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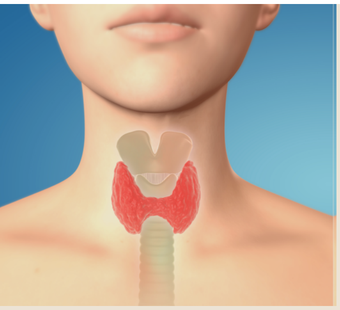

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Thyroid Disorders, Active Component, U.S. Armed Forces, 2008–2017

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This analysis describes the incidence and prevalence of five thyroid disorders (goiter, thyrotoxicosis, primary/not otherwise specified [NOS] hypothyroidism, thyroiditis, and other disorders of the thyroid) among active component service members between 2008 and 2017. During the 10-year surveillance period, the most common incident thyroid disorder among male and female service members was primary/NOS hypothyroidism and the least common were thyroiditis and other disorders of thyroid. Primary/NOS hypothyroidism was diagnosed among 8,641 females (incidence rate: 43.7 per 10,000 person-years [p-yrs]) and 11,656 males (incidence rate: 10.2 per 10,000 p-yrs). Overall incidence rates of all thyroid disorders were 3 to 5 times higher among females compared to males. Among both males and females, incidence of primary/NOS hypothyroidism was higher among non-Hispanic white service members compared with service members in other race/ethnicity groups. The incidence of most thyroid disorders remained stable or decreased during the surveillance period. Overall, the prevalence of most thyroid disorders increased during the first part of the surveillance period and then either decreased or leveled off.

WHAT ARE THE NEW FINDINGS?

More than 40,000 cases of thyroid disorders were diagnosed during the ten-year surveillance period among active component service members. In contrast to previous findings, the current report indicates that the incidence of the five different thyroid disorders remained stable or decreased between 2008 and 2017.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Although thyroid disorders are treatable, hypothyroidism and hyperthyroidism can result in periods of non-deployability, temporary duty profile, or need for medical waiver at the time of diagnosis or if there is a disruption in treatment. More severe cases of hyperthyroidism can take up to 1 year to stabilize, resulting in significant periods of limited deployability.

The thyroid is an endocrine gland in the neck that secretes hormones which control the body's metabolism. Disorders of the thyroid can be broadly classified into two groups: hyperthyroidism, in which the thyroid produces too much hormone, or hypothyroidism, in which the thyroid does not produce enough hormone.

The prevalence of hyperthyroidism in the U.S. is estimated to be 1.3% according to data from the NHANES-III, with the lowest prevalence observed among Mexican Americans and the highest among non-Hispanic whites.[1] Hyperthyroidism can lead to thyrotoxicosis, a term that refers to having an excess of thyroid hormone in the body from any cause.[2] In the U.S., thyrotoxicosis is more common among women, those with other thyroid conditions, and people over 60 years old.[3,4] It is most commonly caused by Graves' disease, an autoimmune disorder affecting the thyroid. However, thyrotoxicosis can also be caused by thyroiditis (inflammation of the thyroid gland causing excess thyroid hormone to leak into the blood stream), thyroid nodules, overconsumption of iodine, or taking too much synthetic thyroid hormone.[3] Symptoms of thyrotoxicosis include restlessness, rapid or irregular heartbeat, muscle weakness, anxiety, fatigue, trouble sleeping, heat intolerance, weight loss, and, in some cases, exophthalmos ("bulging eyes") and enlarged thyroid gland ("goiter"). Goiters are enlarged thyroid glands most commonly due to iodine deficiency. In the U.S., goiters are frequently caused by, and are also a symptom of, hyperthyroidism.[5,6] If left untreated, large goiters can cause difficulty breathing and swallowing.

In the U.S., the prevalence of hypothyroidism is estimated to be 4.6%, with the lowest prevalence observed among non-Hispanic blacks compared to other race/ethnicity groups.[1] Hypothyroidism is most commonly caused by Hashimoto's disease, an autoimmune disorder affecting the thyroid, which is much more common in women than men.[7] Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis, can cause hypothyroidism by impairing the ability of the thyroid to produce thyroid hormones. Hypothyroidism can also be caused by surgical removal of the thyroid or damage from radiation treatment. Symptoms of hypothyroidism include fatigue, depression, weight gain, dry skin, constipation, and muscle and joint pain.[8]

Hyperthyroidism and hypothyroidism can significantly degrade the military operational capabilities of affected service members due to the various symptoms of the disorders. As a result, thyroid disorders are disqualifying conditions for entrance into the U.S. military.[9] However, a 2012 *MSMR* analysis identified more than 37,000 incident cases of thyroid disorders among active component service members between 2002 and 2011.[10] That analysis also documented a marked increase in the incidence rates of thyroid disorder diagnoses among service members during the period, particularly among males; however, this finding may have been due to increased testing for thyroid function disorders during 2002–2011.[10] The current report summarizes the incidence, prevalence, and trends of thyroid disorders other than thyroid cancer among active component service members of the U.S. Armed Forces between 2008 and 2017.

TABLE 1. ICD-9 and ICD-10 codes for thyroid disorders

Description	ICD-9[a]	ICD-10[a]
Goiter	240.*-241.*	E04.*, E01.*
Thyrotoxicosis	242.*	E05.0*-E05.3*, E05.8*, E05.9*
Primary/NOS hypothyroidism	244.9	E03.9, E03.5, E03.8, E02
Thyroiditis	245.*	E06.*
Other disorders of thyroid	246.*	E07.0, E07.1, E07.89, E07.9

[a]An asterisk (*) indicates that any subsequent digit/character is included
NOS, not otherwise specified

METHODS

The surveillance period was January 1, 2008 through December 31, 2017. The surveillance population included all individuals who served in the active component of the Army, Navy, Air Force, or Marine Corps at any time during the surveillance period. Thyroid disorders were identified by diagnostic codes for "disorders of thyroid gland" recorded in standardized records of inpatient and outpatient encounters in military and non-military medical facilities documented in the Defense Medical Surveillance System (DMSS) **(Table 1)**. Medical encounters from the Theater Medical Data Store (TMDS) were also included and were treated as outpatient encounters for the purpose of identifying incident cases. The diagnostic codes were grouped into five types of thyroid disorders based on the ICD coding system: goiter, thyrotoxicosis, primary/not otherwise specified (NOS) hypothyroidism, thyroiditis, and other disorders of thyroid. An incident case was defined by a hospitalization with a case-defining diagnostic code in any diagnostic position or two or more outpatient or in-theater diagnoses of the same thyroid disorder type between 1 and 180 days apart, with at least one of these diagnoses in a primary diagnostic position. One incident case diagnosis per individual per thyroid disorder type was counted. As such, a service member could count as a case for multiple different thyroid disorder types during the surveillance period.

Annual lifetime prevalence of each of the thyroid disorders was also ascertained. Prevalent cases were calculated as the number of service members who had ever been diagnosed with a particular thyroid disorder and who were in service during a given calendar year. Annual lifetime prevalence was calculated as the number of prevalent cases divided by the number of service members in service during a given year. Prevalence was expressed as the number of prevalent cases per 10,000 active component service members.

Individuals who met the case-definition for a specific thyroid disorder prior to the surveillance period (i.e., prevalent cases) were excluded from the incidence rate calculation of that specific thyroid disorder. Among incident cases of thyroid disorders, the numbers of individuals with prior diagnoses of thyroid cancer (ICD-9: 193, 237.4; ICD-10: C73, D44.0) and of each of the four other thyroid disorder types were ascertained.

RESULTS

Between 2008 and 2017, the most common incident thyroid disorder among male and female service members was primary/NOS hypothyroidism and the least common were thyroiditis and other disorders of thyroid **(Table 2, Figure 1)**. During this period, primary/NOS hypothyroidism was diagnosed among 8,641 females (incidence rate: 43.7 per 10,000 person years [p-yrs]) and 11,656 males (incidence rate: 10.2 per 10,000 p-yrs) **(Table 2)**. Crude overall incidence rates of goiter and thyrotoxicosis were lower than for primary/NOS hypothyroidism but higher than for thyroiditis and other thyroid disorders.

Of the service members diagnosed with other disorders of thyroid, 26.0% of females and 19.8% of males had been previously diagnosed with goiter and 17.2% and 14.4% had been previously diagnosed with primary/NOS hypothyroidism, among females and males respectively **(data not shown)**. In addition, 6.6% of female and 8.1% of male service members who were diagnosed with other disorders of thyroid had been previously diagnosed with thyroid cancer.

Overall incidence rates of thyroid disorders among females ranged from 4.3 (primary hypothyroidism) to 6.5 (other disorders of thyroid) times the rates of the respective conditions among males **(Table 2)**. For both sexes, rates of thyrotoxicosis, thyroiditis, and other disorders of the thyroid increased approximately linearly with increasing age, with the greatest difference in incidence between those aged 35-39 years and those aged 40 or more. In contrast, overall rates of goiter and primary/NOS hypothyroidism increased exponentially with increasing age **(Figures 2a, 2b)**. For all thyroid disorder types, the median ages at incident case diagnoses were 3 to 5 years higher among males than females **(data not shown)**.

TABLE 2. Numbers and rates of incident diagnoses of thyroid disorders, by demographic characteristics, active component, U.S. Armed Forces, 2008–2017

	Goiter			Thyrotoxicosis			Primary/ NOS hypothyroidism			Thyroiditis			Other disorders of thyroid		
	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]
All service members	10,022	7.4	---	5,544	4.1	---	20,297	15.1	---	3,571	2.6	---	2,776	2.1	---
All females	5,176	26.0	6.2	2,775	13.9	5.8	8,641	43.7	4.3	1,836	9.1	6.1	1,480	7.4	6.5
All males	4,846	4.2	ref	2,769	2.4	ref	11,656	10.2	ref	1,735	1.5	ref	1,296	1.1	ref
Females by age group															
< 20	109	7.5	ref	104	7.2	ref	263	18.1	ref	49	3.4	ref	47	3.2	ref
20–24	827	12.5	1.7	666	10.1	1.4	1,826	27.7	1.5	337	5.1	1.5	255	3.8	1.2
25–29	1,138	22.6	3.0	728	14.4	2.0	1,986	39.7	2.2	417	8.2	2.4	322	6.4	2.0
30–34	961	31.4	4.2	486	15.8	2.2	1,608	53.0	2.9	368	11.9	3.5	301	9.7	3.0
35–39	940	46.5	6.2	404	19.8	2.8	1,390	70.0	3.9	325	15.7	4.7	261	12.7	3.9
40+	1,201	68.6	9.1	387	21.6	3.0	1,568	92.3	5.1	340	18.8	5.6	294	16.3	5.0
Females by race/ethnicity															
Non-Hispanic white	2,354	25.8	ref	1,055	11.5	ref	5,306	59.2	ref	1,116	12.2	ref	691	7.5	ref
Non-Hispanic black	1,746	33.3	1.3	1,020	19.4	1.7	1,316	25.0	0.4	268	5.0	0.4	472	8.9	1.2
Hispanic	512	17.4	0.7	336	11.4	1.0	1,091	37.5	0.6	240	8.1	0.7	167	5.7	0.8
Asian/Pacific Islander	175	20.9	0.8	128	15.3	1.3	262	31.5	0.5	55	6.5	0.5	51	6.1	0.8
Other/unknown	389	21.5	0.8	236	13.0	1.1	666	37.1	0.6	157	8.6	0.7	99	5.4	0.7
Males by age group															
< 20	38	0.5	ref	85	1.2	ref	210	2.9	ref	22	0.3	ref	14	0.2	ref
20–24	495	1.4	2.6	574	1.6	1.3	1,740	4.8	1.6	243	0.7	2.2	177	0.5	2.5
25–29	710	2.6	4.9	570	2.1	1.8	2,010	7.4	2.5	302	1.1	3.6	230	0.8	4.3
30–34	763	4.2	8.1	495	2.8	2.3	2,057	11.5	3.9	316	1.8	5.8	222	1.2	6.4
35–39	1,000	7.4	14.0	458	3.4	2.9	2,197	16.3	5.6	363	2.7	8.8	234	1.7	8.9
40+	1,840	14.8	28.1	587	4.7	4.0	3,442	28.0	9.6	489	3.9	12.8	419	3.4	17.3
Males by race/ethnicity															
Non-Hispanic white	3,283	4.5	ref	1,449	2.0	ref	8,558	11.9	ref	1,281	1.8	ref	851	1.2	ref
Non-Hispanic black	725	4.4	1.0	622	3.8	1.9	855	5.2	0.4	115	0.7	0.4	184	1.1	0.9
Hispanic	400	2.8	0.6	333	2.3	1.1	1,335	9.2	0.8	202	1.4	0.8	146	1.0	0.9
Asian/Pacific Islander	149	3.5	0.8	163	3.9	1.9	273	6.5	0.5	42	1.0	0.6	46	1.1	0.9
Other/unknown	289	3.8	0.8	202	2.7	1.3	635	8.5	0.7	95	1.3	0.7	69	0.9	0.8

[a]Rate per 10,000 person-years
[b]Incidence rate ratio

Among both males and females, overall incidence rates of primary/NOS hypothyroidism and thyroiditis were higher among non-Hispanic white service members compared with service members in other race/ethnicity groups **(Table 2)**. Among females, rates of goiter, thyrotoxicosis, and other disorders of thyroid were highest among non-Hispanic black service members. Among males, rates of goiter were higher among non-Hispanic black and non-Hispanic white service members, and rates of thyrotoxicosis were highest among non-Hispanic blacks and Asian/Pacific Islanders.

