JANUARY 2021

Volume 28
Number 01

MSMR

MEDICAL SURVEILLANCE MONTHLY REPORT

Attrition Rates and Incidence of Mental Health Disorders in an Attention-Deficit/Hyperactivity Disorder (ADHD) Cohort, Active Component, U.S. Armed Forces, 2014–2018

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Attention-deficit/hyperactivity disorder (ADHD) is a common childhood diagnosis and affects the pool of potential military applicants. Early detection and treatment of ADHD may decrease the risk of developing comorbidities; however, accession policy in place during this study period (2014–2018) disqualified applicants who used ADHD medication for more than 24 months cumulative after age 14. The objective of this study was to assess attrition from military service in newly accessed active component service members diagnosed with ADHD as compared to controls. In addition, attrition rates and incidence rates of mental health diagnoses were assessed in service members with ADHD by treatment status (i.e., treated vs untreated ADHD) where treatment was defined as being dispensed an FDA-approved ADHD medication at least twice within 181 days. Almost two-thirds (64.8%) of newly accessed ADHD cases in 2014 were identified after enlistment medical screening at Military Entrance Processing Stations (MEPS) (i.e., post-MEPS). These post-MEPS ADHD cases accounted for 99.1% of the treated ADHD cases. The vast majority of treated cases (91.0%) were dispensed ADHD medication within 6 months of accession. The treated ADHD group had higher rates of attrition and incidence of mental health disorders during the follow-up period. These study findings highlight the problem of nondisclosure of ADHD among military applicants. Future changes to enlistment standards should consider the optimal way to promote applicant disclosure of ADHD during MEPS screening or for medical waiver review and should discourage withholding an ADHD diagnosis during enlistment.

WHAT ARE THE NEW FINDINGS?

The majority of new military accessions in 2014 with documented ADHD diagnoses within their first year of service were not detected during their MEPS screening physical exam (64.8%), suggesting many new accessions do not disclose previous ADHD diagnoses during enlistment. New accessions in 2014 with ADHD diagnoses who received a prescription for ADHD medication started medication quickly (91.0% within 6 months) and had higher rates of attrition from service and higher incidence rates of comorbid mental health disorders than their untreated ADHD counterparts.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Due to its high prevalence in the U.S. general population, ADHD impacts the pool of military applicants. Future changes to enlistment standards should consider how to optimize or incentivize applicant disclosure of a pre-existing ADHD diagnosis during MEPS screening or service specific medical waiver review and discourage withholding an ADHD diagnosis during enlistment.

Attention-deficit/hyperactivity disorder (ADHD) is a common diagnosis in childhood, characterized by persistent impairing inattention, hyperactivity, and impulsivity. Symptoms are usually recognized in patients before the age of 12.[1] Estimates for the prevalence of ADHD in U.S. children 2–17 years old range from 9–11% while adult ADHD prevalence in the U.S. is estimated at 4.4%.[2] Medication has become a mainstay of treatment with U.S. surveillance data indicating that 62% of children with ADHD in 2016 took medication.[3] ADHD patients frequently have comorbid conditions such as mood, anxiety, and substance use disorders,[2,4–6] but early ADHD treatment with medication may convey some protection against these co-occurring conditions.[7–9]

Due to its high prevalence in the adolescent and adult population, ADHD has readiness and force health impacts on the Department of Defense (DoD) and affects the pool of military applicants.[7] During 2000–2018, the prevalence rate of ADHD in the DoD ranged between 1.7% and 3.9% and has steadily declined since 2011 (E. T. Reeves, MD, unpublished data, 2017). Current DoD accession policy, DoD Instruction (DoDI) 6130.03 (updated in 2018), disqualifies military applicants with diagnosed ADHD if they meet any of the following conditions: 1) had ADHD medication prescribed in the previous 24 months; 2) had an educational plan or work accommodation after 14 years of age; 3) had a history of comorbid mental health disorders; 4) had documentation of adverse academic, occupational, or work performance.[10] The previous updates to DoD accession policy occurred in 2010 and 2005 and disqualified applicants who used ADHD medication for more than 24 months cumulative after the age of 14 years and if there had been medication use in the previous 12 months, respectively.[11] The policy change trends have extended the time period that ADHD-diagnosed accessions to the military had to be without prescribed ADHD medication. Comparing annual rates in 2006–2010 to 2011–2017, this policy change was associated with increased waiver submissions for ADHD (mean of 560/year vs 789/year) and percent applicant disqualifications (36.4%/year vs 46.9%/year) **(Figure 1).**[12] In 2017, ADHD and disruptive behavior disorders were the fifth most frequent diagnoses resulting in medical disqualification of first-time enlisted active component military

applicants (this study's surveillance period was from January 2014 through December 2018).[12] A previous study evaluated ADHD accessions through waiver admissions to the Army and found no change in retention rates; however, that study was conducted well before the current accession policy was in place.[7] Other studies have assessed ADHD and its association with PTSD,[4,6] but no surveillance data have been published on new accession active component service members with ADHD and the effect of medication treatment.

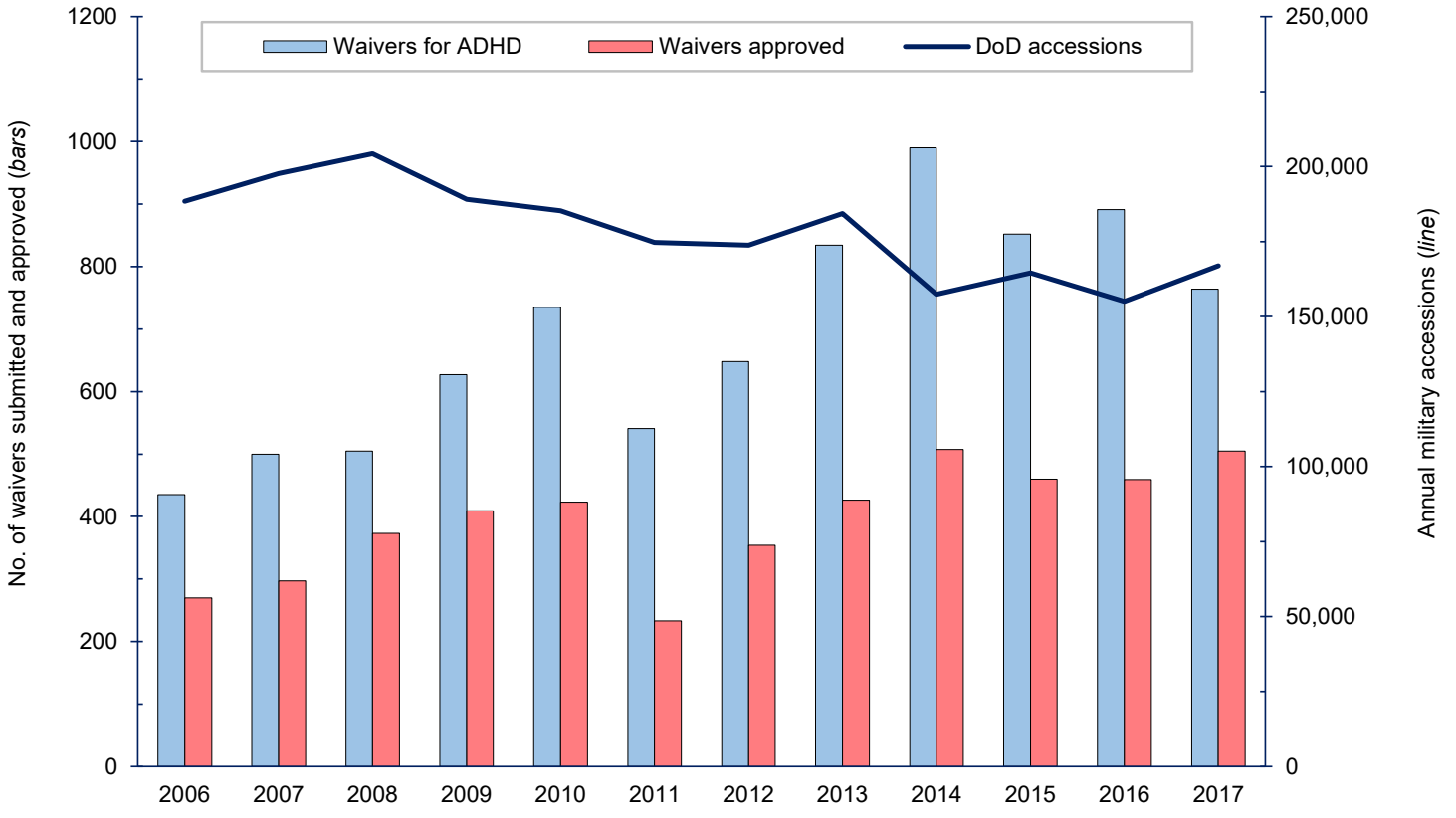
The current study provides evidence-based data relevant to the DoD's medical accession policy. The main objective of this study was to assess attrition from military service in active component service members diagnosed with ADHD compared to matched controls without ADHD. In addition, attrition rates were assessed for service members with ADHD by treatment status. Finally, incidence rates of selected mental health disorder diagnoses were compared between service members with ADHD who were prescribed medication for ADHD and those who were not.

METHODS

This study utilized a retrospective cohort design. The surveillance period was 1 January 2014 through 31 December 2018. The surveillance population included any member of the Army, Navy, Air Force, or Marine Corps who first entered military service in 2014. All data used to identify prevalent cases of ADHD were derived from records routinely maintained in the Defense Medical Surveillance System (DMSS), which is maintained by the Armed Forces Health Surveillance Division (AFHSD). The DMSS includes medical encounter data (e.g. outpatient visits, hospitalizations) of active component members of the U.S. Armed Forces in military and civilian (if reimbursed through the Military Health System) treatment facilities. The DMSS also includes medical screening data from Military Entrance Processing stations (MEPS) and records of prescribed and dispensed medications from the Pharmacy Data Transaction Service (PDTS) which were also used in this analysis.

