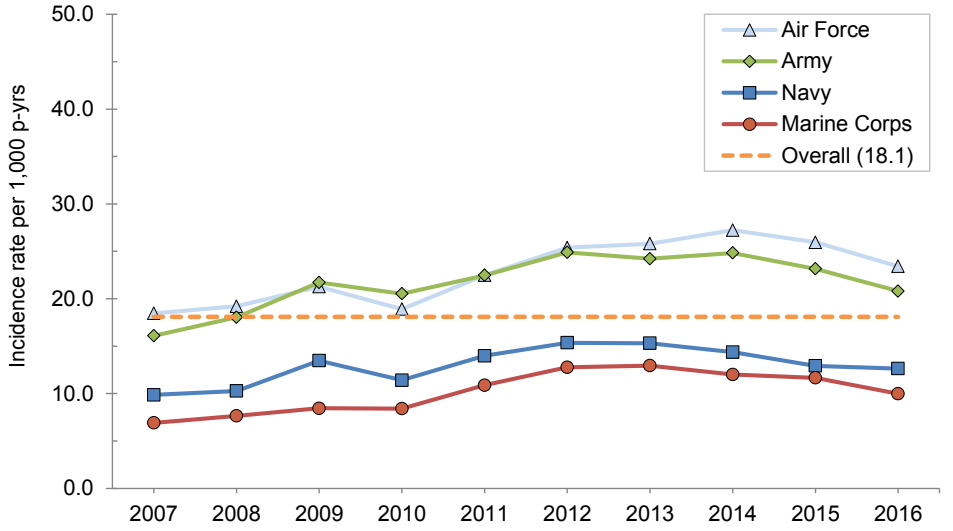


FIGURE 2. Annual incidence rates of fatigue, by service, active component, U.S. Armed Forces, 2007–2016



comorbidities. The complete list of AORs for selected comorbidities diagnosed within 365 days of incident diagnoses of fatigue in 2013 is shown in **Table 6** and visually displayed in **Figure 7**.

EDITORIAL COMMENT

This report documents the counts, rates, and trends of incident diagnoses of fatigue, as well as the burden of fatigue and comorbidities among active component military personnel during 2007–2016. Fatigue is a frequently occurring diagnosis among the active component U.S. military, appearing for the first time in about two out of every 100 previously unaffected service members per year.

In the current study, women were disproportionately affected by fatigue; this observation may be due to the higher rates of mental disorder diagnoses among female service members, as well as higher

FIGURE 3. Annual incidence rates of fatigue, by number of deployments, active component, U.S. Armed Forces, 2007–2016

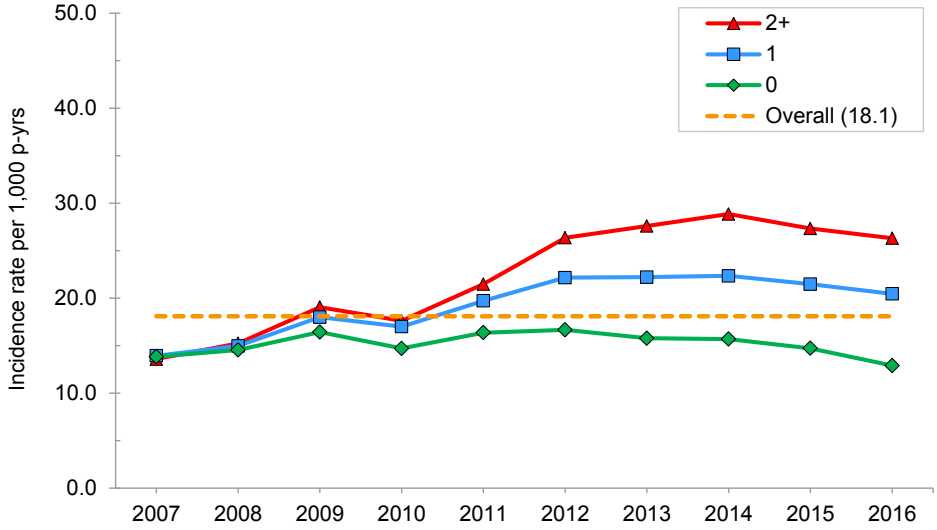


TABLE 3. Healthcare burdens attributable to fatigue, active component, U.S. Armed Forces, 2007–2016