Across all thyroid disorder types, overall incidence rates were higher among service members in the Air Force compared with members of other service branches **(Table 3)**. However, rates of thyrotoxicosis and other disorders of thyroid were similarly high among service members in the Army. Incidence rates of all thyroid disorder types, with the exception of thyrotoxicosis, were higher among senior officers and warrant officers, compared to those in other grades. Finally, service members in healthcare occupations had higher overall incidence rates of all thyroid disorder types compared with those in other occupations.

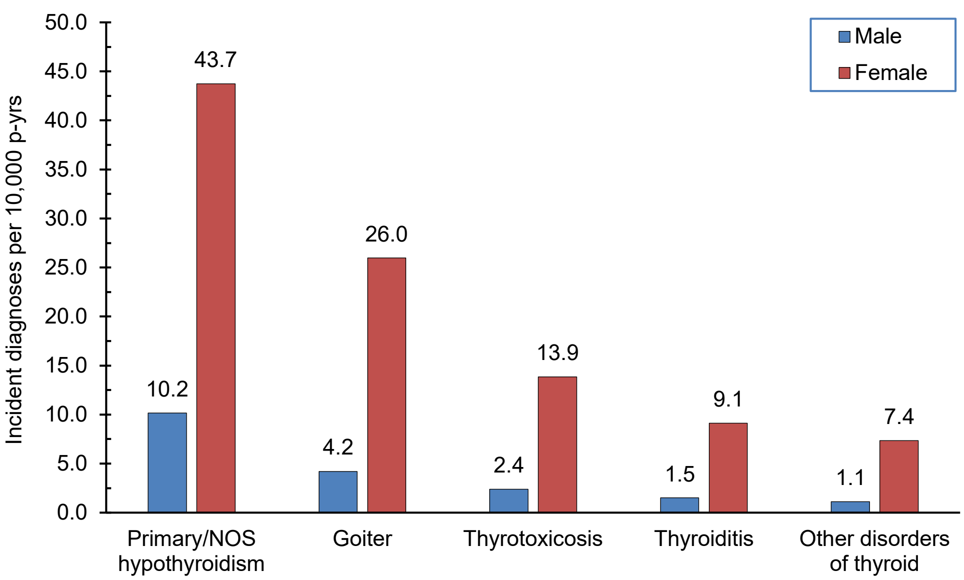
Among males, annual incidence rates for primary/NOS hypothyroidism showed the greatest variation compared to other thyroid disorders during the 10-year surveillance period, with a peak at 12.2 per 10,000 p-yrs in 2013 followed by a decrease to 8.9 per 10,000 p-yrs in 2017 **(Figure 3a)**. Annual rates of the other thyroid disorder types among male service members

TABLE 3. Numbers and rates of incident diagnoses of thyroid disorders, by military characteristics, active component, U.S. Armed Forces, 2008–2017

	Goiter		Thyrotoxicosis		Primary/ NOS hypothyroidism		Thyroiditis		Other disorders of thyroid	
	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
Service										
Army	3,998	7.7	2,493	4.8	9,107	17.6	1,440	2.8	1,242	2.4
Navy	2,003	6.3	1,096	3.4	3,881	12.2	797	2.5	550	1.7
Air Force	3,326	10.4	1,558	4.8	5,868	18.4	1,049	3.3	763	2.4
Marine Corps	695	3.6	397	2.1	1,441	7.5	285	1.5	221	1.1
Rank/grade										
Junior enlisted (E1–E4)	2,246	3.8	2,052	3.5	5,728	9.7	926	1.6	744	1.3
Senior enlisted (E5–E9)	5,074	9.6	2,618	4.9	9,276	17.6	1,688	3.2	1,399	2.6
Junior officer (O1–O3)	980	7.7	408	3.2	2,272	17.9	405	3.2	260	2.0
Senior officer (O4–O10)	1,496	17.6	393	4.6	2,619	31.2	475	5.6	320	3.7
Warrant officer (W1–W5)	226	12.0	73	3.9	402	21.4	77	4.1	53	2.8
Occupation										
Combat-specific[b]	720	3.6	380	1.9	1,947	9.8	276	1.4	191	1.0
Motor transport	241	6.0	192	4.8	464	11.5	82	2.0	73	1.8
Pilot/air crew	311	6.1	83	1.6	493	9.8	111	2.2	64	1.3
Repair/engineering	2,060	5.3	1,245	3.2	4,423	11.3	734	1.9	594	1.5
Communications/intelligence	2,943	9.9	1,674	5.6	5,229	17.7	1,003	3.4	849	2.9
Health care	1,916	16.4	934	8.0	3,738	32.2	702	6.0	499	4.2
Other	1,831	7.1	1,036	4.0	4,003	15.7	663	2.6	506	2.0

[a]Rate per 10,000 person-years
[b]Infantry/artillery/combat engineering/armor

FIGURE 1. Incidence rates of thyroid disorders, by type and sex, active component, U.S. Armed Forces, 2008–2017



were relatively low and stable during the surveillance period. Among females, with the exception of thyroiditis, crude annual incidence rates of each type of thyroid disorder decreased between 2008 and 2017 **(Figure 3b)**. The most pronounced decrease in annual rates among female service members was observed for primary/NOS hypothyroidism (42.5 per 10,000 p-yrs in 2008 to 36.0 per 10,000 p-yrs in 2017).

For both males and females, the prevalence of most thyroid disorders increased during the first part of the surveillance period and then either decreased slightly or leveled off **(Figures 4a, 4b)**. Among female service members, the prevalence of primary/NOS hypothyroidism, goiter, and thyroiditis peaked in 2014, and the prevalences of thyrotoxicosis and other disorders of thyroid

FIGURE 2a. Incidence rates of thyroid disorders, by type and age group, active component males, U.S. Armed Forces, 2008–2017

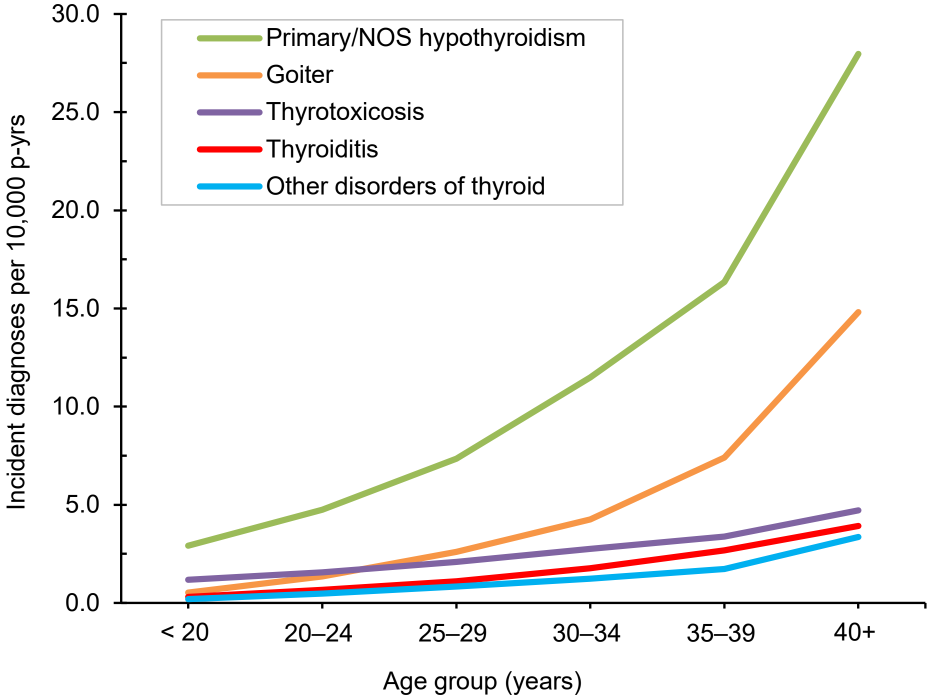
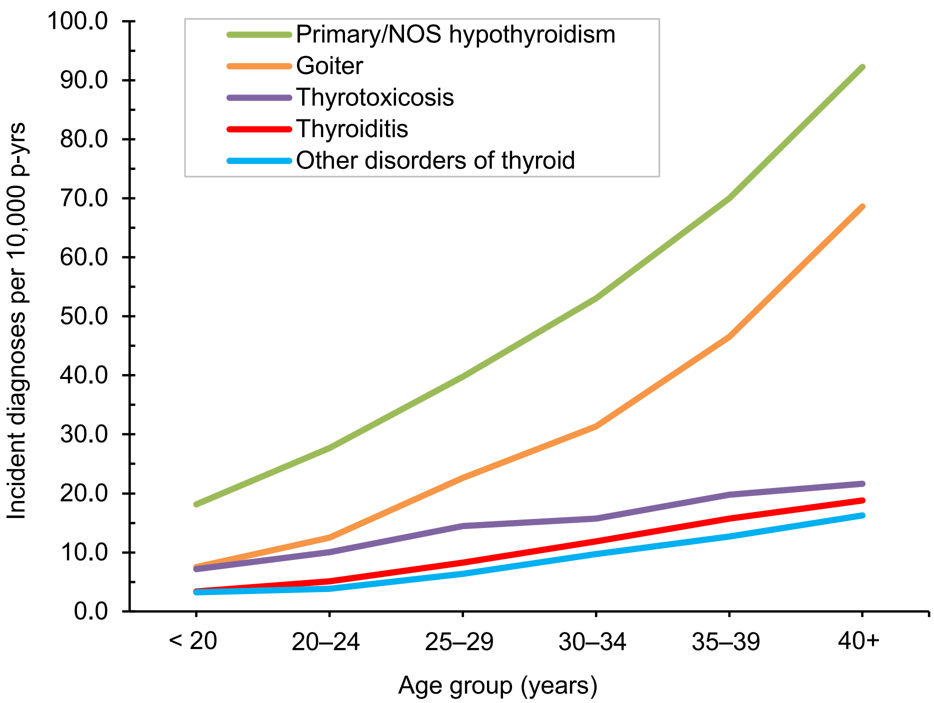


FIGURE 2b. Incidence rates of thyroid disorders, by type and age group, active component females, U.S. Armed Forces, 2008–2017



peaked in 2012. Prevalences of thyrotoxicosis and primary/NOS hypothyroidism similarly peaked among males in 2014; however, the prevalence of thyroiditis peaked in 2016 and that of other disorders of thyroid peaked in 2013. Among male service members, the prevalence of goiter increased steadily throughout the 10-year surveillance period.