For surveillance purposes, an ADHD case was defined as a service member with a qualifying ADHD diagnosis in the first or second diagnostic position for diagnoses assigned during a MEPS medical screening; or 1 hospitalization with any of the qualifying diagnoses of ADHD in the first or second diagnostic position; or 2 outpatient medical encounters within 180 days of each other, with any of the defining diagnoses of ADHD in the first or second diagnostic position; or 1 outpatient/TMDS medical encounter in a psychiatric or mental health

FIGURE 1. Annual ADHD waivers and approvals with total DoD annual accessions, 2006–2017[a]



ADHD, attention-deficit/hyperactivity disorder; DoD, Department of Defense; No., number.
[a]Data from Accession Medical Standards Analysis & Research Activity, Annual Report 2018.[12]

specialty care setting, identified by Medical Expense and Performance Reporting System (MEPRS) code beginning with 'BF'. The International Classification of Diseases, 9th Revision (ICD-9) and International Classification of Diseases, 10th Revision (ICD-10) codes used to identify ADHD cases included all those falling under the parent codes 314 and F90, respectively. Because the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) requires the presence of symptoms prior to age 12 to meet the diagnostic criteria for ADHD, individuals with a diagnosis of ADHD in 2014 were considered to be prevalent cases that existed at the time of accession regardless of when they were formally diagnosed.[1]

All active component service members who entered military service in 2014 and were found to have ADHD diagnoses during a MEPS medical screening or who met the case definition for a new ADHD diagnosis during 2014 were identified. Service members within this cohort were then further classified into 2 groups: ADHD cases that were treated with ADHD medication and ADHD cases who were not treated with ADHD medication.

To qualify as treated, service members had to have pharmacy documentation of being dispensed an FDA licensed drug for the treatment of ADHD at least twice within 6 months (181 days); this criterion is consistent with that employed in previous studies of ADHD medication use.[9] Qualifying ADHD medications included stimulants (amphetamines, methylphenidates), guanfacine (Intuniv), clonidine (Kapvay), and atomoxetine (Strattera). Active component service members dispensed ADHD medication with longer gaps than this threshold were classified as untreated. Because a service member could be admitted to the cohort at any time in 2014, pharmacy data through the first 180 days of 2015 were included in the analysis.

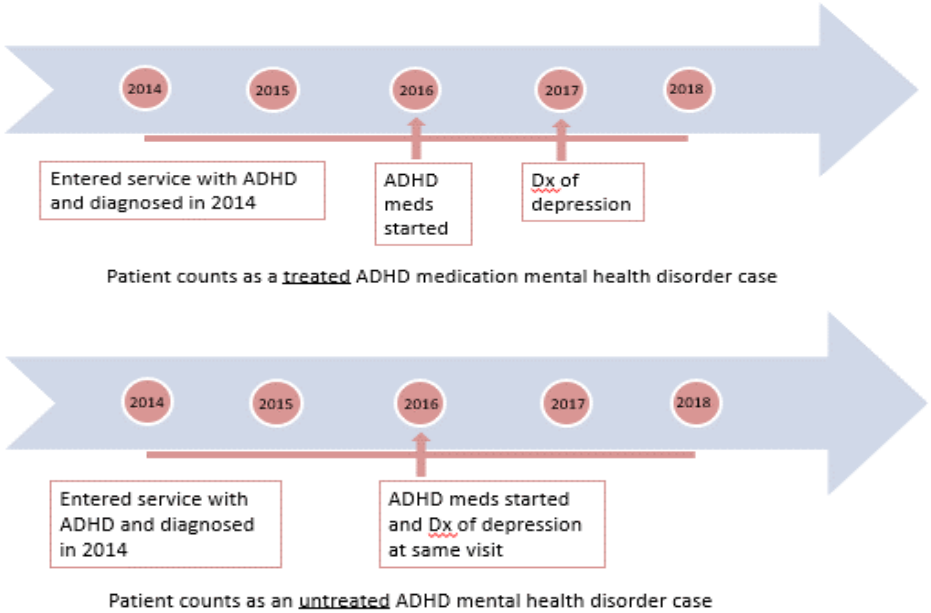
The control group consisted of active component service members without ADHD and matched 1:1 (i.e., case control ratio was 1:1) on age, gender, and date of accession (within 30 days of each ADHD case). Exclusion criteria included a diagnosis of depression, anxiety, or substance-related disorder at accession as documented in the MEPS record or a documented ADHD diagnosis prior to 2014.

The follow-up period for each cohort member and his or her matched control began at 181 days after their initial entry date into service. To assess attrition from service, individuals in each group were followed until 31 December 2018 or until the service member left active service or died. To determine the incidence of mental health disorders, service members were followed until 31 December 2018 or until the service member left active service, died, or received 1 or more of the mental health diagnoses of interest as defined below. To assess attrition, length of service was calculated by summing the number of days a service member was in service.

Occurrences of depressive, anxiety, alcohol- and/or substance-related disorders were ascertained by applying standard AFHSD case definitions.[13] Depressive, anxiety, alcohol- or substance-related disorders were all respectively defined as 1 hospitalization with any of the defining diagnoses (see AFHSD case definitions for full ICD-9 and ICD-10 code lists for each disorder) in the first or second diagnostic position; or 2 outpatient medical encounters, within 180 days of each other, with any of the defining diagnoses in the first or second diagnostic position; or 1 outpatient medical encounter in a psychiatric or mental health care specialty setting, defined by MEPRS code 'BF', with any of the defining diagnoses in the first or second diagnostic position. Service members who received a qualifying mental health disorder diagnosis were associated with the treated ADHD group only if the service member had been dispensed ADHD medication at least 30 days prior to the diagnosis of depressive, anxiety, alcohol- or substance-related disorder **(Figure 2)**.

Descriptive statistics were used to characterize service members in the 3 groups (control without ADHD, ADHD only, and ADHD with medication) who entered the military and were newly diagnosed with ADHD in 2014. The groups were compared on several background variables (i.e., sex, age group, race/ethnicity group, branch of service, and rank/grade) using chi-square tests. To compare the incidence of depressive, anxiety, alcohol- and substance-related disorders diagnosed in these groups, crude incidence rates and their associated 95% confidence intervals were calculated. Finally, Kaplan-Meier curves and the log-rank test were used to examine attrition rates in the study groups over time. All analyses were conducted using SAS/STAT software, version 9.4 (2014, SAS Institute, Cary, NC).

FIGURE 2. Classifying mental health disorders as treated or untreated ADHD cases



Note: ADHD medication treated = dispensed a medication at least twice within 6 months (181 days).
Mental health disorder considered as a treated ADHD case if diagnosed after taking at least 30 days of medication.
ADHD, attention-deficit/hyperactivity disorder; meds, medication; Dx, diagnosis.

TABLE 1. Demographic and military characteristics of treated and untreated ADHD cases in active component military members who entered service during calendar year 2014

	Full study population							Study population after 6-month exclusion applied						
	Treated ADHD cases		Untreated ADHD cases		Controls		p-value	Treated ADHD cases		Untreated ADHD cases		Non-ADHD cases		p-value
	No.	%	No.	%	No.	%		No.	%	No.	%	No.	%	
Total	334	33.5	662	66.5	996	100.0	.	331	53.7	285	46.3	911	100.0	.
Sex														
Male	245	73.3	607	91.7	852	85.5	<.001	244	73.7	265	93.0	779	85.5	<.001
Female	89	26.7	55	8.3	144	14.5		87	26.3	20	7.0	132	14.5	
Age group (years)														
<20	120	35.9	371	56.0	514	51.6	<.001	118	35.6	149	52.3	461	50.6	<.001
20–24	153	45.8	262	39.6	392	39.4		153	46.2	124	43.5	368	40.4	
25–29	45	13.5	28	4.2	74	7.4		44	13.3	12	4.2	67	7.4	
30–34	15	4.5	1	0.2	15	1.5		15	4.5	0	.	14	1.5	
35–39	1	0.3	0	.	1	0.1		1	0.3	0	.	1	0.1	
Race/ethnicity group														
Non-Hispanic white	206	61.7	504	76.1	555	55.7	<.001	204	61.7	237	83.2	506	55.5	<.001
Non-Hispanic black	55	16.5	51	7.7	187	18.8		55	16.6	17	6.0	167	18.3	
Hispanic	48	14.3	49	7.4	150	15.1		48	14.5	19	6.8	138	15.2	
Asian/Pacific Islander	13	3.9	8	1.2	46	4.6		13	3.9	4	1.4	46	5.1	
Other/unknown	12	3.6	50	7.6	58	5.8		11	3.3	8	2.8	54	5.9	
Service														
Army	282	84.4	241	36.4	384	38.6	<.001	280	84.6	171	60.0	351	38.5	<.001
Navy	22	6.6	296	44.7	242	24.3		21	6.3	35	12.3	226	24.8	
Air Force	25	7.5	45	6.8	177	17.8		25	7.6	32	11.2	158	17.4	
Marine Corps	5	1.5	80	12.1	193	19.4		5	1.5	47	16.5	176	19.3	
Rank/grade														
Junior enlisted (E1–E4)	299	89.5	657	99.2	944	94.8	<.001	297	89.7	280	98.2	859	94.3	<.001
Senior enlisted (E5–E9)	0	0	2	0.3	6	0.6		0	.	2	0.7	6	0.7	
Junior officer/warrant officer (O1–O3; W1–W3)	35	10.5	3	0.5	46	4.6		34	10.3	3	1.1	46	5.0	

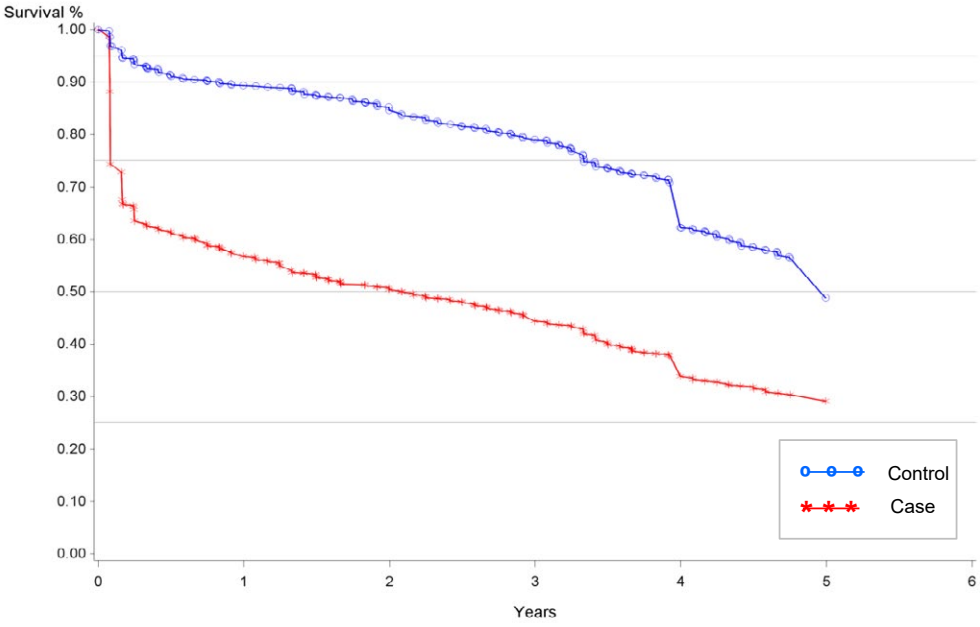
ADHD, attention-deficit/hyperactivity disorder; No. number.