Year	Medical encounters	Individuals affected	Bed days
2007	12,059	9,730	40
2008	13,604	10,820	110
2009	16,483	12,951	53
2010	18,324	14,254	66
2011	19,839	14,994	106
2012	20,979	15,857	103
2013	21,106	16,420	48
2014	20,690	16,239	83
2015	18,945	14,789	64
2016	16,861	13,289	51
Total	162,796	112,014	708

incidences of headaches, thyroid disorders, anemia and even low back pain.[16-20,23] This finding is consistent with studies in civilian populations that show women are at increased risk for fatigue.[1-5] Fatigue increased with age among service members, a trend that is also consistent with studies among civilians.[12] This observation could reflect increased incidence of underlying diseases among older service members, rather than a simple consequence of older age, and the presence of such conditions should be considered in older patients with fatigue. For example, depression, pain, respiratory symptoms, urinary incontinence, hearing difficulty and social isolation have all been shown to be independent risk factors for fatigue in older adults.[12]

The trend showing an increased annual incidence of fatigue among active component service members from 2007 through 2012 coincides with military engagements Operation Enduring Freedom–Afghanistan (OEF-A) from 2001 through 2014 and Operation Iraqi Freedom (OIF) from 2003 through 2011, and similar increases can be seen in the incidence rates of other disorders, especially mental disorders.[18] These increases could reflect increased stressors that accompanied engagement-related deployments, an interpretation that is further supported by the decrease in incident rates from 2015 through 2016, after both

FIGURE 4. Numbers of medical encounters, individuals affected, and hospital bed days for fatigue, by calendar year, active component, U.S. Armed Forces, 2007–2016

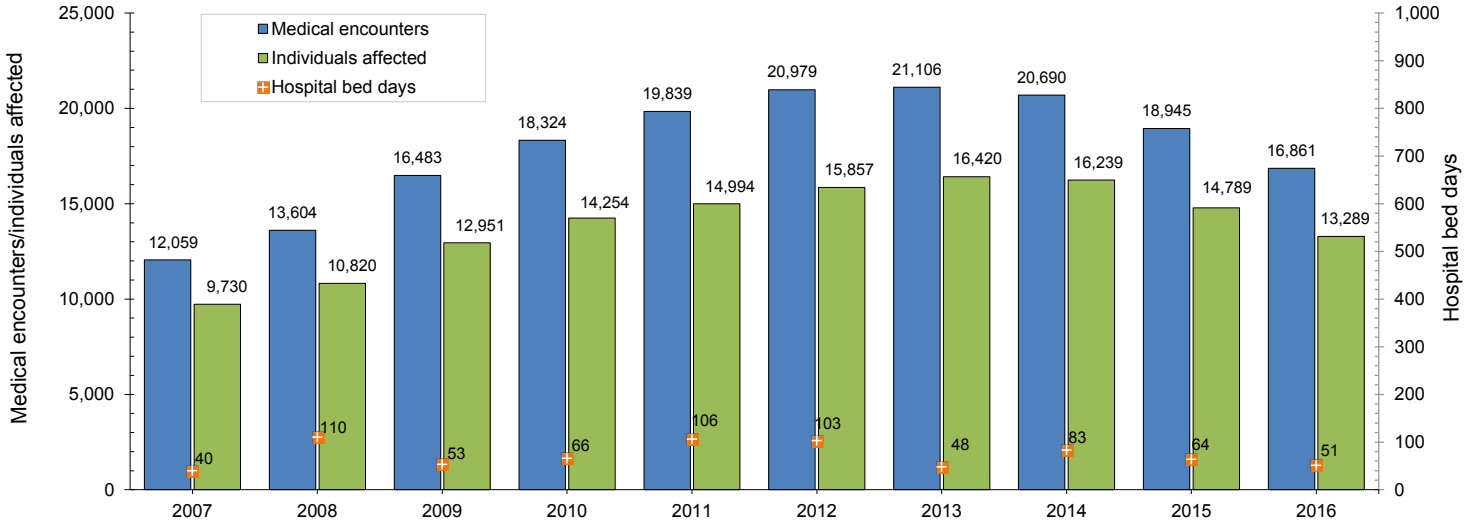


TABLE 4. Burden of most frequent comorbidities among 2013 incident fatigue cases within 365 days of incident fatigue diagnosis (inclusive), active component, U.S. Armed Forces, 2012–2014