EDITORIAL COMMENT

In contrast with a previous *MSMR* report documenting increases in thyroid disorder diagnoses among active component service members between 2002 and 2011, the results of the current analysis indicate that the incidence of thyroid disorders remained stable or decreased between 2008 and 2017. The 2012 *MSMR* report suggested that the increase in incidence during 2002–2011 may have been due, at least in part, to increased screening for thyroid disorders among service members affected by conditions with symptoms similar to those of thyroid disorders (e.g., depression, irritability, PTSD, musculoskeletal pain, sleep disorders), because incidence of these conditions increased sharply during the same period.[10]

Routine screening of young and healthy populations for thyroid disorders is not recommended by the U.S. Preventive Services Task Force, the American Association of Clinical Endocrinologists, or the American Thyroid Association.[11,12] However, because many of the signs and symptoms associated with thyroid dysfunction overlap with the clinical manifestations of other conditions such as sleep, musculoskeletal, and mental health disorders, thyroid function testing is often done to rule out thyroid dysfunction as a cause or exacerbating factor for these conditions that are highly prevalent in the military. The current analysis did not assess rates of screening for thyroid disorders because there was no specific ICD-10 code for thyroid disorder screening (ICD-9 code V77.0 “screening for thyroid disorders” maps to ICD-10 code Z13.29 “encounter for screening for other suspected endocrine disorder”). As a result, the impact of screening for thyroid dysfunction during the 2008–2017 surveillance period is unknown. However, a recent *MSMR* report documented that the incidence of mental health disorders among active component service members declined or remained stable between 2007 and 2016, which could suggest that there was decreased use of thyroid function testing to rule out thyroid dysfunction as a cause of or exacerbating factor for mental health disorders.[13]

FIGURE 3a. Annual incidence rates of thyroid disorders, by type, active component males, U.S. Armed Forces, 2008-2017

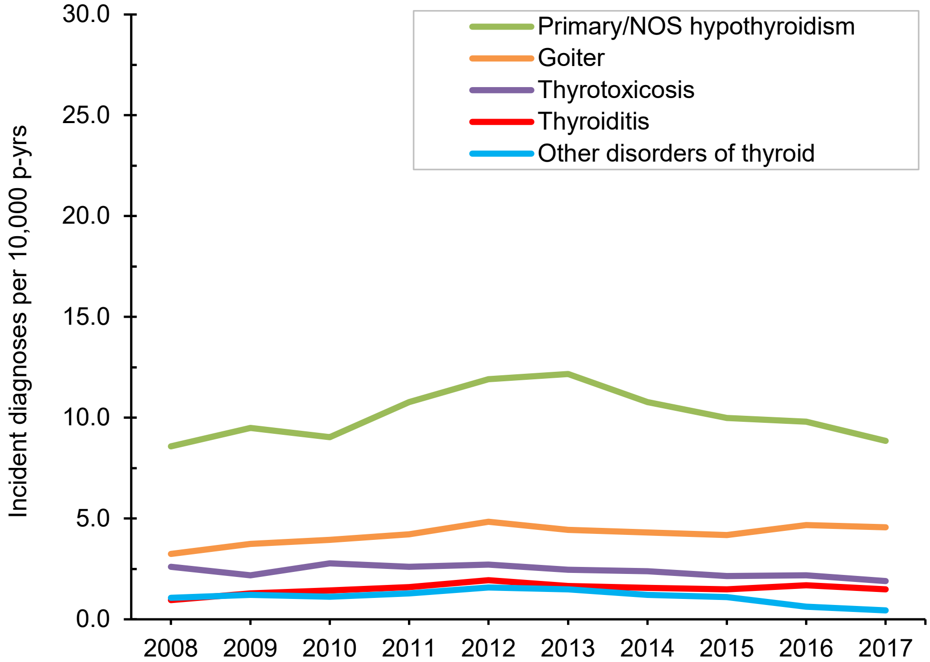
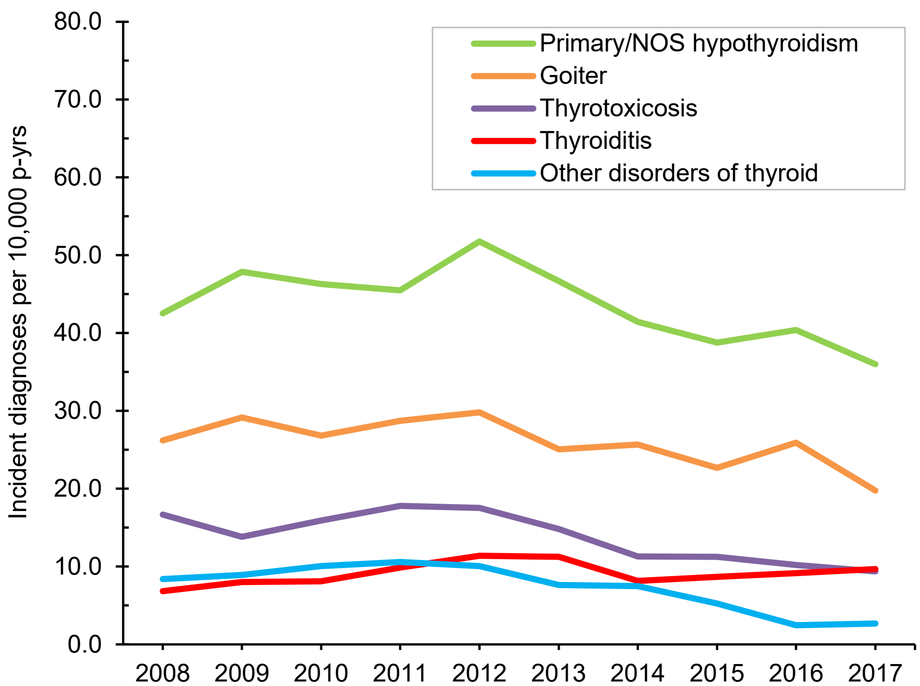


FIGURE 3b. Annual incidence rates of thyroid disorders, by type, active component females, U.S. Armed Forces, 2008-2017



McLeod and colleagues' study of U.S. military personnel during 1997–2011 demonstrated that the incidence of Graves disease, a frequent cause of thyrotoxicosis, was more common among non-Hispanic blacks and Asian/Pacific Islanders compared to non-Hispanic whites.[14] This finding is consistent with the results of the current analysis, which indicate a higher incidence of thyrotoxicosis among non-Hispanic black and Asian/Pacific Islander service members. In contrast, McLeod et al.'s study also found that the incidence of Hashimoto thyroiditis, a common cause of hypothyroidism, was highest among non-Hispanic whites and lowest among non-Hispanic blacks.[14] This is also consistent with the current study's finding that the incidence of thyroiditis was highest among non-Hispanic white service members and lowest among non-Hispanic black service members. Currently, it is unknown whether differences in rates of thyroid disorders by race/ethnicity are due to genetics, environmental exposures (e.g., smoking), or a combination of the two.

Similar to patterns observed in the U.S. civilian population,[4] results of the current study showed that incidence and prevalence of all types of thyroid disorders were much more common among female compared to male service members. One potential risk factor among women is hormone imbalance caused by estrogen dominance.[15] Estrogen receptors are widely expressed in most cells of the immune system and high estrogen levels may lead to deregulation and aberrant activation of the immune system.[16] In addition, pregnancy can put stress on the thyroid gland and autoimmune thyroid disease may be triggered due to the shift in hormone levels or immune function during and after pregnancy.[16,17]

The finding that higher incidence of all thyroid disorders was observed among healthcare personnel is likely related to increased medical awareness, easier access to care, and, perhaps, older age compared to their respective counterparts in other occupations. Higher rates observed among senior enlisted personnel and officers are likely highly correlated with and confounded by age. In addition, higher rates observed among Army and Air Force service members may be related to differences in the demographic distributions of the services.

A significant limitation to this report is that the incidence rates of thyroid disorders were based on diagnoses recorded on standardized medical records. Because of this, the findings reflect the rates of thyroid functional abnormalities that were clinically detected and exclude subclinical dysfunction since not all service members

FIGURE 4a. Annual lifetime prevalence rates of thyroid disorders, by type, active component males, U.S. Armed Forces, 2008–2017

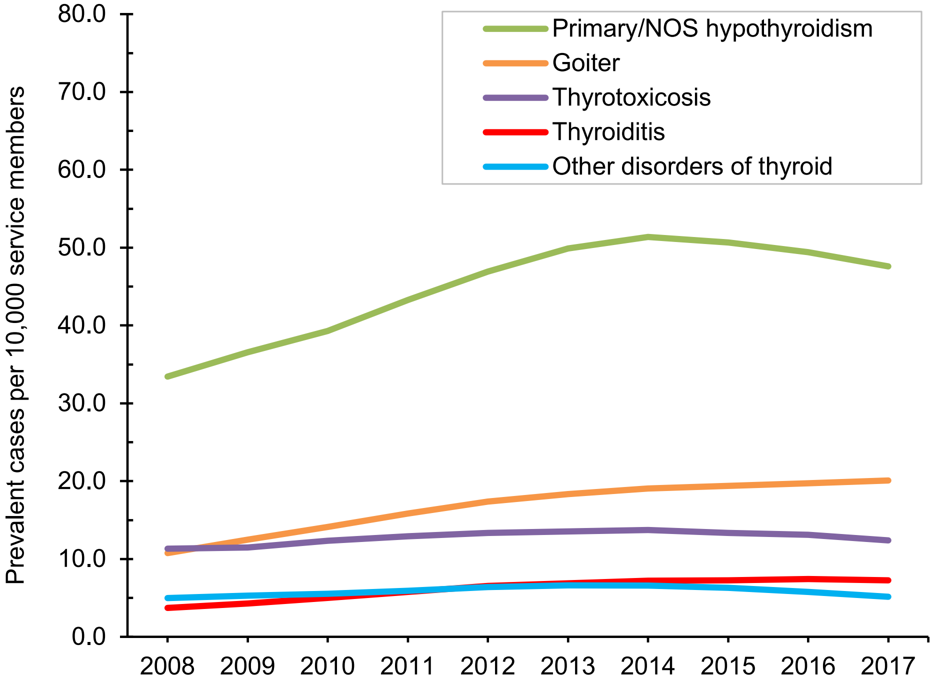
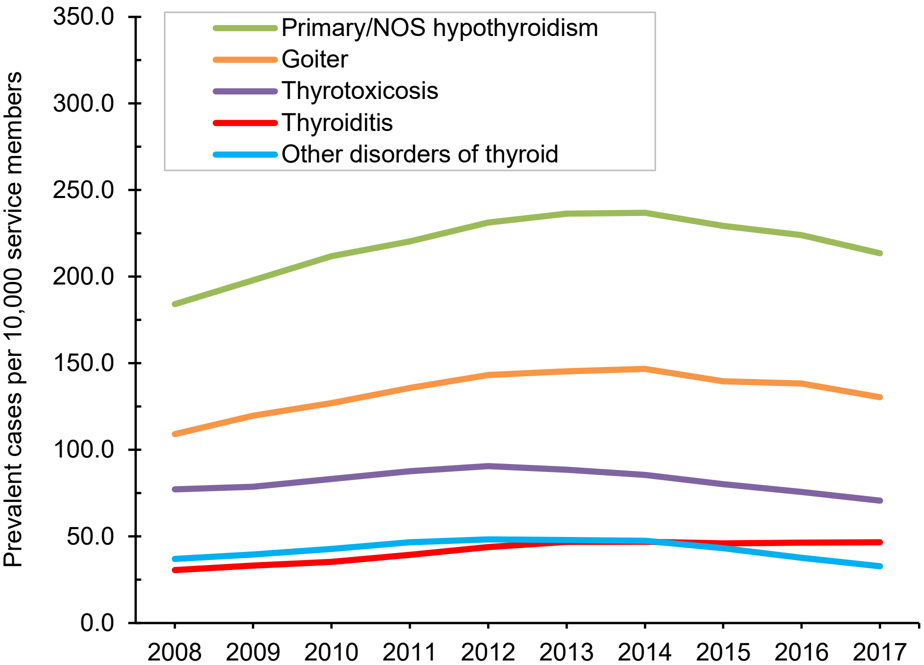


FIGURE 4b. Annual lifetime prevalence rates of thyroid disorders, by type, active component females, U.S. Armed Forces, 2008–2017



are tested for thyroid disorders. Service members may be more likely to be tested for thyroid disorders as a rule-out diagnosis if they are presenting with fatigue, mental health disorders, sleeping disorders, musculoskeletal problems, etc., since these conditions may be viewed as symptoms of possible underlying thyroid disorder. As such, the incidence of thyroid disorders among service members may depend in part on the incidence of these other conditions. Another limitation of the current analysis is related to the implementation of MHS GENESIS, the new electronic health record for the Military Health System. During 2017, medical data from sites that were using MHS GENESIS were not available in DMSS. These sites include Naval Hospital Oak Harbor, Naval Hospital Bremerton, Air Force Medical Services Fairchild, and Madigan Army Medical Center. Therefore, medical encounters and person-time data for individuals seeking care at one of these facilities during 2017 were excluded from the analysis. Findings from this report nevertheless provide useful and updated information regarding the burden of thyroid disorders on the Military Health System.

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Adrenal Gland Disorders, Active Component, U.S. Armed Forces, 2002–2017

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During 2002–2017, the most common incident adrenal gland disorder among male and female service members was adrenal insufficiency and the least common was adrenomedullary hyperfunction. Adrenal insufficiency was diagnosed among 267 females (crude overall incidence rate: 8.2 cases per 100,000 person-years [p-yrs]) and 729 males (3.9 per 100,000 p-yrs). In both sexes, overall rates of other disorders of adrenal gland and Cushing's syndrome were lower than for adrenal insufficiency but higher than for hyperaldosteronism, adrenogenital disorders, and adrenomedullary hyperfunction. Crude overall rates of adrenal gland disorders among females tended to be higher than those of males, with female:male rate ratios ranging from 2.1 for adrenal insufficiency to 5.5 for adrenogenital disorders and Cushing's syndrome. The highest overall rates of adrenal insufficiency for males and females were among non-Hispanic white service members. Among females, rates of Cushing's syndrome and other disorders of adrenal gland were higher among non-Hispanic white service members compared with those in other race/ethnicity groups. In both sexes, the annual rates of adrenal insufficiency and other disorders of adrenal gland increased slightly during the 16-year period.