RESULTS

A total of 996 service members who were newly accessed into the military in 2014 and qualified as an ADHD case were identified. Of the ADHD cases identified, 334 were classified as treated with ADHD medication and 662 were classified as untreated. Compared to the untreated ADHD group, the treated group had relatively higher proportions of females, service members aged 20 years or older, members of racial/ethnic minority groups, Army members, and junior officers. The untreated ADHD group had relatively higher proportions of Navy, Marine Corps, and Air Force members compared to the treated ADHD group **(Table 1)**.

The initial attrition rates in the total ADHD cohort (treated and untreated ADHD groups) and the control group are illustrated in **Figure 3**. Nearly 40% of ADHD

FIGURE 3. Attrition by cohort for active component service members who accessed the service in 2014, comparing those with ADHD 2014 diagnoses and a matched control group without ADHD, 2014–2018



ADHD, attention-deficit/hyperactivity disorder.

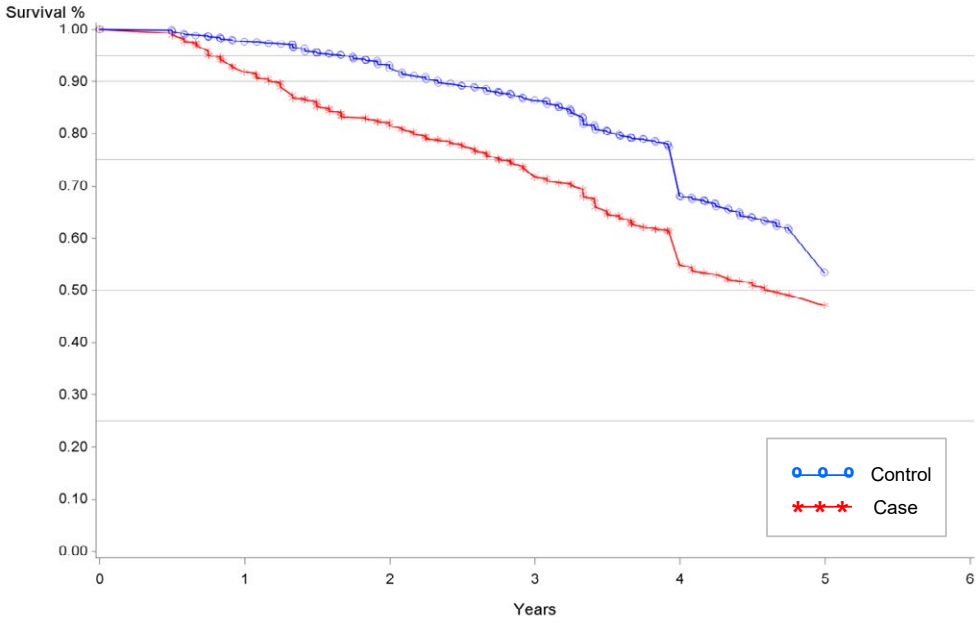
cases left service within the first 6 months of the surveillance period. Since these individuals left the military in less than 6 months, they did not have the opportunity to be a treated ADHD case as defined in this study (dispensed medication at least twice within 6 months). Thus, an additional exclusion was applied for people who did not remain in the military for at least 6 months.

After applying the requirement that service members remained in the military at least 6 months, the ADHD group decreased to 616 individuals (331 treated with medication and 285 untreated), and the non-ADHD (control) group decreased to 911 **(Table 1)**. The relative proportions within the covariates remained similar with the exception of the proportion of untreated service members in the Navy which decreased from 53% (n=296) to 12% (n=35) **(Table 1)**. Although the large initial drop of service members did not remain after applying the requirement for at least 6-months of service, attrition curves comparing ADHD (combined treated and untreated) and non-ADHD groups and treated ADHD, untreated ADHD, and non-ADHD groups were clearly different. The treated ADHD cohort had the highest attrition rates among these groups **(Figures 4, 5)**.

ADHD cases were analyzed according to whether they were detected during MEPS screening encounters or after accession (non-MEPS encounter) **(Table 2)**. Only 35.2% of the ADHD cases were identified with MEPS screening. Almost all of the treated ADHD cohort (328 of 331) were first documented after MEPS, and 91.0% of treated ADHD cases started medication within 6 months of accession. The 3 ADHD cases who were identified during MEPS screening and who went on to start medication during the surveillance period were first dispensed medication over 2 years after accession.

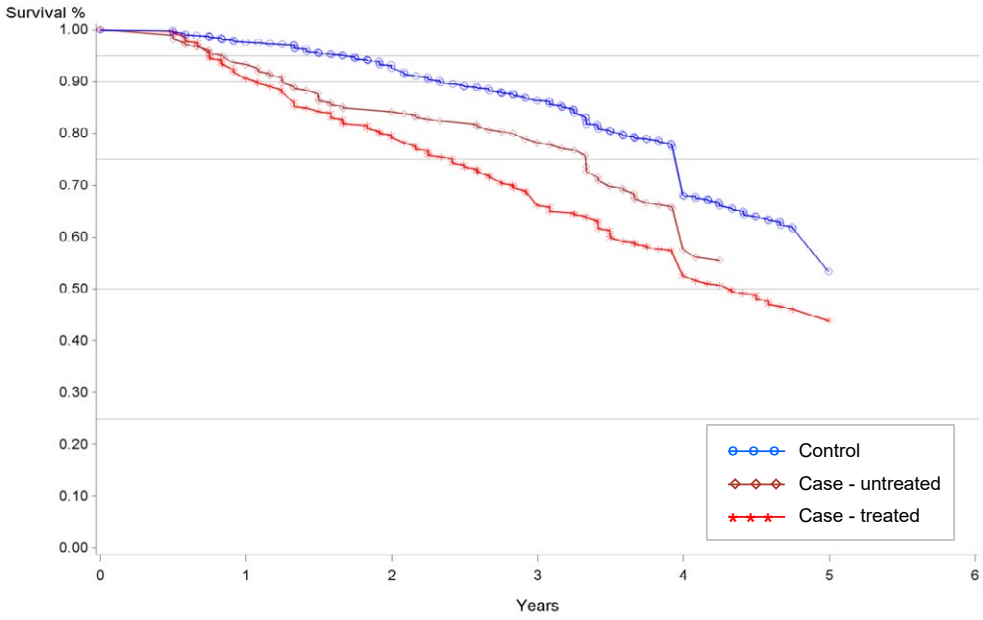
Compared to untreated ADHD and non-ADHD groups, the treated ADHD group had significantly higher crude incidence rates of all mental health disorders with the highest rate observed for anxiety disorders (an individual service member could have had multiple mental health disorders). The untreated ADHD cohort's incidence rates of mental health disorders were not statistically significantly different from the rates among those in the non-ADHD group **(Table 3)**.

FIGURE 4. Attrition by cohort for active component service members who accessed the service in 2014 and remained in the service for at least 6 months, comparing those with ADHD 2014 diagnoses and a matched control group without ADHD, 2014–2018



ADHD, attention-deficit/hyperactivity disorder.

FIGURE 5. Attrition by cohort for active component service members who accessed the service in 2014 and remained in the service for at least 6 months, comparing those with ADHD 2014 diagnoses who did and did not receive specific treatment with a matched control group without ADHD, 2014–2018



ADHD, attention-deficit/hyperactivity disorder.

EDITORIAL COMMENT

This report describes accessions to the military in 2014 with documented ADHD in the same year to examine the impact of the military ADHD enlistment standards in place at that time. Nearly two-thirds of the new accession ADHD cases detected in the first year of service in 2014 were identified after accession and after the MEPS screening process. Service members with treated

ADHD (99.1% of whom were diagnosed after the MEPS screening process) started medications quickly with 91.0% having had drugs prescribed within 6 months of accession. This finding suggests that most treated ADHD cases identified in this study withheld their ADHD diagnosis at accession and then quickly sought treatment after completing basic training. The treated ADHD group had the highest attrition rates over the 5-year surveillance period compared to untreated ADHD and non-ADHD groups and had crude higher incidence rates of mental health disorders.

The ADHD accession policy selects less severe and higher functioning ADHD individuals, but nondisclosure of medical conditions, particularly behavioral health diagnoses, is a difficult problem for accession medical screening to resolve. Previous studies have discussed the problem that more recruits are dismissed annually for withholding an ADHD diagnosis than applicants who are truthful in disclosing the diagnosis.[7] Results of the current study suggest the persistence of this problem, even after multiple policy changes over the past 2 decades. Future changes to enlistment standards should consider how to optimize or incentivize applicant disclosure of ADHD during MEPS screening or for medical waiver review as well as discourage withholding an ADHD diagnosis during enlistment. Potential ways to encourage disclosing ADHD in military applicants could involve different ADHD standards based on a new accession's occupation (difficult to do with MEPS screening as an occupation may not be defined at that time) or emphasizing more relaxed standards with service-based medical waivers after a thorough review and interview with the enlistee. At the same time, nondisclosure of ADHD should be disincentivized with the threat of disqualification from service or other punishment. Additional studies examining ADHD's impact on military readiness, deployment health, and different occupations would help advance and inform accession decisions regarding future ADHD standards.

This is the first study to assess medication dispensed for ADHD in new active component accessions since ADHD enlistment standards were updated in 2010. In addition, this study uses multiple sources of data available in the DMSS which allow for a longitudinal analysis and provide analytic evidence that may inform accession policies in the future.