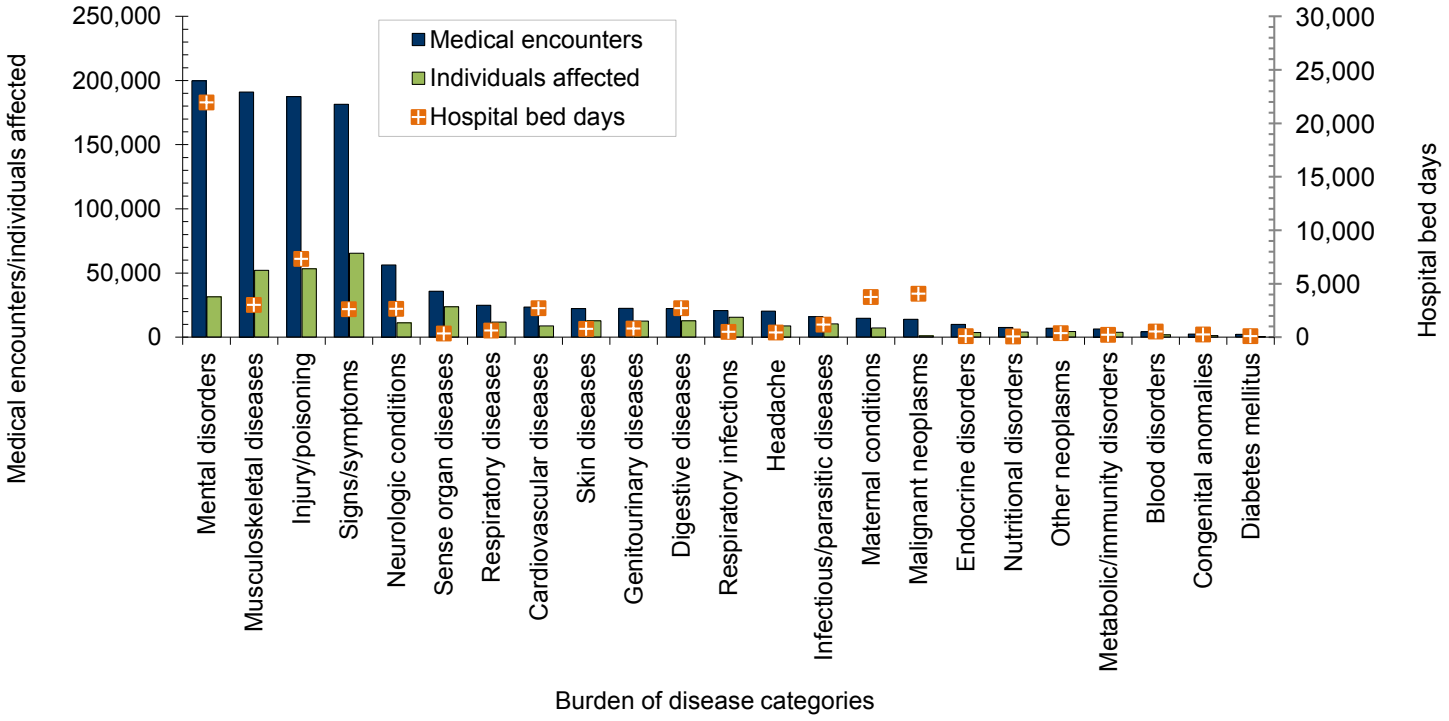
Condition	No. encounters[a]	Rank	% of all encounters	No. service members affected[b]	Rank	% service members affected	Bed days	Rank	Burden category[c]
Joint pain	97,058	1	8.86	12,585	1	3.49	75	109	Injury and poisoning
Other ill-defined conditions	69,970	2	6.39	11,026	2	3.06	1	180	Signs and symptoms
Lumbago	51,995	3	4.75	7,823	3	2.17	77	107	Musculoskeletal diseases
Other specified adjustment reactions	42,815	4	3.91	2,230	25	0.62	5,179	1	Mental disorders
Organic sleep apnea	41,894	5	3.83	6,325	5	1.76	71	113	Neurologic conditions
Anxiety states	22,834	6	2.09	3,759	11	1.04	503	16	Mental disorders
Adjustment reaction with predominant disturbance of other emotions	20,942	7	1.91	3,440	14	0.95	643	10	Mental disorders
Sleep disturbances	16,595	8	1.52	7,392	4	2.05	11	170	Signs and symptoms
Cervicalgia	15,990	9	1.46	3,119	16	0.87	3	178	Musculoskeletal diseases
Depressive disorder, not elsewhere classified	15,517	10	1.42	2,972	18	0.82	971	5	Mental disorders
Major depressive disorder, recurrent episode	14,230	11	1.30	1,157	57	0.32	2,758	3	Mental disorders
Other and unspecified alcohol dependence	13,627	12	1.24	574	120	0.16	2,847	2	Mental disorders
Pain in limb	12,740	13	1.16	4,909	9	1.36	13	168	Musculoskeletal diseases
Abdominal pain	10,922	14	1.00	4,432	10	1.23	243	38	Signs and symptoms
Myopia	9,290	15	0.85	5,868	6	1.63	0	-	Sense organ diseases