WHAT ARE THE NEW FINDINGS?

This is the first *MSMR* report of the incidence of adrenal disorders in the U.S. Armed Forces. These relatively rare disorders were diagnosed in service members 2,356 times during 2002–2017 (rate: 10.7 cases per 100,000 person-years). Rates increased with age, especially over age 30. The most common type of adrenal disorder was adrenal insufficiency.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Because of the relative rarity of these disorders in young adults, their impact on force readiness is limited; however, their occurrence may impair affected individuals' readiness and ability to continue to serve. The causes of these disorders are unknown so there are no force health protection measures that can be implemented.

The adrenal glands are located at the top of each kidney and produce hormones that help regulate metabolism, blood sodium and potassium levels, blood pressure, response to stressors, immune function, and other essential functions.[1] The adrenal glands produce cortisol, aldosterone, catecholamines (epinephrine, norepinephrine, and dopamine), and small amounts of androgens (hormones with testosterone-like function).[1]

Adrenal disorders can be caused by the production of too much or too little of a particular adrenal hormone.[1] Adrenal insufficiency occurs when the outer portion of the adrenal gland (adrenal cortex) does not produce an adequate amount of cortisol.[2] This condition is due to either primary adrenal failure (Addison's disease) or to secondary hypothalamic-pituitary impairment; the former is most often the result of autoimmune destruction of the adrenal cortex and the latter is generally the result of pituitary disease.[2,3] A diagnosis of primary adrenal insufficiency is established on the basis of a poor response to the adrenocorticotropic hormone (ACTH) stimulation test and an elevated blood ACTH level.[4] Adrenal insufficiency is rare with prevalence estimates in Western countries ranging from 82 to 280 cases per million population.[3–12] Individuals affected by this condition may experience fatigue, generalized weakness, loss of appetite, abdominal pain, weight loss, low blood pressure, and salt craving.[3] Both primary and secondary adrenal insufficiency occur more frequently in adult women than in adult men and can be life threatening if untreated.[5,6,13–15] Primary adrenal insufficiency most often appears between the ages of 30 and 50 years while the age at diagnosis of secondary adrenal insufficiency peaks in the sixth decade of life.[5,14]

Cushing's syndrome is a rare disorder caused by chronic exposure to excess cortisol and can be caused by the administration of excessive doses of corticosteroids (exogenous) or the overproduction of cortisol by the adrenal cortex (endogenous).[16] As a screening test for Cushing's syndrome, the Endocrine Society's Clinical Practice guidelines recommend a single test with a high diagnostic accuracy (an overnight 1-mg dexamethasone suppression test, an elevated late night salivary cortisol level, or an elevated free cortisol level in a 24-hour urine specimen).[17] In the U.S., among commercially insured patients under 65 years of age, endogenous Cushing's syndrome has an estimated incidence of between 39.5 and 48.6 cases per million population per year.[18] Common signs and symptoms of Cushing's syndrome include decreased libido, weight gain/obesity, plethora, facial rounding, menstrual changes, hirsutism (male-pattern hair growth on a woman's face, chest and back), hypertension, depression, lethargy, and abnormal glucose tolerance.[16] In general, women are more likely than men to develop Cushing's syndrome; however, both the sex- and age-related distributions vary by the cause of the condition.[16,19,20] Cushing's syndrome is associated with considerable comorbidity and increased mortality.[21] Cardiometabolic (e.g., thromboembolism, hypertension, diabetes, dyslipidemia) and neuropsychiatric comorbidities (e.g., mood disorders) are common as are adverse effects on bone (e.g., decreased osteoblastic and increased osteoclastic activity).[22,23]

Hyperaldosteronism is a rare condition that occurs when the adrenal cortex produces too much aldosterone, a hormone that controls blood pressure by regulating blood sodium and potassium levels.[1] The excess aldosterone is produced either by a tumor in one or both of the adrenal glands (primary aldosteronism—usually a noncancerous adenoma) or by some other condition elsewhere in the body (secondary aldosteronism—e.g., renovascular disease).[1,24] Hyperaldosteronism is associated with the development of adverse cardiometabolic and renal effects that are partly independent of its effects on blood pressure.[24,25] Among high-risk groups of hypertensive patients and those with hypokalemia (low blood potassium level), the Endocrine Society's Clinical Practice guidelines recommend screening for primary hyperaldosteronism using the plasma aldosterone/renin ratio.[26] Studies that have investigated the prevalence of primary hyperaldosteronism report a wide range of estimates (<1%–30%) that vary depending on the characteristics of the study population, healthcare setting, and diagnostic method employed.[27] Hyperaldosteronism occurs more frequently in women than in men with the condition most commonly presenting between the ages of 30 and 50 years.[28]

Adrenogenital disorders are caused by overproduction of adrenocortical steroids (especially those with androgenic or estrogenic effects) and are characterized by masculinization of women, feminization of men, sexual ambiguity, or precocious sexual development of children.[1] This condition may be the result of congenital enzyme defects in steroidgenesis (congenital adrenal hyperplasia) or may be acquired, developing as a result of a tumor or hyperplasia of the adrenal glands.[29] The incidence of congenital adrenal hyperplasia varies according to ethnicity and geographic region. In the U.S., this condition is particularly common in American Indians and Yupik Eskimos (1 in 280 live births).[30] Among U.S. non-Hispanic whites, the incidence has been estimated at 1 in 15,000 live births.[31]

Adrenomedullary hyperfunction is a rare condition that occurs when the inner portion of the adrenal gland (medulla) produces an excess of catecholamines, hormones important for the regulation of metabolism, contractility of cardiac and smooth muscle, and neurotransmission.[32] Common symptoms of adrenomedullary hyperfunction include hypertension, episodic headache, excessive sweating, and tachycardia.[33] This condition is most often due to rare neoplasms called pheochromocytoma.[32] The estimated incidence of pheochromocytoma is 0.8 cases per 100,000 person-years.[33] Diagnosis of this condition is typically made between the ages of 40 and 50 years without pronounced predominance in either sex.[33]

The incidence and prevalence of adrenal disorders in the active component of the U.S. Armed Forces have not been previously described. The current report addresses this gap by examining the incidence, prevalence, and trends of adrenal disorders other than adrenal cancer among the population of active component U.S. service members during 2002–2017.

TABLE 1. ICD-9 and ICD-10 codes for adrenal gland disorders

	ICD-9[a]	ICD-10[a]
Cushing's syndrome	255.0	E24.*
Hyperaldosteronism	255.1*	E26.*
Adrenogenital disorders	255.2*	E25.*
Adrenal insufficiency	255.4*	E27.1, E27.2, E27.40, E27.49
Adrenomedullary hyperfunction	255.6*	E27.5
Other disorders of adrenal gland	255.3, 255.5, 255.8, 255.9	E27.0, E27.3, E27.8, E27.9

[a]An asterisk (*) indicates that any subsequent digit/character is included

METHODS

The surveillance period was January 1, 2002 through December 31, 2017. The surveillance population consisted of all individuals who served in the active component of the Army, Navy, Air Force, or Marine Corps at any time during the surveillance period. Adrenal gland disorders were identified by diagnostic codes for "disorders of adrenal gland" recorded in standardized records of inpatient and outpatient encounters in military and nonmilitary medical facilities documented in the Defense Medical Surveillance System (DMSS) **(Table 1)**. The diagnostic codes were grouped into six types of adrenal gland disorders: Cushing's syndrome, hyperaldosteronism, adrenogenital disorders, adrenal insufficiency, adrenomedullary hyperfunction, and other disorders of adrenal gland.

An incident case was defined by hospitalization with a case-defining diagnostic code in any diagnostic position or two or more outpatient diagnoses of the same adrenal disorder type between 1 and 180 days apart, with at least one of these diagnoses in a primary diagnostic position. One incident case diagnosis per individual per adrenal disorder type was counted. As such, a service member could be counted as a case for multiple different adrenal disorder types during the surveillance period. Individuals who met the case definition for a specific adrenal gland disorder prior to the surveillance period (i.e., prevalent cases) were excluded from the incidence rate calculation of that disorder. Incidence rates were calculated as incident adrenal gland disorder diagnoses per 100,000 person years (p-yrs) of active component service. Both deployed and non-deployed person time was used in the denominator.

Among incident cases of adrenal gland disorders, the numbers of individuals with prior diagnoses of adrenal gland cancer (ICD-9: 194.0, 237.2; ICD-10: C74.*, D44.1*) and each of the five other adrenal gland disorder types were ascertained.

Lifetime prevalence of the diagnoses of each of the six adrenal disorder types was estimated for each year in the 16-year surveillance period. The numerator for annual lifetime prevalence calculations consisted of service members who had ever been diagnosed with a particular adrenal gland disorder and who were in service during the given calendar year. The denominator for annual prevalence calculations consisted of the total number of active component service members who served at any time during the given year. Annual prevalence estimates were calculated as the number of prevalent cases per 100,000 active component service members.

RESULTS

From 2002 through 2017, the most common incident adrenal gland disorder among male and female service members was adrenal insufficiency and the least common was adrenomedullary hyperfunction **(Table 2; Figure 1)**. Adrenal insufficiency was diagnosed among 267 females (crude overall incidence rate: 8.2 cases per 100,000 p-yrs) and 729 males (crude overall incidence rate: 3.9 cases per 100,000 p-yrs) during this period **(Table 2)**. Among both male and female service members, crude overall incidence rates of other disorders of adrenal gland and Cushing's syndrome were lower than for adrenal insufficiency but higher than for hyperaldosteronism, adrenogenital disorders, and adrenomedullary hyperfunction.

Of the service members diagnosed with other disorders of adrenal gland, 10.1% (n=23) of females and 6.7% (n=31) of males had been previously diagnosed with adrenal insufficiency. In addition, 5.3% (n=12) of female service members with incident diagnoses of other disorders of adrenal gland had prior diagnoses of Cushing's syndrome **(data not shown)**. Of the service members diagnosed with adrenomedullary hyperfunction, 15.2% (n=5) of males and 50.0% (n=2) of females had been previously diagnosed with other disorders of adrenal gland. Furthermore, 12.1% (n=4) of male service members who were diagnosed with adrenomedullary hyperfunction had been previously diagnosed with adrenal gland cancer.

Crude overall incidence rates of adrenal gland disorders among females tended to be higher than those of males, with female:male rate ratios ranging from 2.1 for adrenal insufficiency to 5.5 for adrenogenital disorders and Cushing's syndrome **(Table 2)**. Adrenomedullary hyperfunction was the only condition for which males and females had a similar incidence (0.2 cases per 100,000 p-yrs for males and 0.1 cases per 100,000 p-yrs for females). Among service members of both sexes, overall rates of adrenal insufficiency and other disorders of adrenal gland increased approximately exponentially with increasing age; the greatest differences in overall incidence rates were between those aged 35–39 years and those aged 40 years or older **(Figures 2a, 2b; Table 3)**. Among males, rates of Cushing's syndrome increased monotonically with age. A similar pattern in rates of this condition was observed among females for all but the oldest age group (40+ years) **(Table 3)**. Rates of hyperaldosteronism were relatively low among members of the youngest age groups for both sexes. However, among females, the greatest difference in incidence rates of this condition were observed between those aged 25–29 years and those aged 30–34 years whereas the greatest difference in rates among males was between those aged 30–34 years and those aged 35 years or older **(Figures 2a, 2b; Table 3)**. Rates of adrenogenital disorders among female service members were highest among those in the age groups spanning 20–34 years. In contrast, rates of this condition among male service members increased approximately linearly with increasing age. Across all age groups among both sexes, rates of adrenomedullary hyperfunction were relatively low.

Descriptive analysis of age at incident case diagnosis by sex showed that, for Cushing's syndrome, other disorders of adrenal gland, and hyperaldosteronism, the median ages at incident case diagnoses were two to 7 years higher among males than females **(data not shown)**. The median age at incident diagnosis of adrenogenital disorders was 10 years higher among males than females. In contrast, the median age at incident diagnosis of adrenomedullary hyperfunction was 5.5 years higher among females than among males **(data not shown)**.