Multiple limitations to this study should be considered. This analysis used data from PDTS which identified whether ADHD medications had been dispensed to active component service members with ADHD diagnoses. However, these data cannot be used to assess the medication adherence of these patients. Furthermore, patients with ADHD in this study could be prescribed ADHD medications for other medical conditions (FDA-approved indications or off-label use) or obtain ADHD medications by other means without a prescription. In addition, the population of patients who were dispensed ADHD medication could be different (e.g., have more severe symptoms or comorbid conditions) from the population of ADHD patients who were not dispensed medication. ADHD diagnosis data were derived from ICD-9 and ICD-10 coded medical encounters or from the MEPS tables

TABLE 2. Service members identified as ADHD cases stratified by identification at MEPS screening vs identification after military accession and by time to starting ADHD medication

	Total	%	MEPS Cases	%	Non-MEPS Cases	%
Total service members with ADHD	616	.	217	35.2	399	64.8
Treated	331	.	3	0.9	328	99.1
Length of time to start medication						
<6 months	301	91.0	0	0.0	301	91.8
6–24 months	14	4.2	0	0.0	14	4.2
>24 months	16	4.8	3	100.0	13	3.9

ADHD, attention-deficit/hyperactivity disorder; MEPS, military entrance processing station.

TABLE 3. Incidence rates of mental health disorders in treated versus untreated ADHD cases

	Treated ADHD			Untreated ADHD			Non-ADHD		
	No.	Rate[a]	95% CI	No.	Rate[a]	95% CI	No.	Rate[a]	95% CI
Total service members	331			285			911		
All mental health disorders	159	174.5	147.4–201.6	59	62.3	46.4–78.2	145	41.6	4.8–48.4
Depression	74	68.5	52.9–84.1	27	27.1	16.9–37.4	61	17.0	12.8–21.3
Anxiety	108	110.0	89.3–130.7	20	20.3	11.4–29.2	69	19.3	14.7–23.8
Substance-related	33	28.9	19.0–38.8	8	7.9	2.4–13.3	18	4.9	2.7–7.2
Alcohol-related	44	39.1	27.6–50.7	20	20.0	11.3–28.8	52	14.4	10.5–18.6

[a]Incidence rate per 1,000 person-years.
ADHD, attention-deficit/hyperactivity disorder; No., number; CI, confidence interval.

according to standardized health surveillance case definitions which could underestimate the prevalence of ADHD, especially in service members not actively being treated with medication for ADHD or withholding information at MEPS assessment (misclassification bias).

The DoD must continue to evaluate its accession policies related to ADHD, since the condition impacts the military enlistment pool. The observation of potentially undisclosed ADHD cases with worse outcomes in this study illustrates problems and challenges for the military when recruits do not truthfully reveal a previous ADHD diagnosis. Additional studies could further explore the issues identified in this analysis related to ADHD in new accessions and contribute to the enhanced readiness of service members with ADHD.

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Disclaimer: The views expressed herein are those of the authors and do not necessarily reflect official policy or position of Uniformed Services University of the Health Sciences, the Department of Defense, or Departments of the Army, Navy, or Air Force.

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Brief Report

The Prevalence of Attention-Deficit/Hyperactivity Disorder (ADHD) and ADHD Medication Treatment in Active Component Service Members, U.S. Armed Forces, 2014–2018

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Attention-deficit/hyperactivity disorder (ADHD) is a common diagnosis in childhood, characterized by persistent impairing inattention, hyperactivity, and impulsivity with symptoms recognized in patients before age 12.[1] Since ADHD is the most common pediatric neurodevelopmental disorder diagnosed in the U.S., this condition has readiness and force health importance to the Department of Defense (DoD), and its high prevalence in the adolescent and adult civilian population affects the pool of military applicants.[2] Current DoD accession policy lists ADHD as disqualifying for military applicants if they meet any of the following conditions: ADHD medication prescribed in the previous 24 months, an educational plan or work accommodation after age 14, a history of comorbid mental health disorders, or documentation of adverse academic, occupational, or work performance.[3]

The prevalence of ADHD in U.S. children aged 2–17 is estimated to range from 9–11% with approximately two-thirds of children with ADHD having at least 1 other mental, emotional, or behavioral disorder.[4] In 2016, U.S. surveillance data revealed that 62% of children diagnosed with ADHD currently take medication for the condition.[5] Although symptoms can resolve after childhood, the most recent estimate of overall prevalence of adult ADHD in the U.S. is 4.4%.[4] Unpublished data from an analysis conducted using Defense Medical Surveillance System (DMSS) data, demonstrated annual ADHD prevalence estimates ranging from 1.7–3.7% in the active component from 2000–2016 with a peak prevalence in 2011 (E. T. Reeves, MD, unpublished data, 2017). Although patients with ADHD are more likely to have comorbid mood, anxiety, and substance use disorders,[4,6–8] patients receiving ADHD medications may be protected from the development of these associated mental health conditions.[9,10]

The last major change to DoD accession policy standards for ADHD occurred in 2010 and resulted in more restrictive requirements (no medications for more than 24 months cumulative after age 14 instead of the previous requirement of no medications within 12 months of enlistment). Although services can accept applicant waivers with less stringent restrictions (e.g., the Air Force will consider waivers for recruits stable off medications for 15 months), ADHD diagnosis is consistently a common disqualifier for military service. In 2017, ADHD and disruptive behavior disorders were the fifth most frequent medical disqualification of first-time enlisted active component military applicants.[11] Although previous studies have evaluated the impact of ADHD on retention rates[2] (also E. T. Reeves, MD, unpublished data, 2017) and its association with post-traumatic stress disorder (PTSD),[6,8] no surveillance data have been published on recent estimates of the prevalence of ADHD diagnoses in active component military personnel or on what proportion of active component service members with ADHD are dispensed ADHD medications. The primary objectives of this study were to determine the prevalence of ADHD diagnoses among active component service members from 2014 through 2018 and the proportion of these service members who were prescribed medications to treat the condition.

METHODS

This descriptive study utilized a surveillance period from 1 January 2014 through 31 December 2018. The surveillance population included any member of the Army, Navy, Air Force, or Marine Corps who served in the active component at any point during the surveillance period. All data used to identify prevalent cases of ADHD were derived from records routinely stored in the DMSS, which is maintained by the Armed Forces Health Surveillance Division (AFHSD). DMSS includes medical encounter data (e.g., outpatient visits, hospitalizations) of active component members of the U.S. Armed Forces in military and civilian (if reimbursed through the Military Health System) treatment facilities. The DMSS also includes medical screening data from Military Entrance Processing Stations (MEPS) and records of prescribed and dispensed medications from the Pharmacy Data Transaction Service (PDTS) which were also included in this analysis.

For surveillance purposes, an ADHD case was defined as a qualifying ADHD diagnosis in the first or second diagnostic position for diagnoses assigned during MEPS medical screening; or 1 hospitalization with any of the qualifying diagnoses of ADHD in the first or second diagnostic position; or 2 outpatient medical encounters within 180 days of each other, with any of the defining diagnoses of ADHD in the first or second diagnostic position; or 1 outpatient/TMDS medical encounter in a psychiatric or mental health specialty care setting, identified by a Medical Expense and Performance Reporting System (MEPRS) code beginning with 'BF', with a

qualifying diagnosis of ADHD in the first or second diagnostic position. The International Classification of Diseases, 9th Revision (ICD-9) and International Classification of Diseases, 10th Revision (ICD-10) codes used to identify ADHD cases included all those falling under the parent codes 314 and F90, respectively.

Individuals with a diagnosis of ADHD at any time during the surveillance period were assumed to be prevalent cases at the time of accession regardless of when they were formally diagnosed, since the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) requires the presence of symptoms prior to age 12 to meet the diagnostic criteria for ADHD.[1]

To qualify as treated for ADHD, service members had to have a PDTS record documenting that they had been dispensed an FDA-licensed drug for the treatment of ADHD at least twice within 6 months (181 days) which is consistent with previous research.[10] Active component service members dispensed ADHD medication with longer gaps than this threshold were classified as untreated. Medications used for the treatment of ADHD included stimulants (amphetamines, methylphenidates), guanfacine (Intuniv), clonidine (Kapvay), and atomoxetine (Strattera). **Table 1** presents a comprehensive list of ADHD medications used in the current analysis.

Crude annual prevalences of ADHD in the active component of the military during 2014–2018 were calculated and reported as percentages. In these calculations, the numerator was the number of prevalent cases of ADHD in active component service members and the denominator included all active component service members in service as of 30 June in the specified year. The proportion of active component service members diagnosed with ADHD who had been dispensed ADHD medication as defined above was calculated. Service members for whom ADHD medication was dispensed (treated) and those for whom ADHD medication was not dispensed (untreated) were compared on several background variables (i.e., sex, age group, race/ethnicity group, education level, marital status, branch of service, rank/grade, and military occupation) using chi-square tests. All analyses were conducted using SAS/STAT software, version 9.4 (2014, SAS Institute, Cary, NC).

RESULTS

During the 5-year surveillance period, the crude annual ADHD prevalence among the active component declined from 3.9% in 2014 (n=58,691) to 2.8% in 2018 (n=41,338) **(Figure 1)**. Compared to their respective counterparts, service members with less than a high school education, those who were divorced or widowed, non-Hispanic whites, Army members, senior enlisted members, and those in healthcare occupations had higher overall prevalence rates of ADHD. Females and males had similar annual and overall prevalence estimates **(Figure 2, Table 2)**. Junior enlisted (E1–E4) service members trended down from the group with the second highest prevalence in 2014 to the group with the lowest prevalence in 2018 **(Table 2, Figure 3)**.

The proportion of prevalent ADHD cases who were prescribed ADHD medication during the surveillance period was 60.2%. During the surveillance period, the majority of medications prescribed were stimulants alone (78.9–79.6%) compared to combined stimulant and non-stimulant (16.5–17.4%) or non-stimulant only (3.6%–3.9%) regimens **(Figure 4)**. ADHD patients were more likely to be dispensed medication if they were older than 25 years of age, above junior enlisted rank (E1–E4), divorced/widowed, or in a healthcare occupation **(Table 3)**.