Dyspnea and respiratory abnormalities	9,099	16	0.83	5,007	8	1.39	21	160	Signs and symptoms
Chest pain	7,994	17	0.73	3,522	13	0.98	280	33	Signs and symptoms
Major depressive disorder, single episode	7,854	18	0.72	955	74	0.27	1,518	4	Mental disorders
Adjustment disorder with depressed mood	7,622	19	0.70	1,724	37	0.48	619	12	Mental disorders
Acute upper respiratory infections of unspecified site	7,378	20	0.67	5,334	7	1.48	5	176	Respiratory infections
Backache, unspecified	7,293	21	0.67	2,774	21	0.77	26	155	Musculoskeletal diseases
Headache	6,925	22	0.63	3,629	12	1.01	98	89	Headache
Other disorders of muscle ligament and fascia	6,919	23	0.63	1,945	30	0.54	623	11	Musculoskeletal diseases
Pain in thoracic spine	6,717	24	0.61	2,056	27	0.57	1	180	Musculoskeletal diseases
Other general symptoms	6,666	25	0.61	1,591	43	0.44	48	133	Signs and symptoms
Unspecified adjustment reaction	6,492	26	0.59	1,945	30	0.54	192	50	Mental disorders
Unspecified essential hypertension	6,129	27	0.56	2,398	23	0.67	81	104	Cardiovascular diseases
Degeneration of thoracic or lumbar intervertebral disc	6,123	28	0.56	1,686	39	0.47	177	57	Musculoskeletal diseases
Displacement of thoracic or lumbar intervertebral disc without myelopathy	5,871	29	0.54	1,492	47	0.41	391	20	Musculoskeletal diseases
Overweight/obese	5,677	30	0.52	2,880	19	0.80	0	-	Nutritional disorders