During the surveillance period, the highest overall incidence rates of adrenal insufficiency for males and females were among non-Hispanic white service members **(Table 3)**. Among both sexes, rates of hyperaldosteronism were highest among non-Hispanic black service members. Among females, rates of Cushing's syndrome and other disorders of adrenal gland were higher among non-Hispanic white service members compared with those in other race/ethnicity groups. Rates of other disorders of adrenal gland among male service members were highest among those of other/unknown race/ethnicity **(Table 3)**.

Overall incidence rates of adrenal insufficiency and Cushing's syndrome were higher among service members in the Air Force compared with members of other service branches whereas rates of other disorders of adrenal gland were highest among Army members **(Table 2)**. Across all adrenal disorder types, overall incidence rates were lowest among Marine Corps members. With the exception of adrenogenital disorders and adrenomedullary hyperfunction, rates were higher among senior officers, compared to those in other grades. Service members in healthcare occupations had the highest overall incidence rates of all adrenal gland disorders except adrenomedullary hyperfunction **(Table 2)**.

Due to the small number of cases each year, incidence rates were collapsed into 4-year groupings to assess changes over time. During the 16-year surveillance period, the incidence of Cushing's syndrome and hyperaldosteronism among males remained relatively low and stable **(Figure 3a)**. Notably, the incidence of adrenal insufficiency among males increased from a low of 2.1 cases per 100,000 p-yrs during the 2002–2005 period to a high of 5.4 cases per 100,000 p-yrs during the 2014–2017 period. Annual rates of other disorders of adrenal gland among males increased from a low of 1.2 cases per

TABLE 2. Numbers and rates of incident diagnoses of adrenal gland disorders, active component, U.S. Armed Forces, 2002–2017

	Cushing's syndrome			Hyperaldosteronism			Adrenal insufficiency			Adrenogenital disorders			Adrenomedullary hyperfunction			Other disorders of adrenal gland		
	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]
Total	328	1.5	--	209	1.0	--	996	4.5	--	96	0.4	--	37	0.2	--	690	3.1	--
Sex																		
Male	168	0.9	ref	145	0.8	ref	729	3.9	ref	49	0.3	ref	33	0.2	ref	462	2.5	ref
Female	160	4.9	5.47	64	2.0	2.5	267	8.2	2.1	47	1.4	5.5	4	0.1	0.7	228	7.0	2.8
Age group (years)																		
< 20	4	0.3	ref	4	0.3	ref	35	2.3	ref	1	0.1	ref	0	0.0	ref	13	0.9	ref
20–24	65	0.9	3.4	19	0.3	1.0	197	2.7	1.2	22	0.3	4.6	5	0.1	1.0	110	1.5	1.8
25–29	83	1.7	6.2	19	0.4	1.4	190	3.8	1.6	20	0.4	6.0	8	0.2	1.0	127	2.5	2.9
30–34	54	1.6	6.1	26	0.8	3.0	164	4.9	2.1	17	0.5	7.7	5	0.2	1.0	107	3.2	3.7
35–39	59	2.2	8.5	57	2.2	8.2	176	6.7	2.9	17	0.6	9.8	11	0.4	1.0	121	4.6	5.3
40+	63	2.7	10.2	84	3.6	13.7	234	10.1	4.3	19	0.8	12.4	8	0.3	1.0	212	9.2	10.6
Race/ethnicity																		
Non-Hispanic white	198	1.5	ref	79	0.6	ref	639	4.8	ref	60	0.4	ref	25	0.2	ref	431	3.2	ref
Non-Hispanic black	69	1.9	1.3	97	2.6	4.5	173	4.7	1.0	19	0.5	1.2	5	0.1	0.7	137	3.7	1.2
Hispanic	34	1.3	0.9	15	0.6	1.0	91	3.5	0.7	12	0.5	1.0	5	0.2	1.0	60	2.3	0.7
Asian/Pacific Islander	10	1.2	0.8	5	0.6	1.0	28	3.4	0.7	1	0.1	0.3	0	0.0	0.0	14	1.7	0.5
Other/unknown	17	1.2	0.8	13	0.9	1.5	65	4.5	1.0	4	0.3	0.6	2	0.1	0.7	48	3.4	1.0
Service																		
Army	117	1.4	ref	82	1.0	ref	416	5.1	ref	49	0.6	ref	17	0.2	ref	305	3.7	ref
Navy	80	1.5	1.0	63	1.2	1.2	177	3.3	0.6	21	0.4	0.7	9	0.2	0.8	147	2.7	0.7
Air Force	107	2.0	1.4	59	1.1	1.1	313	5.8	1.1	21	0.4	0.7	9	0.2	0.8	182	3.4	0.9
Marine Corps	24	0.8	0.6	5	0.2	0.2	90	3.0	0.6	5	0.2	0.3	2	0.1	0.3	56	1.9	0.5
Rank/grade																		
Junior enlisted (E1–E4)	96	1.0	ref	39	0.4	ref	302	3.2	ref	29	0.3	ref	7	0.1	ref	179	1.9	ref
Senior enlisted (E5–E9)	166	1.9	1.9	113	1.3	3.2	470	5.4	1.7	47	0.5	1.8	25	0.3	3.9	367	4.2	2.3
Junior officer (O1–O3, W1–W3)	34	1.5	1.5	21	0.9	2.3	109	4.8	1.5	13	0.6	1.9	3	0.1	1.8	54	2.4	1.3
Senior officer (O4–O10, W4–W5)	32	2.2	2.2	36	2.5	6.2	115	8.1	2.6	7	0.5	1.6	2	0.1	1.9	90	6.3	3.4
Occupation																		
Combat-specific[c]	26	0.8	ref	11	0.4	ref	141	4.6	ref	11	0.4	ref	3	0.1	ref	97	3.1	ref
Motor transport	6	0.9	1.1	7	1.1	3.0	30	4.6	1.0	3	0.5	1.3	1	0.2	1.6	22	3.3	1.1
Pilot/air crew	10	1.2	1.4	6	0.7	2.0	33	3.9	0.9	3	0.4	1.0	1	0.1	1.2	18	2.2	0.7
Repair/engineering	71	1.1	1.3	53	0.8	2.3	235	3.6	0.8	28	0.4	1.2	11	0.2	1.8	166	2.6	0.8
Communications/ intelligence	114	2.3	2.8	57	1.2	3.3	249	5.1	1.1	19	0.4	1.1	9	0.2	1.9	173	3.5	1.1
Health care	57	3.0	3.6	40	2.1	6.0	134	7.1	1.6	16	0.8	2.4	4	0.2	2.2	98	5.2	1.7
Other	44	1.1	1.3	35	0.9	2.4	174	4.2	0.9	16	0.4	1.1	8	0.2	2.0	116	2.8	0.9

[a]Rate per 100,000 person-years
[b]Incidence rate ratio
[c]Infantry/artillery/combat engineering/armor

100,000 p-yrs in the 2002–2005 period to a peak of 3.0 cases per 100,000 p-yrs in the 2010-2013 and 2014-2017 periods. Among females, the incidence of adrenal insufficiency and Cushing's syndrome peaked during the 2010–2013 period at 10.5 and 6.1 cases per 100,000 p-yrs, respectively **(Figure 3b)**. In contrast, rates of hyperaldosteronism and other disorders of the adrenal gland increased gradually during the surveillance period. The number of cases for adrenomedullary hyperfunction and adrenogenital disorders were too small to assess trends over time.

The pattern of annual prevalence rates of adrenal insufficiency during 2002–2017 were broadly similar for both sexes with an increase in prevalence between 2002

TABLE 3. Numbers and rates of incident diagnoses of adrenal disorders, by sex, age, and race/ethnicity, active component, U.S. Armed Forces, 2002-2017

	Cushing's syndrome			Hyperaldosteronism			Adrenal insufficiency			Adrenogenital disorders			Adrenomedullary hyperfunction			Other disorders of adrenal gland		
	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]	No.	Rate[a]	IRR[b]
All service members	328	1.5	--	209	1.0	--	996	4.5	--	96	0.4	--	37	0.2	--	690	3.1	--
Females by age group																		
< 20	4	1.6	ref	4	1.6	ref	4	1.6	ref	1	0.4	ref	0	0.0	ref	4	1.6	ref
20–24	29	2.6	1.6	11	1.0	0.6	43	3.8	2.4	18	1.6	4.1	0	0.0	1.0	41	3.7	2.3
25–29	46	5.9	3.7	8	1.0	0.7	56	7.2	4.6	12	1.5	3.9	0	0.0	1.0	44	5.6	3.6
30–34	29	6.1	3.9	16	3.4	2.1	56	11.8	7.5	9	1.9	4.8	1	0.2	1.0	41	8.7	5.5
35–39	29	8.7	5.5	12	3.6	2.3	47	14.1	9.0	3	0.9	2.3	1	0.3	1.0	39	11.7	7.4
40+	23	7.9	5.0	13	4.4	2.8	61	20.8	13.3	4	1.4	3.5	2	0.7	1.0	59	20.2	12.8
Females by race/ethnicity																		
Non-Hispanic white	86	5.6	ref	31	2.0	ref	141	9.2	ref	25	1.6	ref	3	0.2	ref	121	7.9	ref
Non-Hispanic black	41	4.6	0.8	23	2.6	1.3	77	8.7	0.9	12	1.4	0.8	1	0.1	0.6	64	7.2	0.9
Hispanic	23	5.3	0.9	6	1.4	0.7	20	4.6	0.5	8	1.8	1.1	0	0.0	0.0	21	4.8	0.6
Asian/Pacific Islander	2	1.5	0.3	1	0.8	0.4	6	4.6	0.5	0	0.0	0.0	0	0.0	0.0	8	6.1	0.8
Other/unknown	8	3.0	0.5	3	1.1	0.6	23	8.5	0.9	2	0.7	0.5	0	0.0	0.0	14	5.2	0.7
Males by age group																		
< 20	0	0.0	ref	0	0.0	ref	31	2.5	ref	0	0.0	ref	0	0.0	ref	9	0.7	ref
20–24	36	0.6	1.0	8	0.1	1.0	154	2.5	1.0	4	0.1	1.0	5	0.1	1.0	69	1.1	1.6
25–29	37	0.9	1.0	11	0.3	1.0	134	3.2	1.3	8	0.2	1.0	8	0.2	1.0	83	2.0	2.7
30–34	25	0.9	1.0	10	0.4	1.0	108	3.8	1.5	8	0.3	1.0	4	0.1	1.0	66	2.3	3.2
35–39	30	1.3	1.0	45	2.0	1.0	129	5.6	2.3	14	0.6	1.0	10	0.4	1.0	82	3.6	5.0
40+	40	2.0	1.0	71	3.5	1.0	173	8.5	3.5	15	0.7	1.0	6	0.3	1.0	153	7.6	10.5
Males by race/ethnicity																		
Non-Hispanic white	112	0.9	ref	48	0.4	ref	498	4.2	ref	35	0.3	ref	22	0.2	ref	310	2.6	ref
Non-Hispanic black	28	1.0	1.1	74	2.6	6.5	96	3.4	0.8	7	0.3	0.8	4	0.1	0.8	73	2.6	1.0
Hispanic	11	0.5	0.5	9	0.4	1.0	71	3.3	0.8	4	0.2	0.6	5	0.2	1.2	39	1.8	0.7
Asian/Pacific Islander	8	1.2	1.2	4	0.6	1.4	22	3.2	0.8	1	0.1	0.5	0	0.0	0.0	6	0.9	0.3
Other/unknown	9	0.8	0.8	10	0.9	2.1	42	3.6	0.9	2	0.2	0.6	2	0.2	0.9	34	2.9	1.1

[a]Rate per 100,000 person-years
[b]Incidence rate ratio

and 2012. This increase was followed by a slight decrease until 2015, after which rates increased through the end of the surveillance period **(Figures 4a, 4b)**. For males, annual prevalence of other disorders of adrenal gland increased steadily during 2002–2015 and then decreased during the last two years of the surveillance period. Prevalence of this condition among females showed a similar pattern but with a peak occurring in 2013. Annual prevalence of Cushing's syndrome and hyperaldosteronism among males was relatively stable throughout the 16-year period. In contrast, prevalence of these two conditions among females showed an overall increase during the period. Among females, prevalence of adrenogenital disorders increased slightly during 2002–2017.