EDITORIAL COMMENT

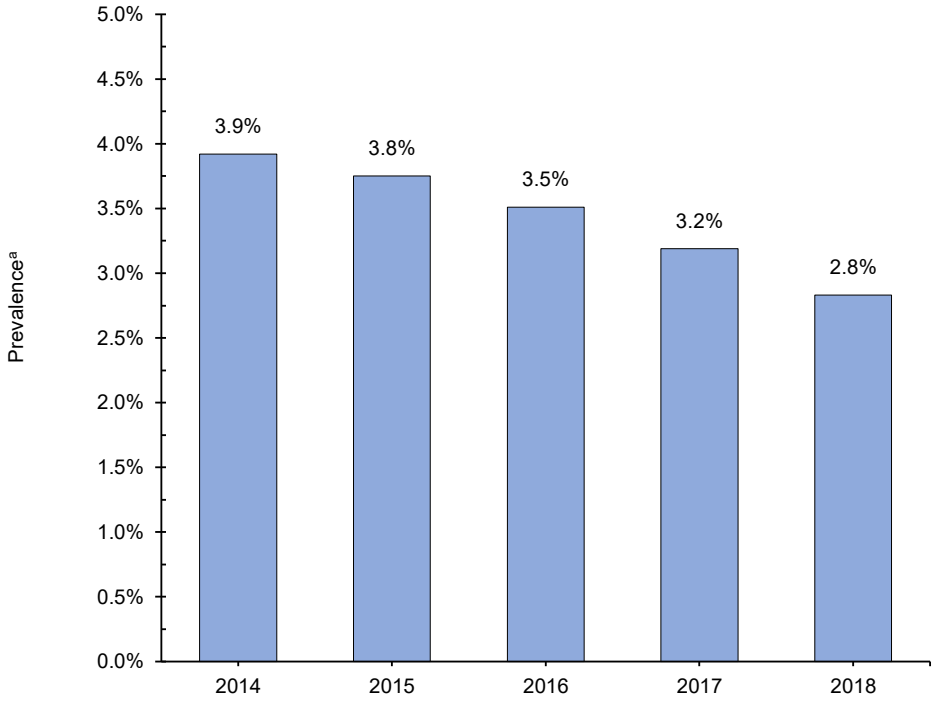
This report documents the prevalence and medication trends of ADHD among the active component service members during 2014–2018. Previous unpublished data on crude annual ADHD prevalence in the active component prior to 2014 revealed that a peak prevalence occurred in 2011 (E. T. Reeves, MD, unpublished data, 2017). The current study demonstrated a continued decline in the crude annual prevalence of ADHD in the military since the ADHD

TABLE 1. List of approved ADHD medications by drug class, generic drug name, and brand name

Drug class	Drug name	Brand name(s)
Stimulant - amphetamine	Amphetamine, mixed salts	Adderall (XR)
	Dextroamphetamine sulfate	Dexedrine (Spansules), Dextroamphetamine ER, Dextrostat
	Lisdexamphetamine dimesylate	Vyvanse
	Methamphetamine	Desoxyn
Stimulant - methlyphenidate	Methylphenidate	Concerta, Daytrana, Metadate CD/ED, Methylin (ER), Ritalin (LA/SR)
	Dexmethylphenidate HCl	Focalin (XR)
Non-stimulant	Guanfacine	Intuniv
	Clonidine	Kapvay
	Atomeoxetine	Strattera

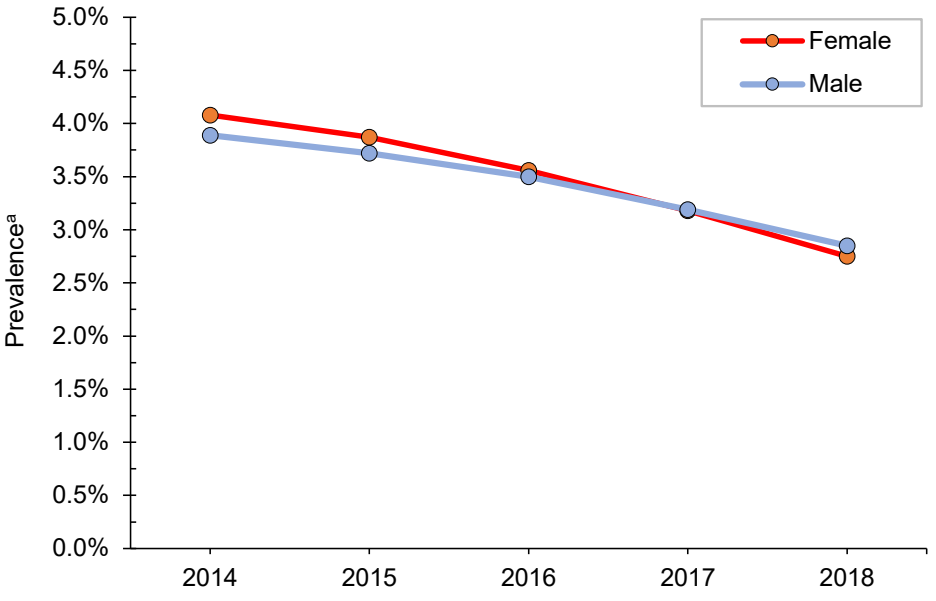
ADHD, attention-deficit/hyperactivity disorder.

FIGURE 1. Crude annual ADHD prevalence, active component, U.S. Armed Forces, 2014—2018



[a]The number of prevalent cases of ADHD in a given year divided by the number of active component members in service as of 30 June of that year.
ADHD, attention-deficit/hyperactivity disorder.

FIGURE 2. Annual ADHD prevalence, by sex, active component, U.S. Armed Forces, 2014—2018



[a]The number of prevalent cases of ADHD in a given year divided by the number of active component members in service as of 30 June of that year.
ADHD, attention-deficit/hyperactivity disorder.

accession medical standard became more restrictive in 2010, particularly among junior enlisted (E1–E4) service members whose crude annual ADHD prevalence was lower than all other rank groups in 2018. In contrast, national adult ADHD prevalence rose during this same timeframe.[12]

The ADHD population in the DoD differs from that in the U.S. civilian population on several key demographic characteristics. Female and male service members have similar prevalences whereas adult males are approximately twice as likely to be diagnosed with ADHD compared to females in the U.S. civilian population.[4,5,13] Possible explanations for this finding include that the true ADHD prevalence in males and females may be more similar than previous research has suggested when performing comparable occupations or indicates that males with ADHD may have characteristics (such as more recent medication use) selecting them to be disqualified from the military enlistment process at higher rates than females. Additionally, annual ADHD prevalences among service members in healthcare occupations were consistently more than 2 times the prevalences of those in other occupations. The reasons for this difference are unknown but may reflect better access to care, more knowledge about ADHD and treatment options, greater acceptance by coworkers, and/or less physical exertion-based/more sedentary jobs compared to other military occupations.

Medication dispensed for ADHD in the military (60%) represents a proportion similar to that in the U.S. civilian population (62%).[4,14] These data and the distribution of medication for ADHD patients should be informative for commanders and providers. For example, stimulant medication, as a controlled substance, can only be prescribed for 3 months at a time, which complicates the deployment readiness of service members with ADHD.

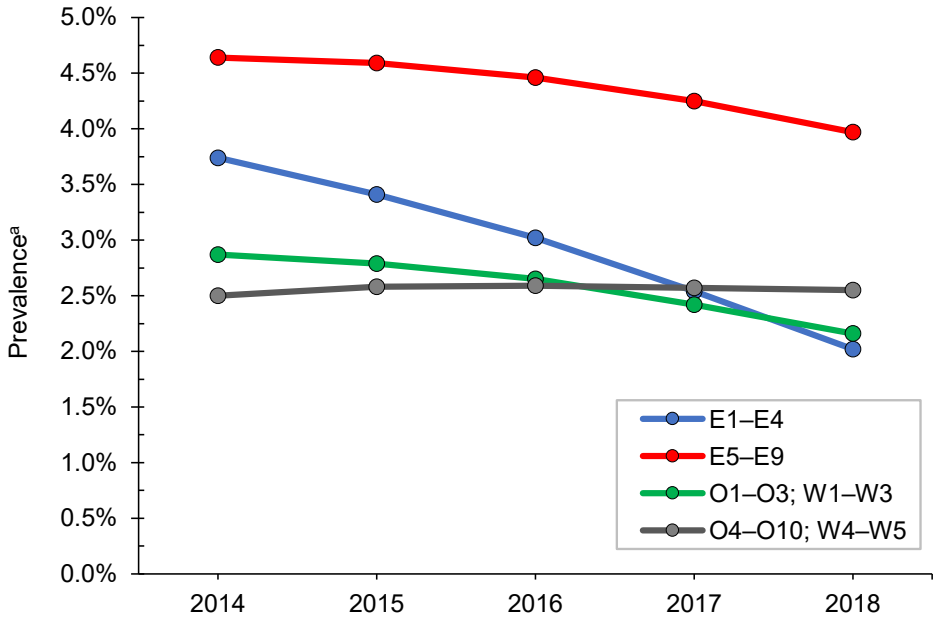
Several limitations should be considered when interpreting the results of this study. The current study used data on medications dispensed to active component service members through PDTS, but the medication adherence of these patients could not be assessed. Furthermore, patients with ADHD in this study

TABLE 2. Counts of prevalent cases, and prevalence rates of ADHD stratified by demographic and military characteristics, active component, U.S. Armed Forces, 2014–2018