[a]Medical encounters: total hospitalizations and ambulatory visits for the condition (with no more than one encounter per individual per day per condition)

[b]Individuals with at least one hospitalization or ambulatory visit for the condition

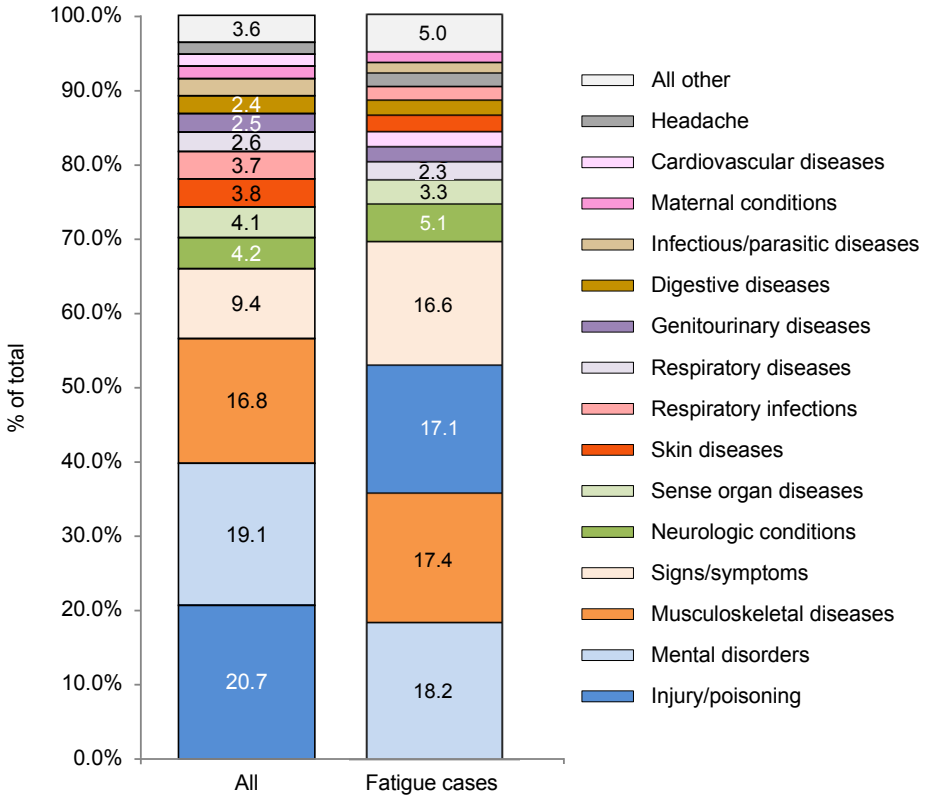
[c]Major categories and conditions defined in the Global Burden of Disease Study, The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Murray, CJ and Lopez, AD, eds. Harvard School of Public Health (on behalf of the World Health Organization and The World Bank), 1996:120–122.

FIGURE 5. Numbers of medical encounters,[a] individuals affected,[b] and hospital bed days during 2012–2014, by burden of disease category,[c] active component service members with incident fatigue in 2013, U.S. Armed Forces



[a]Medical encounters: total hospitalizations and ambulatory visits for the condition (with no more than one encounter per individual per day per condition)
[b]Individuals with at least one hospitalization or ambulatory visit for the condition
[c]Major categories and conditions defined in the Global Burden of Disease Study[34]

FIGURE 6. Percentage of medical encounters, attributable to burden of disease categories, active component, U.S. Armed Forces, 2013, and for active component service members with incident fatigue in 2013, during 2012–2014



operations had ended. Alternatively, this decrease from 2015 through 2016 could be the result of changes in coding patterns with the introduction of ICD-10 codes in late 2015.

Fatigue accounts for a large healthcare burden in the active component military. For instance, in 2016, about 13,000 unique service members had at least one healthcare encounter during which a diagnosis of fatigue was recorded in the first diagnostic position. Those service members had about 17,000 such encounters during the year (average of 46 per day) and the encounters were associated with 51 hospital bed days (average of 4 per month). The relatively low number of bed days reflects the fact that fatigue is mostly diagnosed and treated in the outpatient setting. Comparing these burden data to prior *MSMR* data, the burden of fatigue in 2016 among the active component U.S. military was on par with the burden of benign skin neoplasms and kidney stones, and would rank No. 60 overall (out of nearly 4,000 conditions) on the list of most burdensome conditions reported in 2016.[15]

TABLE 5. Characteristics of nested case-control study population, active component, U.S. Armed Forces, 2012–2014

	Fatigue		No fatigue		Overall		
	N	%	N	%	N	%	p-value
Total	16,969	100	16,969	100	33,938	100	
Race/ethnicity							
Non-Hispanic white	10,221	60	10,031	59	20,252	60	<.0001
Non-Hispanic black	3,081	18	2,954	17	6,035	18	
Hispanic	1,947	11	2,018	12	3,965	12	
Other/unknown	1,720	10	1,966	12	3,686	11	
Service							
Army	7,053	42	6,497	38	13,550	40	<.0001
Air Force	3,078	18	4,045	24	7,123	21	
Navy	5,179	31	4,374	26	9,553	28	
Marine Corps	1,659	10	2,053	12	3,712	11	
Military rank/grade							
Junior enlisted (E1–E4)	5,472	32	5,412	32	10,884	32	<.0001
Senior enlisted (E5–E9)	8,516	50	7,498	44	16,014	47	
Junior officer (O1–O4)	1,974	12	2,716	16	4,690	14	
Senior officer (O5–O10)	730	4	1,036	6	1,766	5	
Warrant officer (W01–W05)	277	2	307	2	584	2	
Military occupation							
Combat-specific[a]	1,812	11	2,006	12	3,818	11	<.0001
Motor transport	432	3	417	2	849	3	
Pilot/air crew	408	2	774	5	1,182	3	
Repair/engineering	4,335	26	4,506	27	8,841	26	
Communications/intelligence	4,355	26	4,028	24	8,383	25	
Health care	2,434	14	2,046	12	4,480	13	
Other/unknown	3,193	19	3,192	19	6,385	19	