EDITORIAL COMMENT

Adrenal disorders are rare conditions but when present can significantly reduce the operational fitness of affected military members. As such, current adrenal dysfunction or any history of adrenal dysfunction requiring treatment or hormone replacement, is a disqualifying condition for entrance into the U.S. military.[34] However, because the majority of adrenal disorders generally are diagnosed among those over 30 years of age, newly incident diagnoses of these conditions are likely to affect service members later in their military careers. Conditions requiring referral to a medical evaluation board include adrenal insufficiency requiring replacement therapy, Cushing's syndrome, primary hyperaldosteronism when resulting in uncontrolled hypertension and/or hypokalemia, pheochromocytoma, and salt-wasting congenital adrenal hyperplasia.[35]

FIGURE 1. Incidence rates of adrenal gland disorders by type, by sex, active component, U.S. Armed Forces, 2002–2017

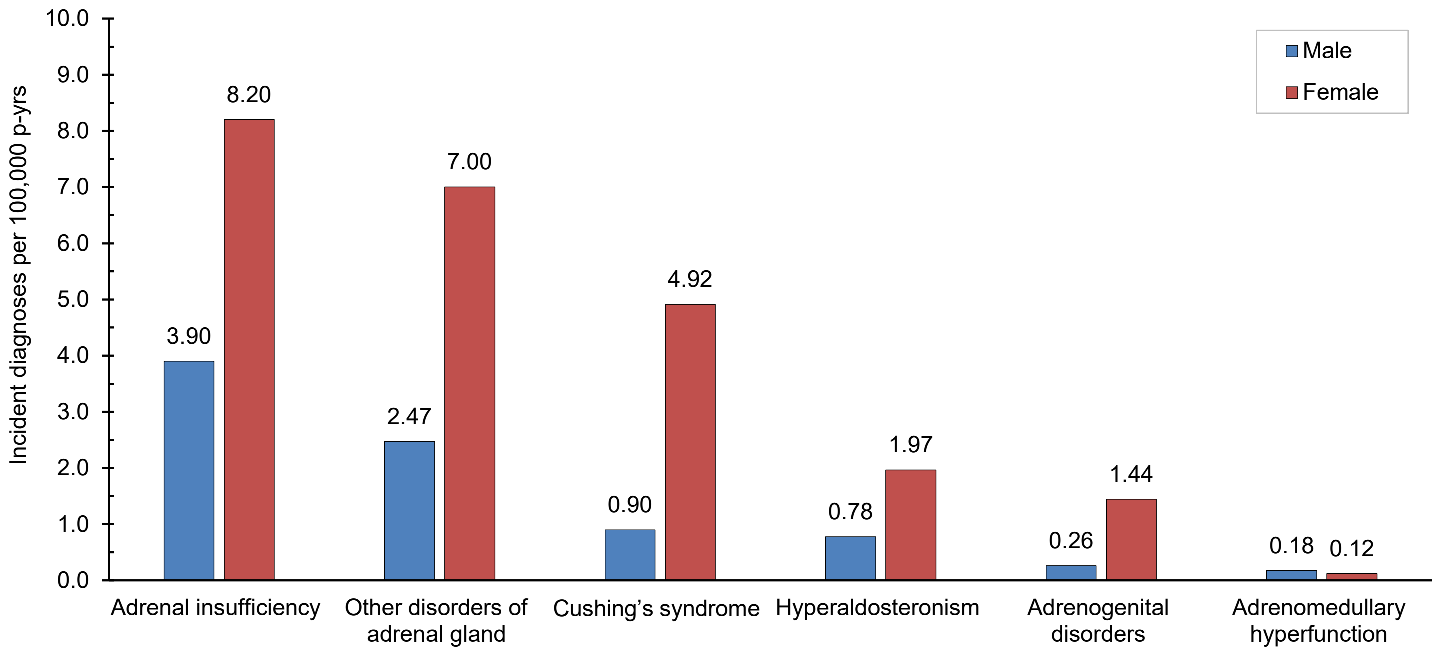
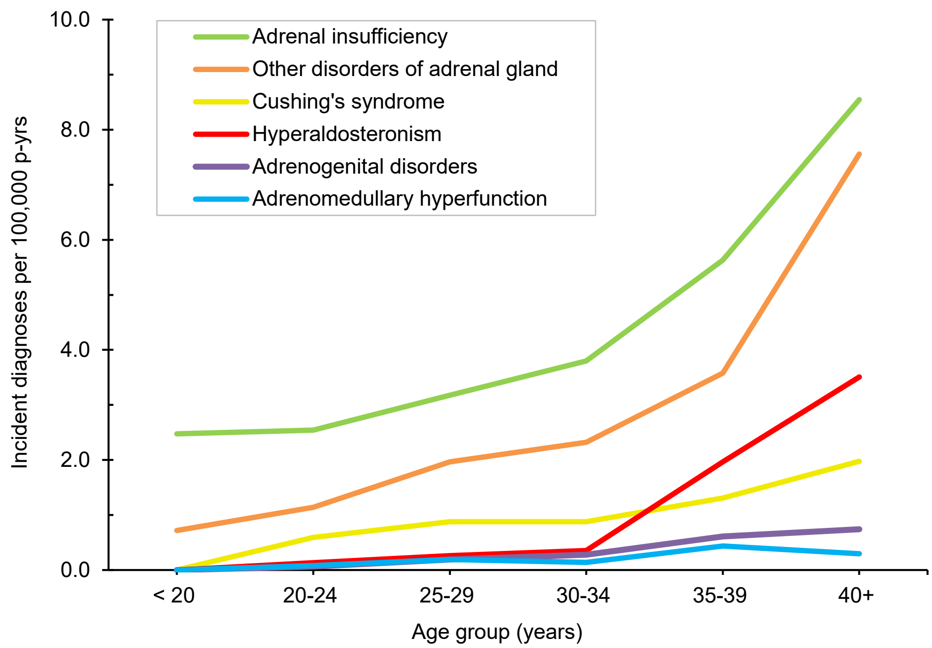


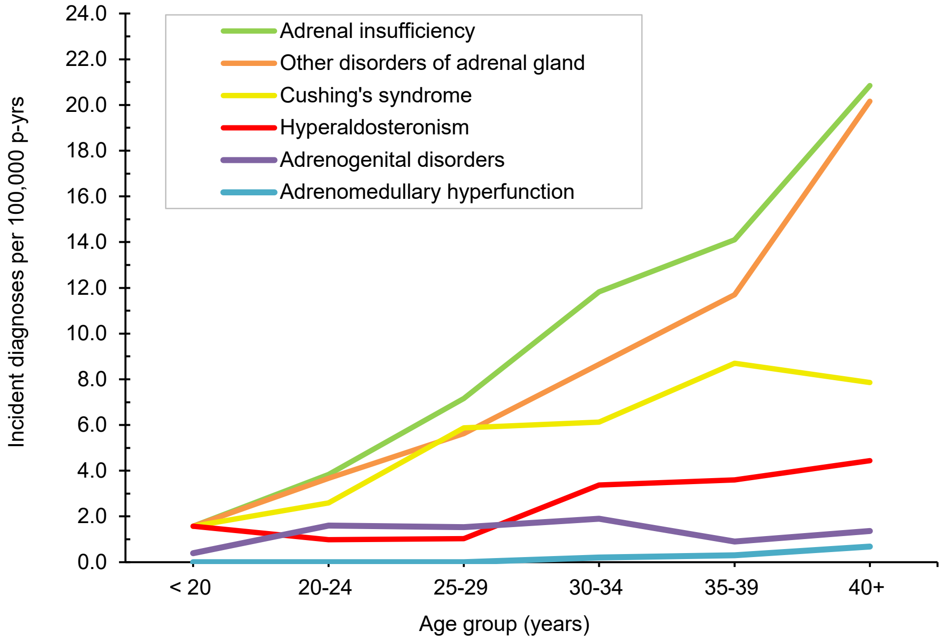
FIGURE 2a. Incidence rates of adrenal gland disorders, by type and age group, active component males, U.S. Armed Forces, 2002–2017



The incidence and prevalence of the adrenal disorders of interest have not been well characterized, particularly in the U.S. general population. Consistent with findings from studies of adrenal disorders in the general populations of other Western countries,[6,14,17,26] results of the current study showed that the incidence and prevalence of the types of adrenal disorders considered here, with the exception of adrenomedullary hyperfunction, occur more frequently in females than in males. The finding that the highest overall incidence rates of all adrenal disorders except adrenomedullary hyperfunction were observed among service members in healthcare occupations is likely due to heightened medical awareness, easier access to care, and, perhaps, older age compared to their respective counterparts in other occupations. The pattern of higher rates of adrenal disorders (with the exception of adrenogenital disorders and adrenomedullary hyperfunction) observed among senior officers compared to those in other grades is likely highly associated with and confounded by age. In addition, the finding that overall rates of all adrenal disorder types were lowest among Marine Corps members may be related to differences in the age distributions of the services.

Data on trends in incidence and prevalence of adrenal disorders in the general U.S. population during a comparable time period were not available at the time of this report, thus precluding comparisons to the current results. Because the current analysis did not assess rates of screening for adrenal disorders, it is unclear if, or to what degree, changes in screening practices may have factored into any of the temporal patterns in incidence reported here. Current recommendations for screening and clinical practice guidelines for all adrenal disorders are available from

FIGURE 2b. Incidence rates of adrenal gland disorders, by type and age group, active component females, U.S. Armed Forces, 2002–2017



not included as not all service members are tested for adrenal disorders. An additional limitation of the current analysis is related to the implementation of MHS GENESIS, the new electronic health record for the Military Health System. During 2017, medical data from sites that were using MHS GENESIS were not available in DMSS. These sites include Madigan Army Medical Center, Air Force Medical Services Fairchild, Naval Hospital Bremerton, and Naval Hospital Oak Harbor. Consequently, medical encounters and person-time data for individuals who received care at these facilities during 2017 were not included in the analysis. Despite these limitations, findings from this report make a useful contribution to the literature on the overall incidence of adrenal disorders among a demographically diverse population and provide new information regarding temporal changes in the incidence of these conditions by sex.

the Endocrine Society at: https://www.endocrine.org/guidelines-and-clinical-practice/clinical-practice-guidelines/.

One important limitation of the current analysis is that the incidence rates of adrenal disorders were based on diagnoses recorded on standardized medical records. Given this, the findings reflect the rates of adrenal functional abnormalities that were clinically detected; subclinical dysfunction was

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FIGURE 3a. Incidence rates of adrenal gland disorders, by type and 4-year time period, active component males, U.S. Armed Forces, 2002–2017

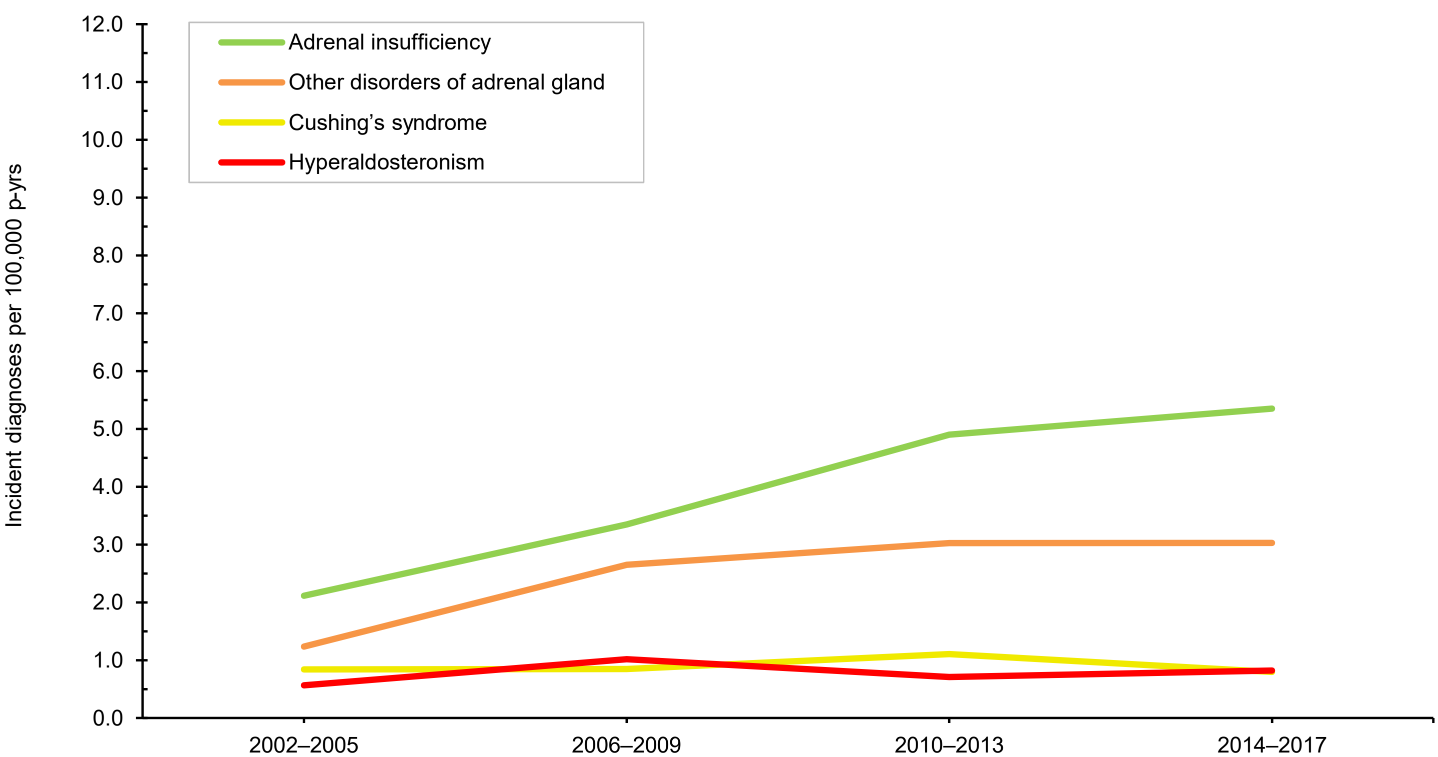

FIGURE 3b. Incidence rates of adrenal gland disorders, by type and 4-year time period, active component females, U.S. Armed Forces, 2002–2017