	2014		2015		2016		2017		2018		2014–2018	
	No	%	No	%	No	%	No	%	No	%	No	%
Total	58,691	3.9	54,674	3.8	50,721	3.5	46,228	3.2	41,338	2.8	70,231	3.2
Sex												
Male	49,385	3.9	45,896	3.7	42,520	3.5	38,714	3.2	34,659	2.9	59,342	3.2
Female	9,306	4.1	8,778	3.9	8,201	3.6	7,514	3.2	6,679	2.8	10,889	3.0
Age group (years)												
<20	3,523	2.6	3,051	2.2	2,610	1.8	2,068	1.3	1,472	0.9	2,461	1.4
20–24	16,903	3.6	15,159	3.3	13,421	2.9	11,563	2.5	9,525	2.0	17,860	2.4
25–29	15,295	4.4	13,922	4.2	12,671	3.9	11,340	3.5	10,079	3.1	18,206	3.6
30–34	10,917	4.8	10,550	4.7	10,116	4.6	9,435	4.4	8,637	4.0	13,007	4.3
35–39	6,788	4.3	6,739	4.4	6,802	4.5	6,763	4.4	6,724	4.3	9,951	4.5
40–49	4,894	3.5	4,864	3.6	4,682	3.7	4,637	3.8	4,485	3.8	7,988	3.7
50+	371	2.4	389	2.6	419	2.8	422	2.8	416	2.8	758	2.5
Race/ethnicity group												
Non-Hispanic white	40,541	4.6	37,314	4.4	34,250	4.1	31,009	3.8	27,691	3.4	48,789	3.8
Non-Hispanic black	5,931	2.5	5,673	2.4	5,366	2.3	4,931	2.1	4,398	1.9	7,102	2.0
Hispanic	6,893	3.4	6,657	3.2	6,405	3.0	5,915	2.6	5,297	2.3	8,130	2.5
Aasian/Pacific Islander	1,318	2.4	1,263	2.2	1,173	2.0	1,095	1.8	999	1.7	1,548	1.8
Other/unknown	4,008	3.7	3,767	3.6	3,527	3.4	3,278	3.1	2,953	2.8	4,662	3.1
Education level												
Less than high school	218	6.5	171	6.0	139	5.7	110	5.1	93	4.8	199	5.5
High school	40,116	4.1	36,197	3.8	32,573	3.5	28,688	3.1	24,686	2.6	45,569	3.1
Some college	8,624	4.7	8,615	4.8	8,619	4.7	8,415	4.7	7,934	4.4	11,895	4.5
College	5,396	3.0	5,387	3.0	5,199	2.8	4,918	2.6	4,726	2.5	6,959	2.7
Advanced degree	3,181	2.7	3,235	2.8	3,317	2.9	3,336	2.8	3,234	2.7	4,493	2.8
Unknown	1,156	3.4	1,069	3.2	874	2.9	761	2.6	665	2.3	1,116	2.8
Marital status												
Single, never married	19,689	3.3	18,160	3.0	16,625	2.7	13,929	2.2	11,834	1.9	21,730	2.3
Married	35,492	4.3	33,177	4.2	30,971	4.0	28,591	3.8	26,084	3.5	42,831	3.8
Other	3,488	5.3	3,323	5.4	3,119	5.3	3,702	5.1	3,411	4.7	5,654	5.0
Unknown	22	2.4	14	1.5	6	0.6	6	0.6	9	0.8	16	1.0
Service												
Army	28,486	5.0	25,887	4.7	23,190	4.3	20,381	3.8	17,605	3.3	33,099	3.9
Navy	12,003	3.4	11,690	3.3	11,113	3.1	10,381	2.9	9,429	2.6	14,560	2.9
Air Force	12,894	3.7	12,124	3.6	11,834	3.5	11,301	3.3	10,501	3.0	15,583	3.2
Marine Corps	5,308	2.4	4,973	2.3	4,584	2.2	4,165	1.9	3,803	1.8	6,989	2.0
Rank/grade												
Junior enlisted (E1–E4)	24,680	3.7	22,108	3.4	19,581	3.0	16,415	2.5	13,035	2.0	28,162	2.7
Senior enlisted (E5–E9)	27,117	4.6	25,861	4.6	24,714	4.5	23,763	4.3	22,614	4.0	34,095	4.1
Junior officer/warrant officer (O1–O3; W1–W3)	4,418	2.9	4,246	2.8	3,996	2.7	3,642	2.4	3,289	2.2	4,538	2.4
Senior officer/warrant officer (O4–O10; W4–W5)	2,476	2.5	2,459	2.6	2,430	2.6	2,408	2.6	2,400	2.6	3,436	2.6
Military occupation												
Combat-specific[a]	8,347	3.8	7,553	3.6	6,776	3.3	5,891	2.9	5,076	2.5	9,734	2.9
Motor transport	1,595	3.6	1,420	3.3	1,274	3.0	1,130	2.6	976	2.2	1,940	2.8
Pilot/air crew	331	0.6	301	0.6	250	0.5	236	0.5	212	0.4	349	0.5
Repair/engineering	15,386	3.5	14,201	3.3	13,326	3.1	12,201	2.9	10,985	2.6	18,424	2.9
Communications/ intelligence	12,590	3.9	11,867	3.7	11,107	3.5	9,795	3.2	9,019	2.9	14,830	3.2
Healthcare	12,062	9.0	11,600	9.0	10,767	8.5	9,792	7.8	8,718	6.9	13,810	7.6
Other/unknown	8,380	3.1	7,732	2.9	7,221	2.7	7,183	2.4	6,352	2.1	11,144	2.5

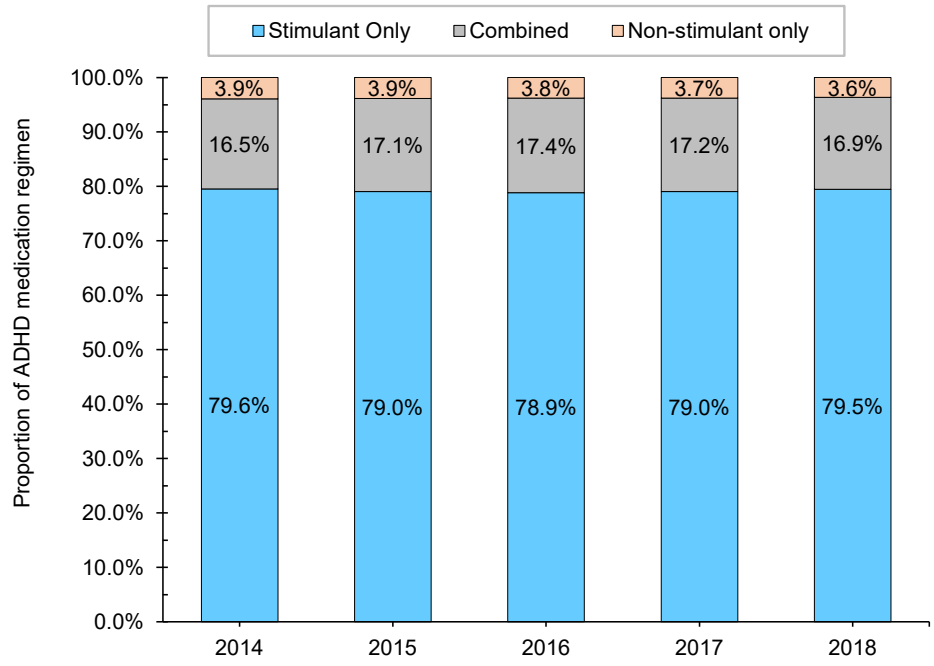
[a]Infantry/artillery/combat engineering/armor.
ADHD, attention-deficit/hyperactivity disorder; No., number.

FIGURE 3. Annual ADHD prevalence, by rank, active component, U.S. Armed Forces, 2014—2018



[a]The number of prevalent cases of ADHD in a given year divided by the number of active component members in service as of 30 June of that year.
ADHD, attention-deficit/hyperactivity disorder.

FIGURE 4. Percentages of ADHD cases, by type of ADHD medication regimen, active component, U.S. Armed Forces, 2014—2018



ADHD, attention-deficit/hyperactivity disorder.

could have been prescribed the medications for other medical conditions (FDA-approved indications or off-label use) or have obtained medications by other means without a prescription. Observational studies are subject to bias. For example, the population of patients who had ADHD medication dispensed might be different (e.g., more severe symptoms or comorbid diseases) from the population of ADHD patients without medication. Diagnostic data were derived from coded medical encounters, including medical examination at MEPS, according to standardized health surveillance case definitions; however, this method may underestimate the prevalence of ADHD, especially in service members not actively being treated with medication for ADHD or who were deliberately withholding information related to prior ADHD diagnosis at MEPS assessment (i.e., misclassification bias). The earliest year of data collection was 2014 because of the inability to link to pharmacy data prior to that year.

In conclusion, this study found a decreasing trend in crude annual ADHD prevalence in the active component from 2014–2018. In terms of military readiness, a decrease in prevalence lessens the demand on commanders and medical practitioners to make decisions about whether or not ADHD is a waiverable condition for deployments; however, this must be balanced with the effects that a strict ADHD accession policy has on limiting the pool of military applicants. Continued research and discussions should focus on the optimal ADHD accession military standard. Future studies should evaluate the impact of deployment on ADHD patients, the high prevalence of ADHD in healthcare occupations, and differences among service members with ADHD accessed to the military through various methods (i.e., MEPS, waivers, withholding the diagnosis, new ADHD diagnosis).

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Disclaimer: The views expressed herein are those of the authors and do not necessarily reflect official policy or position of Uniformed Services University of the Health Sciences, the Department of Defense, or Departments of the Army, Navy, or Air Force.

TABLE 3. Counts of prevalent cases of ADHD by treatment status, active component, U.S. Armed Forces, 2014-2018

	Medication Dispensed		Medication Not Dispensed		
	No.	%	No.	%	p-value
Total	42,289	100.0	27,942	100.0	
Sex					
Male	34,618	81.9	24,724	88.5	<.0001
Female	7,671	18.1	3,218	11.5	
Age group (years)					
<20	1,824	4.3	7,078	25.3	<.0001
20–24	13,253	31.3	10,073	36.1	
25–29	11,961	28.3	5,042	18.0	
30–34	7,716	18.3	2,939	10.5	
35–39	4,670	11.0	1,705	6.1	
40–49	2,708	6.4	1,040	3.7	
50+	157	0.4	65	0.2	
Race/ethnicity group					
Non-Hispanic white	28,336	67.0	20,453	73.2	<.0001
Non-Hispanic black	4,394	10.4	2,708	9.7	
Hispanic	5,485	13.0	2,645	9.5	
Asian/Pacific Islander	1,077	2.6	471	1.7	
Other/unknown	2,997	7.1	1,665	6.0	
Education level					
Less than high school	114	0.3	84	0.3	<.0001
High school	17,110	40.5	17,893	64.0	
Some college	3,023	7.2	1,454	5.2	
College	2,222	5.3	1,315	4.7	
Advanced degree	1,097	2.6	544	2.0	
Unknown	18,723	44.3	6,652	23.8	
Marital status					
Single, never married	8,807	20.8	12,944	46.3	<.0001
Married	14,043	33.2	8,263	29.6	
Other	19,431	46.0	6,662	23.8	
Unknown	8	0.0	73	0.3	
Service					
Army	20,479	48.4	12,495	44.7	<.0001
Navy	8,871	21.0	5,718	20.5	
Air Force	9,395	22.2	6,218	22.3	
Marine Corps	3,544	8.4	3,511	12.6	
Rank/grade					
Junior enlisted (E1–E4)	19,188	45.4	19,115	68.4	<.0001
Senior enlisted (E5–E9)	17,895	42.3	6,964	24.9	
Junior officer/warrant officer (O1–O3; W1–W3)	3,898	9.2	1,307	4.7	
Senior officer/warrant officer (O4–O10; W4–W5)	1,308	3.1	556	2.0	
Military occupation					
Combat-specific[a]	5,815	13.8	3,461	12.4	<.0001
Motor transport	1,020	2.4	1,054	3.8	
Pilot/air crew	145	0.3	143	0.5	
Repair/engineering	10,350	24.5	6,369	22.8	
Communications/intelligence	8,950	21.2	4,529	16.2	
Healthcare	10,381	24.6	3,202	11.5	
Other/unknown	5,628	13.3	9,184	32.9	

[a]Infantry/artillery/combat engineering/armor.
ADHD, attention-deficit/hyperactivity disorder; No., number.