Note: Covariates are the values at time of fatigue diagnosis.
[a]Infantry/artillery/combat engineering
[b]Infantry/artillery/combat engineering

In the comorbidity analysis, mental disorders and musculoskeletal diseases accounted for the highest disease-related burdens among those with incident fatigue (each found in greater than 5% of patients with fatigue), and they were both independently associated with fatigue in the case-control study. These categories of disease have been reported to be the top two causes of fatigue in civilians.[6]

Sleep problems, obstructive sleep apnea, headache, respiratory, abdominal and cardiovascular symptoms, and tobacco use disorder were each found in about 1%–5% of patients with fatigue and were also independently associated with fatigue in the case-control study. Male hypogonadism, thyroid disorders, anemia, malignancy, and hyperlipidemia were found in less than 1% of those with fatigue **(data not shown)** but were independently associated with fatigue. Based on these findings, clinicians might be able to better diagnose underlying causes of fatigue by asking questions about the diseases and symptom groups for all of these aforementioned conditions.

Highly-associated conditions like thyroid disorder, sleep problems and anemia, should always be a part of a clinician's differential diagnosis (though they may not occur commonly), as should malignancy, which is a diagnosis that can cause substantially greater morbidity and mortality if undetected.[31]

Study limitations include the definition for fatigue, which allowed only one incident case of fatigue per service member in a lifetime. In reality, individuals may have multiple incident cases of fatigue due to disparate etiologies, but such information was not captured. There was also the potential for differential misclassification of fatigue by providers. For example, providers may be more likely to document fatigue in a patient with a disease known to cause fatigue, such as hypothyroidism, than in a patient without such a disease.

In addition, there may have been confounding by time in service or low socioeconomic status (shown to be associated with greater levels of fatigue[32]), which were not controlled for in these analyses. Finally, the comorbidities assessed may or may not have been the causes of fatigue. Moreover, because this analysis did not attempt to distinguish between causes and effects of fatigue, it was not possible to clarify the issue of whether or not an associated comorbidity such as depression was the cause or effect of fatigue or if they had a common cause.[33]

In summary, fatigue is a common diagnosis with high incidence and burden among service members in the active component of the U.S. military. Several comorbid diagnoses are associated with fatigue, providing a list of potential causes of fatigue when its origin is unclear. This list could be used to guide investigations of the cause of fatigue. By focusing on the most frequent and highly associated conditions, clinicians have the opportunity to more rapidly diagnose and treat the underlying cause of service member fatigue, which would likely lead to fewer lost work days and improved readiness.