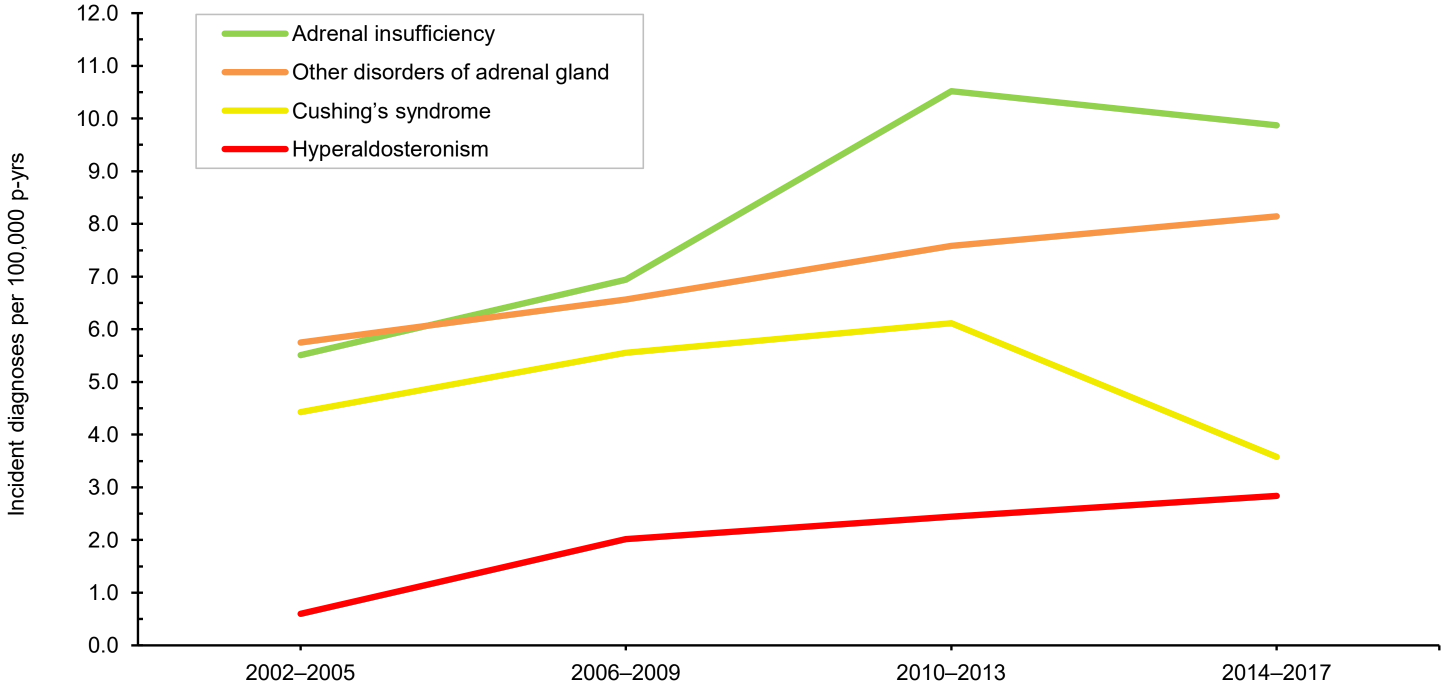

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FIGURE 4a. Annual lifetime prevalence rates of adrenal gland disorders, by type, active component males, U.S. Armed Forces, 2002–2017

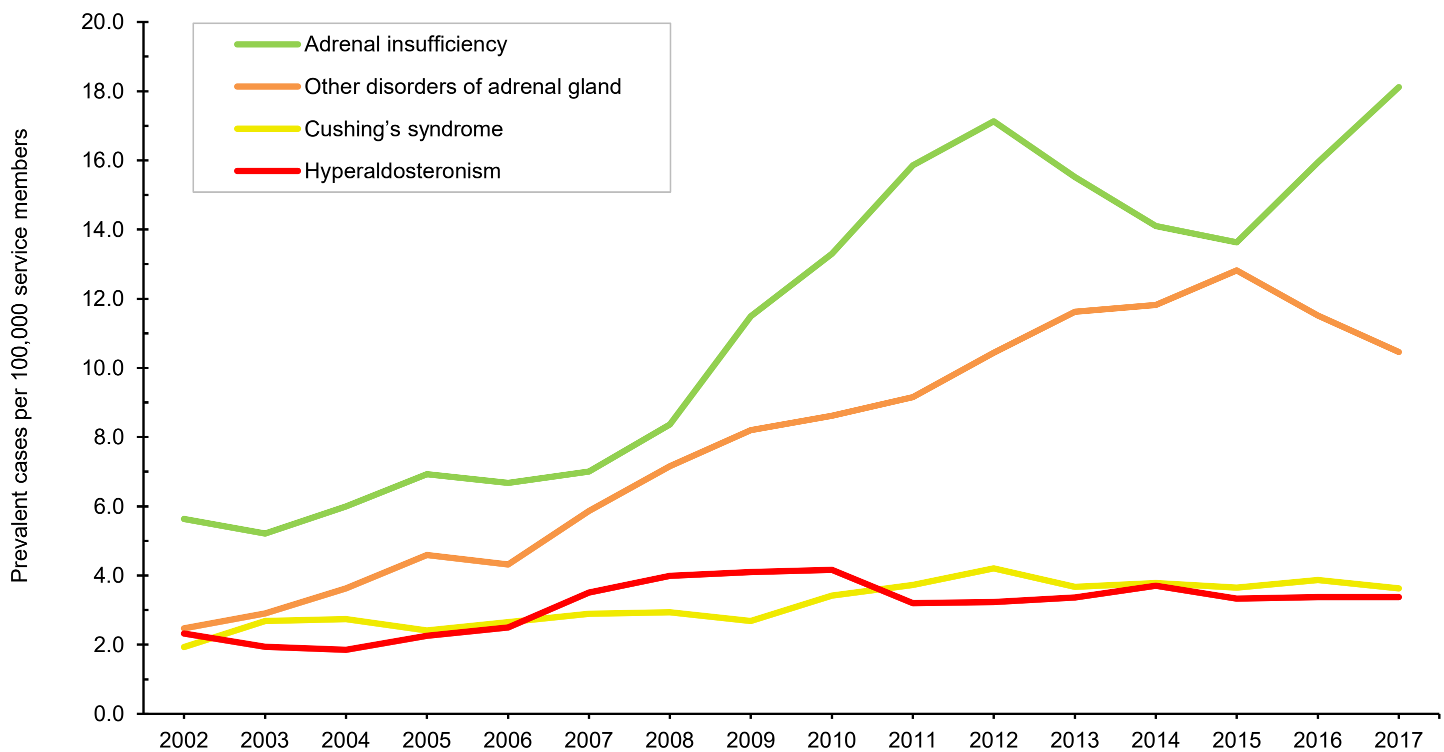
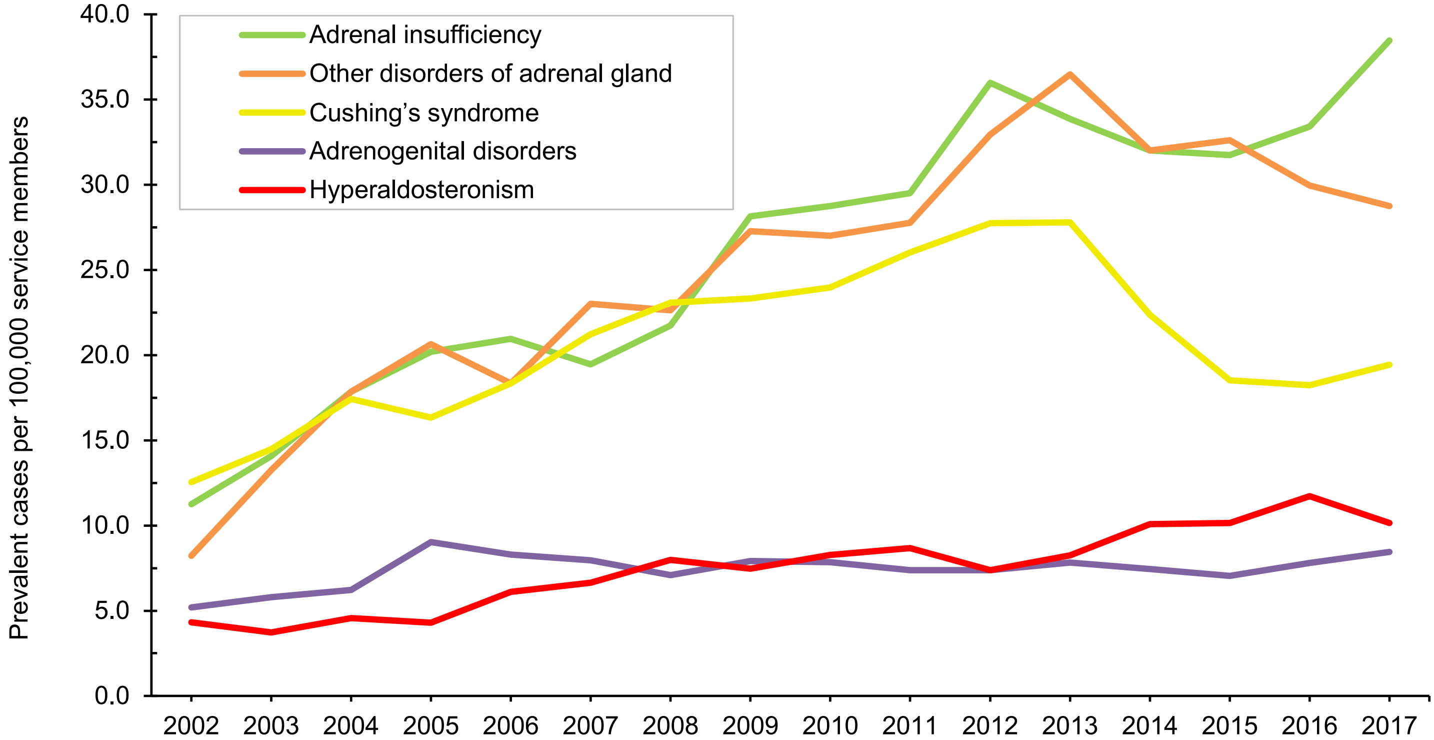


FIGURE 4b. Annual lifetime prevalence rates of adrenal gland disorders, by type, active component females, U.S. Armed Forces, 2002–2017



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WORLD AIDS DAY, observed on 1 December each year since 1988, is an international day focused on raising awareness of efforts to stop new HIV infections, support those affected by HIV, and remember those who have died of HIV-related diseases.