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Exertional Rhabdomyolysis and Sickle Cell Trait Status in the U.S. Air Force, January 2009–December 2018

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Sickle cell trait (SCT) is associated with incident exertional rhabdomyolysis, but its effect on disease progression and severity is poorly understood. Of 377 exertional rhabdomyolysis cases diagnosed between 2009 and 2018 in the active component of the U.S. Air Force, 200 had records available for chart review, and 185 of these had known SCT status. Pre- and post-event data were stratified by SCT status, and serum chemistry changes among SCT-positive (n=11) and SCT-negative (n=174) airmen were compared using Wilcoxon-Mann-Whitney tests. Of the 200 cases with records available for chart review, 110 (55.0%) were hospitalized; 98 (56.3%) of the 174 who were SCT-negative were hospitalized. Also hospitalized were 4 (36.4%) of the 11 who were SCT-positive, and 8 (53.3%) of the 15 with unknown SCT status. Of the 7 airmen who were admitted to intensive care, 4 required hemodialysis, and 1 underwent a fasciotomy; all 7 were SCT-negative. Alterations in creatine kinase, potassium, creatinine, troponin I, and hemoglobin were statistically equivalent between those with and without SCT. Providers should maintain a high index of suspicion for exertional rhabdomyolysis, especially in warm climates and in the context of high-intensity activities, but should not presume that the presence of SCT portends a higher risk of complications or worse clinical outcomes.

WHAT ARE THE NEW FINDINGS?

Between 2009 and 2018, 377 active component members of the U.S. Air Force developed exertional rhabdomyolysis, according to the Armed Forces Health Surveillance Division (AFHSD) case definition. Two hundred cases were available for chart review, most of which included a documented sickle cell trait (SCT) test result. Medical intervention requirements and sequelae were statistically similar between SCT-positive (n=11) and SCT-negative (n=174) airmen.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Exertional rhabdomyolysis is a potentially serious condition demanding a vigilant approach. For all suspected cases, regardless of SCT status, healthcare providers should thoroughly review potential contributing factors and pre-existing comorbidities and intervene to prevent complications. Although SCT is a risk factor for developing exertional rhabdomyolysis, it does not appear to influence its progression or severity.

Exertional rhabdomyolysis is pathological breakdown of skeletal muscle resulting from physical activity. Depending on the rate and severity of myonecrosis, patients may experience debilitating pain, renal failure, cardiac arrhythmia, compartment syndrome, and splenic infarction.[1] The diagnosis of exertional rhabdomyolysis is clinical and should be made when severe muscle symptoms (e.g., pain and stiffness) and laboratory evidence of myonecrosis (usually defined as a serum creatine kinase [CK] level at least 5 times the upper limit of normal) follow a bout of physical activity.[2] Across the U.S. Armed Forces, exertional rhabdomyolysis is more common among males, non-Hispanic blacks, Marines, recruits, members of major ground combat units, and those with sickle cell trait (SCT).[3,4] In rare cases during exercise, individuals with SCT may develop a severe metabolic crisis known as exertional collapse associated with sickle cell trait (ECAST), which can be accompanied by exertional rhabdomyolysis and is frequently fatal.[5]

At an October 2019 summit on ECAST, hosted by the Consortium for Health and Military Performance (CHAMP), military and civilian experts from across the U.S. shared best practices and enumerated several knowledge gaps. One key question from the summit drew interest from health policymakers in the U.S. Air Force: Is exertional rhabdomyolysis experienced differently in service members with and without SCT? The present study sought to answer this question through chart reviews of exertional rhabdomyolysis cases over a 10-year period, focusing on context, triggers, progression, and severity.

METHODS

Air Force Personnel Center (AFPC) files were used to identify those who served in the active component of the U.S. Air Force for at least 1 day between 1 January 2009 and 31 December 2018. The Military Health System Data Mart (M2), which includes diagnoses made at military treatment facilities (direct care) and at outside facilities reimbursed by TRICARE (purchased care), was used to identify exertional rhabdomyolysis cases. Cases were assigned using the Armed Forces Health Surveillance Division (AFHSD) surveillance case definition, which requires a hospitalization or outpatient medical encounter with a case-defining ICD-9 or

ICD-10 code in any diagnostic position, an associated condition code in any diagnostic position, and no exclusionary condition code in any diagnostic position.[6] AFPC and M2 data were merged by social security number. Incident cases were retained in the final dataset, based on the first case-defining diagnosis during the surveillance period.

For all incident exertional rhabdomyolysis cases, charts were systematically reviewed by the principal investigator (BW) in the Armed Forces Health Longitudinal Technology Application (AHLTA) and the Health Artifact and Image Management Solution (HAIMS) to abstract the following information into Microsoft Excel 2013 (Microsoft Corporation, Redmond, WA): SCT status; location and activity at the time of the exertional rhabdomyolysis event (or the most recent precipitating activity documented in the chart); presence or absence of preexisting anemia or renal disease (considered absent if not mentioned in any clinical notes with an exertional rhabdomyolysis diagnosis); use of supplements, stimulants, statins, antipsychotics, and alcohol, as documented in any notes diagnosing exertional rhabdomyolysis (considered absent if not mentioned in these notes); presence or absence of hospitalization, intensive care unit admission, hemodialysis, fasciotomy, and splenic infarction; hemoglobin and hematocrit values prior to the event (considered baseline) and nadir values after the event; date and time of the initial and peak values of serum CK and serum potassium; and peak values of serum blood urea nitrogen, troponin I, and lactate dehydrogenase. Greater-than signs in CK values were dropped (e.g., ">2000" was recorded as "2000") to allow for statistical calculations. For CK and potassium, an hourly rate of change was calculated as $\Delta v/\Delta t$, where $\Delta v = \text{value}_{peak} - \text{value}_{initial}$ and $\Delta t = \text{time}_{peak} - \text{time}_{initial}$. The Aeromedical Services Information Management System was used to retrieve SCT status for airmen with no results documented in AHLTA or HAIMS.

Values of blood analytes were compared by SCT status. Shapiro-Wilk tests were used to determine that all variables were non-normally distributed. Therefore, the Wilcoxon-Mann-Whitney test was used to compare median differences between those with and without SCT. Significance was established at a 2-sided p value of .05. Given the small number of observations among those with SCT, exact p values were obtained using the Monte Carlo estimation. Clinical and laboratory data from the Microsoft Excel database were deidentified prior to analysis in SAS/STAT software, version 9.4 (2014, SAS Institute, Cary, NC). This study was commissioned by the Air Force Medical Readiness Agency to inform healthcare policy and was approved by the Air Force Research Laboratory Institutional Review Board.

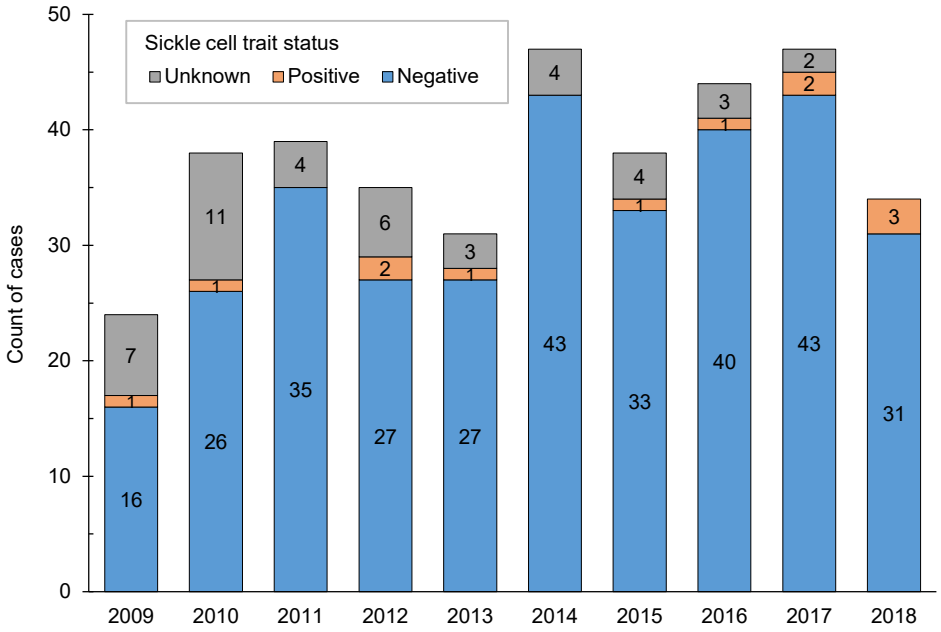
RESULTS

A total of 377 airmen met the case definition of exertional rhabdomyolysis, with an annual range of 24–47 cases. Of the 333 cases with documented SCT status, 12 (3.6%) were positive for SCT **(Figure)**. Their mean age was 27.3 years (range: 17–47 years), and males accounted for 348 (92.3%) cases **(data not shown)**.

Electronic medical charts were available for 200 (53.1%) cases, of whom 174 (87.0%) were SCT-negative, 11 (5.5%) were SCT-positive, and 15 (7.5%) had unknown SCT status. Events occurred on or near 66 military installations around the world, led by Joint Base San Antonio, TX (n=20); Hurlburt Field, FL (n=19); Joint Base Pearl Harbor, HI (n=9); Sheppard Air Force Base, TX (n=8); Davis-Monthan Air Force Base, AZ (n=8); and Fort Bragg, NC (n=7) **(data not shown)**. Antecedent activities were the Air Force Fitness Assessment (n=39); leisure-time exercise other than running, to include playing sports and hiking (n=36); running (n=35); ruck marching (n=24); other military training, to include land navigation, combative exercises, and drilling (n=24); weightlifting (n=12); and yardwork or housework (n=5). Sixteen cases were reported as occurring at rest, and 9 had no documented activity. Among airmen with SCT, 5 (45.5%) were participating in the Air Force Fitness Assessment **(data not shown)**.

A variety of over-the-counter supplements were documented as having been used by the cases: pre-workout products (n=9); energy drinks and weight loss supplements (n=5); multivitamins (n=4); melatonin (n=3); fish oil (n=2); protein

FIGURE. Exertional rhabdomyolysis counts, by calendar year and sickle cell trait status, active component, U.S. Air Force, 2009–2018 (n=377)



powder (n=2); medium-chain triglyceride oil (n=1); vitamin D (n=1); and unspecified products (n=3) **(data not shown)**. Brand names mentioned in charts included Jack3D, Nitraflex, C4, Hypershot, Monster, 5-hour Energy, Hydroxycut, and Ripped Fuel. One airman was taking prescribed dextroamphetamine-amphetamine, 6 were taking prescribed statins, and 12 reported alcohol use proximate to the event; none had documented use of antipsychotics **(data not shown)**. Among airmen with SCT, 1 reported fish oil supplementation and 1 reported recent alcohol use **(data not shown)**.