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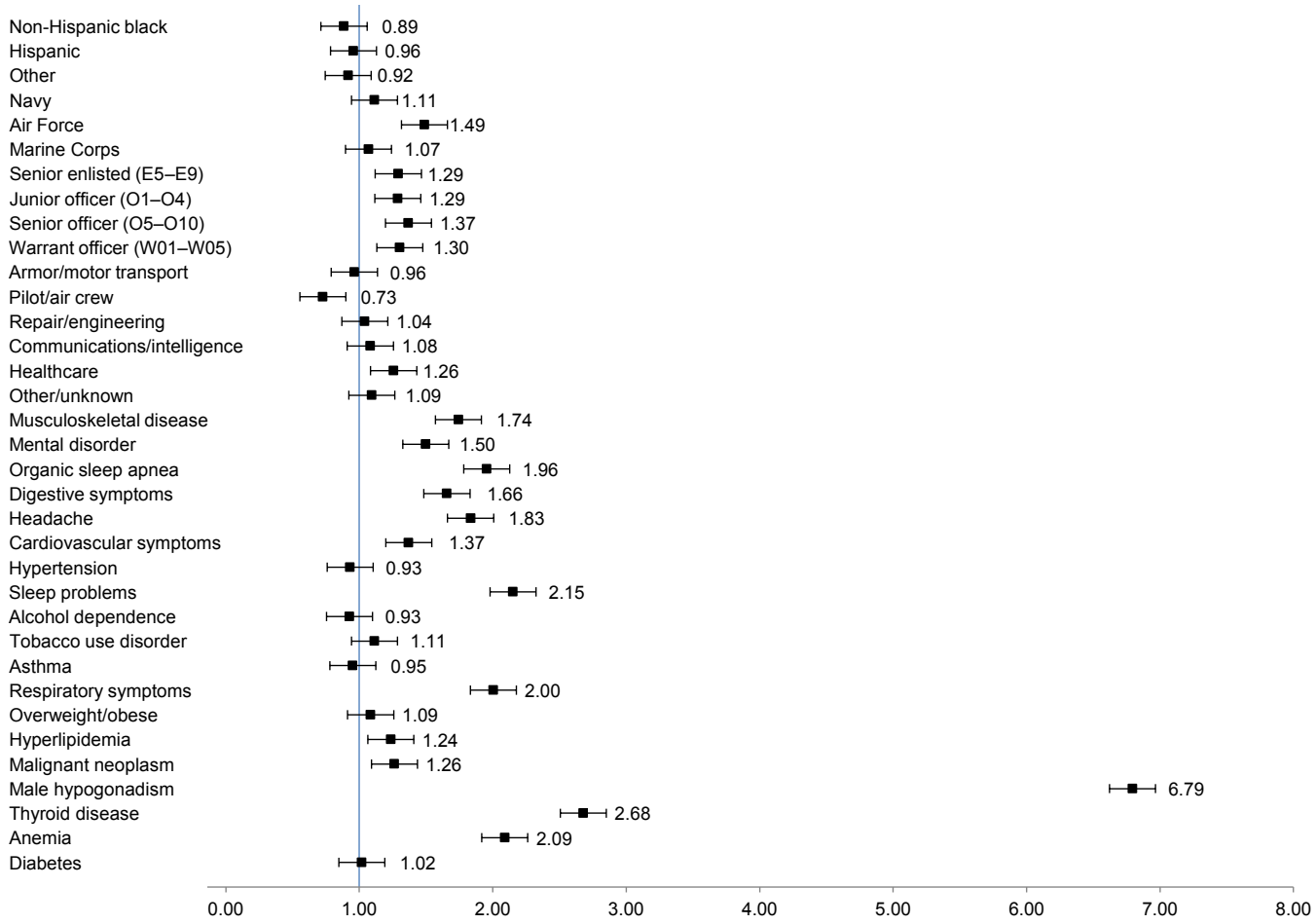
TABLE 6. Crude and adjusted odds ratios (AORs) for fatigue among age- and sex-matched cases and controls, by subgroup, active component, U.S. Armed Forces, 2012–2014