Five cases had a past history of anemia and 3 had kidney disorders, including 2 with nephrolithiasis and 1 with renal dysplasia. None of the SCT-positive airmen had preexisting comorbidities **(data not shown)**.

A total of 110/200 (55.0%) airmen were hospitalized: 98/174 (56.3%) without SCT, 4/11 (36.4%) with SCT, and 8/15 (53.3%) with unknown SCT status **(data not shown)**. Among those hospitalized, 7 were admitted to an intensive care unit; 4 required hemodialysis; and 1 underwent a fasciotomy. All intensive care unit cases were SCT-negative. No splenic infarctions were recorded among the cases **(data not shown)**.

Serum chemistry results varied markedly (e.g., while the vast majority of cases had at least 1 CK result, only 5 had a lactate dehydrogenase result) **(Table)**. The median initial and peak CK levels were 1,231 U/L and 1,811 U/L, respectively, with a median rise of 80.4 U/L/hr. Three airmen experienced a peak CK greater than 100,000 U/L, and 4 had a CK rise exceeding 2000 U/L/hr. Among those with a pre-event (i.e., baseline) and lower post-event hemoglobin (n=96), the median decline was 11.8%, with a range of 0.6% to 41.0%. Airmen with and without SCT had serum chemistry values that were not statistically significantly different **(Table)**.

TABLE. Serum chemistry findings associated with exertional rhabdomyolysis events, by sickle cell trait status, active component, U.S. Air Force, 2009–2018

Marker	Total (n=200)	SCT-negative (n=174)	SCT-positive (n=11)	p-value[a]
Creatine kinase (reference range: 40 – 200 U/L)				
Initial, No.	181	162	8	.111
Median, U/L	1,231	1,323	827	
Min – max, U/L	80 – 271,000	80 – 271,000	225 – 7.971	
Peak, No.	181	162	8	.431
Median, U/L	1,811	1,824	1,285	
Min – max, U/L	80 – 271,000	80 – 271,000	225 – 12,144	
Rate of rise, No.[b]	56	48	3	.985
Median, U/L/hr	80.4	79.4	96.5	
Min – max, U/L/hr	0.1 – 6.086	0.1 – 6,086	69.8 – 96.8	
Potassium (reference range: 3.5 – 5.3 mM/L)				
Initial, No.	175	157	7	.775
Median, mM/L	4	4	4	
Min – max, mM/L	3.0 – 7.2	3.0 – 7.2	3.4 – 4.7	
Peak, No.	175	157	7	.557
Median, mM/L	4.2	4.2	4.3	
Min – max, mM/L	3.2 – 7.4	3.2 – 7.4	3.4 – 4.7	
Rate of rise, No.[b]	80	74	2	.885
Median, mM/L/hr	0.041	0.014	0.106	
Min – max, mM/L/hr	0.001 – 0.440	0.002 – 0.440	0.003 – 0.209	
Creatinine (reference range: 0.6 – 1.5 mg/dL)				
Peak, No.	179	161	7	.859
Median, mg/dL	1.4	1.4	1.3	
Min – max, mg/dL	0.7 – 14.2	0.7 – 14.2	1.2 – 2.2	
Blood urea nitrogen (reference range: 8 – 23 mg/dL)				
Peak, No.	175	157	7	.056
Median, mg/dL	18	19	14	
Min – max, mg/dL	7 – 72	7 – 72	12 – 24	
Troponin I (reference range: <0.04 ng/mL)				
Peak, No.	66	54	6	.580
Median, ng/mL	0.03	0.03	0.05	
Min – max, ng/mL	<0.001 – 1.78	<0.001 – 1.78	0.01 – 0.28	
Lactate dehydrogenase (reference range: 140 – 280 U/L)				
Peak, No.	5	5	0	--
Median, U/L	386	386	--	
Min – Max, U/L	324 – 3,087	324 – 3,087	--	
Hemoglobin decline				
No.[c]	96	87	3	.364
Median, %	11.8	11.6	16.6	
Min – max, %	0.6 – 41.0	0.6 – 41.0	0.1 – 0.22	
Hematocrit decline				
No.[c]	93	84	3	.598
Median, %	12.2	11.7	18.2	
Min – max, %	0.2 – 42.0	0.2 – 42.0	6.5 – 19.2	

SCT, sickle cell trait; No., number.
Note: reference ranges vary by laboratory; figures represent typical ranges provided by laboratories involved in this case series.
[a]Exact two-sided p-value based on Monte Carlo estimation, comparing SCT negative and SCT positive.
[b]Reflects cases with a documented rise.
[c]Reflects cases with a pre-event (baseline) value and a lower post-event value.

EDITORIAL COMMENT

During a recent 10-year surveillance period, 377 active component U.S. airmen met the case definition for exertional

rhabdomyolysis. Those with SCT, who traditionally represent 1.0%[7] to 1.2%[8] of the Air Force population, comprised 3.6% of cases—supporting an association between SCT and incident exertional rhabdomyolysis that has been documented in other studies.[9,10] This increased risk of disease incidence may not indicate increased risk of disease severity. In a cohort of black U.S. soldiers exposed to universal training precautions, Nelson and colleagues found a similar hazard of all-cause mortality for those with and without SCT (hazard rate=0.99; 95% confidence interval [CI]: 0.46–2.13), even though the former had a greater hazard of exertional rhabdomyolysis (hazard rate=1.54; 95% CI: 1.12–2.12).[9] No SCT-positive airmen in the present study required intensive care unit admission, hemodialysis, or fasciotomy, and their serum chemistry findings were similar to their SCT-negative peers. This may reflect more intensive pre-hospital interventions among SCT-positive airmen, such as aggressive rehydration and supplemental oxygen use, or it may indicate that SCT status is more instrumental in the inception rather than the progression of exertional rhabdomyolysis.

Mitigating health risks among SCT-positive service members remains vital,[11,12] but the results of this study (i.e., the predominance of cases and the prevalence of sequelae among SCT-negative airmen) underscore the importance of universal precaution strategies and healthcare system responses for all service members demonstrating signs and symptoms of exertional rhabdomyolysis. Population health policies should focus on the documented risk factors for exertional rhabdomyolysis: insufficient acclimatization to the environment and to the physical activity demand; strenuous exertion in hot and humid climates; and use of statins and over-the-counter supplements, especially stimulants.[2] The findings of this study suggest that increased vigilance is required at training installations located in warm climates and during high-intensity activities such as running, ruck marching, and fitness testing.

Males accounted for 92.3% of exertional rhabdomyolysis cases, despite making up 79.8% of the active duty Air Force population at the conclusion of the surveillance period.[13] This sex-based discrepancy in exertional rhabdomyolysis has been documented elsewhere. Across the active component of the U.S. Armed Forces in 2019, females had a 60% lower incidence rate of the condition,[3] and in a cohort of black U.S. Army soldiers who served between 2011 and 2014, females had a 49% lower hazard rate than males.[9] Although nonmodifiable, male sex is a risk factor for exertional rhabdomyolysis that clinicians should consider in their evaluations.

This study has additional clinical implications, highlighting issues with confirming the diagnosis of exertional rhabdomyolysis. Remarkably, 53 of the cases in this study had a peak serum CK less than 5 times the upper limit of normal, the diagnostic threshold for the condition, which was "designed for high sensitivity [despite] low specificity."[2] An additional 16 cases were noted to have symptoms beginning at rest. Therefore, over one-third of cases in this sample did not meet the diagnostic criteria for exertional rhabdomyolysis established by a DoD Clinical Practice Guideline.[2] A high index of suspicion for exertional rhabdomyolysis is encouraged, but healthcare providers should ensure that suspected cases have a history of recent exertion and meet all clinical and laboratory features of the condition before diagnosing it. This is especially important because the diagnosis carries implications for retention versus separation from military service. Finally, the vast majority of charts did not mention over-the-counter supplement use, which may indicate a simple lack of documentation or, more troubling, a lack of inquiry. Given the high prevalence of energy drinks[14] and supplement use[15] in the military, and the association between some over-the-counter products and exertional rhabdomyolysis,[16] providers should assess, document, and counsel patients regarding these important details.

These public health and clinical considerations should be interpreted in light of the study's limitations. First, charts were available for just over half of all cases, mostly because charts from purchased care facilities had not been uploaded into HAIMS. While the unavailability of records reduced statistical power, any introduced bias was likely non-differential by SCT status. Second, if supplements were not documented in the medical chart, nonuse was assumed; it is likely that true use exceeded that reported in this study. Third, greater-than symbols, which were present in 12 CK values, had to be ignored in the analysis, resulting in an underestimate of the initial and peak CK values, and possibly an underestimate in the rate of CK rise. Fourth, the small number of cases among SCT-positive airmen limited the statistical power to detect a difference in outcomes based on SCT status. Fifth, case ascertainment relied on a diagnostic code-based definition[6] that may not have captured all cases of exertional rhabdomyolysis in the population, just as the chart reviews suggested imperfect specificity in the case definition.

It is well-established that SCT-positive service members are at greater risk for exertional rhabdomyolysis. Results of this study suggest that SCT status may not modify the likelihood of complications thereof. These findings do not undermine the importance of SCT screening and education, which appear to mitigate the risk of death associated with SCT.[17] Rather, this study highlights the importance of universal strategies to prevent, diagnose, and treat exertional rhabdomyolysis in all service members, regardless of SCT status. Moreover, this retrospective analysis reveals a pattern of misdiagnosis and weak documentation of exertional rhabdomyolysis, which may reflect inadequate training of healthcare providers. Further investigation is warranted, including on the impact of SCT on duty limitations and military attrition secondary to exertional rhabdomyolysis.

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Acknowledgements: The authors thank Dr. Alisa Simon and Mr. James Escobar, U.S. Air Force School of Aerospace Medicine, for assisting with data acquisition.

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Uniformed Services University of the Health Sciences, the Air Force, the Department of Defense, or the U.S. Government.

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Medical Surveillance Monthly Report (MSMR)
Armed Forces Health Surveillance Division
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Silver Spring, MD 20904

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ISSN 2158-0111 (print)
ISSN 2152-8217 (online)