Variable	Crude OR	95% CI	p-value	AOR	95% CI	p-value
Total						
Race/ethnicity						
White, non-Hispanic	ref	-	-	ref	-	-
Black, non-Hispanic	1.02	0.97–1.09	.431	0.89	0.82–0.96	.002
Hispanic	0.95	0.89–1.01	.120	0.96	0.88–1.04	.321
Other	0.86	0.80–0.92	<.0001	0.92	0.84–1.00	.062
Service						
Army	ref	-	-	ref	-	-
Navy	0.70	0.66–0.74	.009	1.11	1.03–1.21	.008
Air Force	1.09	1.04–1.15	<.0001	1.49	1.38–1.60	<.0001
Marine Corps	0.74	0.69–0.80	<.0001	1.07	0.97–1.18	.174
Military rank/grade						
Junior enlisted (E1–E4)	ref	-	-	ref	-	-
Senior enlisted (E5–E9)	1.09	1.02–1.17	.043	1.29	1.18–1.41	<.0001
Junior officer (O1–O4)	0.70	0.64–0.76	<.0001	1.29	1.15–1.44	<.0001
Senior officer (O5–O10)	0.60	0.53–0.69	.001	1.37	1.15–1.63	<.001
Warrant officer (W01–W05)	0.83	0.69–0.99	<.0001	1.30	1.03–1.66	.030
Military occupation						
Combat-specific[a]	ref	-	-	ref	-	-
Motor transport	1.16	1.00–1.35	.049	0.96	0.79–1.17	.711
Pilot/air crew	0.58	0.50–0.66	<.0001	0.73	0.60–0.87	.001
Repair/engineering	1.08	1.00–1.16	.061	1.04	0.94–1.16	.451
Communications/intelligence	1.23	1.13–1.33	<.0001	1.08	0.97–1.20	.144
Health care	1.37	1.25–1.50	<.0001	1.26	1.11–1.42	<.001
Other/unknown	1.12	1.04–1.22	.005	1.09	0.98–1.22	.113
Musculoskeletal disorders						
No	ref	-	-	ref	-	-
Yes	2.96	2.81–3.12	<.0001	1.74	1.64–1.86	<.0001
Mental disorders						
No	ref	-	-	ref	-	-
Yes	3.23	3.06–3.41	<.0001	1.50	1.40–1.61	<.0001
Obstructive sleep apnea						
No	ref	-	-	ref	-	-
Yes	4.86	4.51–5.24	<.0001	1.96	1.78–2.15	<.0001
Abdominal/digestive symptoms						
No	ref	-	-	ref	-	-
Yes	2.76	2.63–2.90	<.0001	1.66	1.56–1.76	<.0001
Headache						
No	ref	-	-	ref	-	-
Yes	3.40	3.21–3.61	<.0001	1.83	1.71–1.97	<.0001
Cardiovascular symptoms						
No	ref	-	-	ref	-	-
Yes	2.50	2.36–2.63	<.0001	1.37	1.28–1.47	<.0001
Hypertension						
No	ref	-	-	ref	-	-
Yes	1.89	1.75–2.03	<.0001	0.93	0.84–1.03	.155
Sleep disturbance						
No	ref	-	-	ref	-	-
Yes	4.83	4.55–5.13	<.0001	2.15	2.00–2.32	<.0001
Alcohol dependence						
No	ref	-	-	ref	-	-
Yes	1.94	1.67–2.26	<.0001	0.93	0.76–1.13	.448
Tobacco use disorder						
No	ref	-	-	ref	-	-
Yes	1.69	1.59–1.79	<.0001	1.11	1.03–1.20	.005
Asthma						
No	ref	-	-	ref	-	-
Yes	2.30	2.03–2.60	<.0001	0.95	0.81–1.12	.534
Respiratory symptoms						
No	ref	-	-	ref	-	-
Yes	3.94	3.71–4.19	<.0001	2.00	1.86–2.16	<.0001
Overweight/obese						
No	ref	-	-	ref	-	-
Yes	1.98	1.87–2.11	<.0001	1.09	1.00–1.17	.044
Hyperlipidemia						
No	ref	-	-	ref	-	-
Yes	1.79	1.67–1.93	<.0001	1.24	1.12–1.36	<.0001
Malignant neoplasms						
No	ref	-	-	ref	-	-
Yes	1.76	1.52–2.04	<.0001	1.26	1.04–1.53	.018
Male hypogonadism						
No	ref	-	-	ref	-	-
Yes	9.98	7.95–12.52	<.0001	6.79	5.24–8.82	<.0001
Thyroid disease						
No	ref	-	-	ref	-	-
Yes	3.62	3.13–4.18	<.0001	2.68	2.24–3.20	<.0001
Blood disorders						
No	ref	-	-	ref	-	-
Yes	2.75	2.44–3.11	<.0001	2.09	1.79–2.44	<.0001
Diabetes						
No	ref	-	-	ref	-	-
Yes	2.17	1.75–2.69	<.0001	1.02	0.77–1.35	.896

[a]Infantry/artillery/combat engineering

FIGURE 7. Adjusted[a] odds ratios for fatigue among age- and sex-matched cases and controls, by selected characteristics and comorbidities, active component, U.S. Armed Forces, 2012–2014



[a]Adjusted for all covariates in this table, as well as race, rank, and occupation; refence groups are those without conditions listed.

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