In the September 2017 issue (Vol. 24 No. 9) of the *MSMR*, Okulicz et al. reviewed the progress of the U.S. military's HIV program and highlighted some of the challenges that remain in providing the most comprehensive and state-of-the art care to HIV-infected service members. To access this article, go to www.Health.mil/MSMR/

Incidence and Prevalence of the Metabolic Syndrome Using ICD-9 and ICD-10 Diagnostic Codes, Active Component, U.S. Armed Forces, 2002–2017

Valerie F. Williams, MA, MS; Gi-Taik Oh, MS; Shauna Stahlman, MPH, PhD

This report uses ICD-9 and ICD-10 codes (277.7 and E88.81, respectively) for the metabolic syndrome (MetS) to summarize trends in the incidence and prevalence of this condition among active component members of the U.S. Armed Forces between 2002 and 2017. During this period, the crude overall incidence rate of MetS was 7.5 cases per 100,000 person-years (p-yrs). Compared to their respective counterparts, overall incidence rates were highest among Asian/Pacific Islanders, Air Force members, and warrant officers and were lowest among those of other/unknown race/ethnicity, Marine Corps members, and junior enlisted personnel and officers. During 2002–2017, the annual incidence rates of MetS peaked in 2009 at 11.6 cases per 100,000 p-yrs and decreased to 5.9 cases per 100,000 p-yrs in 2017. Annual prevalence rates of MetS increased steadily during the first 11 years of the surveillance period reaching a high of 38.9 per 100,000 active component service members in 2012, after which rates declined slightly to 31.6 per 100,000 active component service members in 2017. Validation of ICD-9/ICD-10 diagnostic codes for MetS using the National Cholesterol Education Program Adult Treatment Panel III criteria is needed to establish the level of agreement between the two methods for identifying this condition.

WHAT ARE THE NEW FINDINGS?

This analysis confirmed that the incidence of metabolic syndrome (MetS) among service members steadily increases with advancing age. However, because the specific MetS ICD codes tend to be underutilized in patient records, this analysis' estimates of incidence greatly underestimate rates that have been derived using biologic thresholds for the five components of the syndrome.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

MetS is a medically disqualifying condition for appointment, enlistment, or induction into military service. Significant impacts on force readiness include administrative discharges for failure to meet weight standards, non-deployability due to type 2 diabetes diagnosis requiring medication, and increased potential for cardiovascular disease in deployed environments.

The metabolic syndrome (MetS) is a cluster of cardiometabolic risk factors that is associated with increased risk of multiple chronic diseases and premature mortality.[1,2] MetS is characterized by abdominal obesity, dyslipidemia (elevated plasma triglycerides and/or reduced high density lipoprotein [HDL] cholesterol), elevated fasting plasma glucose level, and hypertension.[2] The association between MetS and increased risk of multiple chronic diseases (e.g., cardiovascular disease, chronic liver disease, chronic kidney disease, arthritis, and several types of cancer) and all-cause mortality is well established.[3–10] However, there is some uncertainty regarding whether MetS confers risk over and above its individual components.[11,12] Regardless of whether MetS is considered to have unique predictive value, the importance of identifying and managing its individual components to decrease morbidity and mortality associated with diabetes and cardiovascular disease is undisputed.[2,11,13]

The importance of MetS was highlighted in 2001 with the approval of the ICD-9 code, 277.7, for "dysmetabolic syndrome X".[14] However, studies using data from the National Hospital Discharge Survey and the National Ambulatory Medical Care Survey as well as large U.S. civilian administrative databases have found that a diagnosis of MetS is rarely recorded in these data using the designated ICD code.[15–18] Given this under-recording, most efforts to better estimate the public health burden of MetS in the civilian population have relied on biologic thresholds of five components of MetS (elevated waist circumference, elevated triglyceride level, reduced HDL cholesterol level, elevated blood pressure, and elevated fasting blood glucose level). These efforts have been complicated by the lack of consistency in the clinical parameters used to define MetS; however, the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) criteria are one of the most widely agreed upon criteria for MetS.[19] These criteria do not include the designated ICD code for MetS but define MetS by the presence of at least three of the five components based on laboratory and vital data. Studies using this definition and data from the National Health and Nutrition Examination Survey (NHANES) estimated the overall age-adjusted prevalence of MetS in 1988–1994 to be 25.3%.[20] In 1999–2006, the overall age-adjusted prevalence declined slightly to 25.0%[20] and then increased to 34.3% in 2007–2014.[21] Examination of trends from 2007 through 2014 showed that the prevalence of MetS remained relatively stable in all age, sex, and race/ethnicity groups.[21]

The majority of studies that have examined the prevalence of MetS among U.S. military personnel have done so among specific subpopulations (e.g., soldiers at accession, veterans with or without cardiovascular disease or diabetes mellitus, those exposed to environmental hazards).[22–34] However, few studies have examined the prevalence of MetS among active component service members.[34] Using electronic health record data from the Military Health System (MHS) Management Analysis and Reporting Tool and the NCEP-ATPIII criteria for defining MetS, Herzog et al. demonstrated a trend of decreasing prevalence of MetS among a sample of active duty service members during fiscal years 2009–2012.[34] Age-adjusted MetS prevalence among male service members in the sample decreased from 24.7% in 2009 to 21.1% in 2012. The decrease in age-adjusted prevalence was not as pronounced among female service members (10.0% in 2009 to 8.3% in 2012).[34]

To determine and document the long term trends in diagnoses of MetS in the active component population, the current report summarizes trends in the incidence and prevalence of MetS using the ICD-9 and ICD-10 codes for this condition among active component members of the U.S. Armed Forces during 2002–2017.

METHODS

The surveillance period was January 1, 2002 through December 31, 2017. The surveillance population consisted of all individuals who served in the active component of the Army, Navy, Air Force, or Marine Corps at any time during the surveillance period. Cases of MetS were identified by ICD-9 diagnostic code 277.7 and ICD-10 code E88.81 recorded in standardized records of inpatient and outpatient encounters in military and non-military medical facilities documented in the Defense Medical Surveillance System (DMSS).

An incident case of MetS was defined by hospitalization with a case-defining diagnostic code in any diagnostic position or by two or more outpatient diagnoses between 1 and 180 days apart, with at least one of these diagnoses in a primary diagnostic position. An individual could be counted as an incident case of MetS once per lifetime. Individuals who met the case-definition for MetS prior to the surveillance period (i.e., prevalent cases) were excluded from the incidence rate calculation. Incidence rates were calculated as incident MetS diagnoses per 100,000 person years (p-yrs) of active component service. Both deployed and non-deployed person time were used in the denominator.

Lifetime prevalence of the diagnoses of MetS was estimated for each year in the 16-year surveillance period. The numerator for annual lifetime prevalence calculations consisted of service members who had ever been diagnosed with MetS and who were in service during the given calendar year. The denominator for annual prevalence calculations consisted of the total number of active component service members who served at any time during the given year. Annual prevalence estimates were calculated as the number of prevalent cases per 100,000 active component service members.

RESULTS

During 2002–2017, a total of 1,639 active component service members received incident diagnoses of MetS, for a crude overall incidence rate of 7.5 cases per 100,000 p-yrs **(Table 1)**. The overall incidence of MetS among females was more than twice that of males (13.9 per 100,000 p-yrs and 6.4 per 100,000 p-yrs, respectively). Crude overall rates of MetS increased with increasing age; the greatest percent increase in overall incidence rates occurred between those aged 30–34 years and those aged 35–39 years or older **(Table 1)**. Across all cases, the median age at the time of incident MetS diagnosis was 36 years (interquartile range [IQR]=30–41) with females having a much younger median age at diagnosis (31 years; IQR=26–38) compared to males (38 years; IQR=32–42) **(data not shown)**.

Compared to their respective counterparts, overall incidence rates were highest among Asian/Pacific Islanders (9.8 per 100,000 p-years), Air Force members (9.4 per 100,000 p-yrs), and warrant officers (17.8 per 100,000 p-yrs) and lowest among those of other/unknown race/ethnicity (6.7 per 100,000 p-yrs), Marine Corps members (1.9 per 100,000 p-yrs), and junior enlisted personnel and officers (2.8 and 4.3 per 100,000 p-yrs, respectively). Stratification by military occupation revealed that crude overall rates of MetS were highest among healthcare workers (13.4 per 100,000 p-yrs) and lowest among those in combat-specific occupations (4.4 per 100,000 p-yrs) **(Table 1)**. Of active component service members with known locations of military assignment, overall incidence of MetS was highest among those stationed in the Northeastern region of the U.S. (17.6 per 100,000 p-yrs) and lowest among those stationed overseas (2.3 per 100,000 p-yrs) or in the West (7.9 per 100,000 p-yrs).

During 2002–2017, the crude annual incidence rates of MetS peaked in 2009 at 11.6 cases per 100,000 p-yrs and decreased to 5.9 cases per 100,000 p-yrs in 2017 **(Figure 1)**. Crude annual prevalence rates of MetS increased steadily during the first 11 years of the surveillance period reaching a high of 38.9 per 100,000 active component service members in 2012, after which rates declined slightly to 31.6 per 100,000 active component service members in 2017 **(Figure 2)**.

EDITORIAL COMMENT

The results of the current study show a trend of steadily increasing prevalence of MetS diagnoses (based on ICD-9/ICD-10 codes alone) among active component service members between 2002 and 2012 followed by a slight decline during the subsequent five years. In contrast, the findings of Herzog et al. demonstrated a decrease in MetS prevalence in a sample of active duty service members between 2009 and 2012,[34] while the MetS prevalence estimates for the general U.S. population (NHANES) remained relatively stable during 2009–2014.[21] However, because the estimates from the Herzog et al. and U.S. general population-based studies used different sets of modified NCEP-ATP III criteria to identify MetS cases, they are not directly comparable to those obtained in the current analysis which used only ICD-9/ICD-10 diagnostic codes. The most

TABLE 1. Numbers and rates of incident diagnoses of the metabolic syndrome, by demographic and military characteristics, active component, U.S. Armed Forces, 2002–2017

	No.	Rate[a]
Total	1,639	7.5
Sex		
All females	453	13.9
All males	1,186	6.4
Age group		
< 20	4	0.3
20–24	148	2.1
25–29	251	5.0
30–34	269	8.1
35–39	403	15.4
40+	564	24.4
Race/ethnicity		
Non-Hispanic white	948	7.1
Non-Hispanic black	304	8.3
Hispanic	212	8.1
Asian/Pacific Islander	80	9.8
Other/unknown	95	6.7
Service		
Army	644	7.9
Navy	434	8.1
Air Force	505	9.4
Marine Corps	56	1.9
Rank		
Junior enlisted (E1–E4)	267	2.8
Senior enlisted (E5–E9)	1,086	12.5
Junior officer (O1–O3)	87	4.3
Senior officer (O4–O10))	148	10.8
Warrant officer (W1–W5)	51	17.8
Occupation		
Combat-specific[b]	137	4.4
Motor transport	47	7.2
Pilot/air crew	57	6.8
Repair/engineering	443	6.9
Communications/intelligence	445	9.1
Health care	252	13.4
Other	258	6.3
Geographic region of military assignment[c]		
Northeast	110	17.6
Midwest	124	9.7
South	879	9.1
West	420	7.9
Overseas	105	2.3
Unknown/missing	1	0.3

[a]Rate per 100,000 person years
[b]Infantry/artillery/combat engineering/armor
[c]Within the U.S., categorization was based on U.S. Census Bureau regions (www.census.gov/geo/reference/webatlas/regions.html).

comparable prevalence estimate available at the time of this report was obtained from a recent study of cardiometabolic risk factors among soldiers who accessed into the U.S. Army during 2001–2011. Using the ICD-9 diagnostic code to identify MetS cases, Hruby et al. obtained a prevalence estimate of 31.2 MetS diagnoses per 100,000 Army entrants during the 11-year period.[17]

Despite the major differences in case definitions used in studies of the prevalence of MetS, several broad findings of the current analysis are consistent with the literature. The age-related rise in the prevalence of MetS is well established and has been attributed to the development of central obesity in middle age associated with overeating and a decline in physical activity.[35,36] In contrast to the results of general population-based studies using NHANES data and the findings of Herzog and colleagues' study of MetS prevalence among a sample of active duty service members, overall rates of MetS in the current study were higher in women than in men.[21,34,37] The reasons for this difference are unclear but are likely related to sex differences in the prevalence of individual MetS components in the study population.[37] The pattern of lower incidence rates observed among junior enlisted and junior officers compared to those in other grades is likely highly correlated and confounded by age. In addition, the finding that overall incidence rates of MetS were lowest among Marine Corps members may be related to differences in the age and obesity distributions of the services.[38,39] The decline in the prevalence of MetS during the surveillance period might be due to earlier identification of MetS and/or more aggressive management of its component conditions. Data on trends in incidence of MetS in the general U.S. population using ICD diagnostic codes (either alone or in conjunction with other diagnostic codes and/or laboratory data relevant to components of MetS) during a comparable time period were not available at the time of this report, thus precluding comparisons to the current results. This lack of comparable results is likely due, at least in part, to the under-recording of MetS using the designated ICD code in U.S. civilian administrative databases.

Whether the designated ICD code for MetS is underutilized in the MHS is

FIGURE 1. Number of incident cases and annual incidence rates of metabolic syndrome, active component, U.S. Armed Forces, 2002–2017

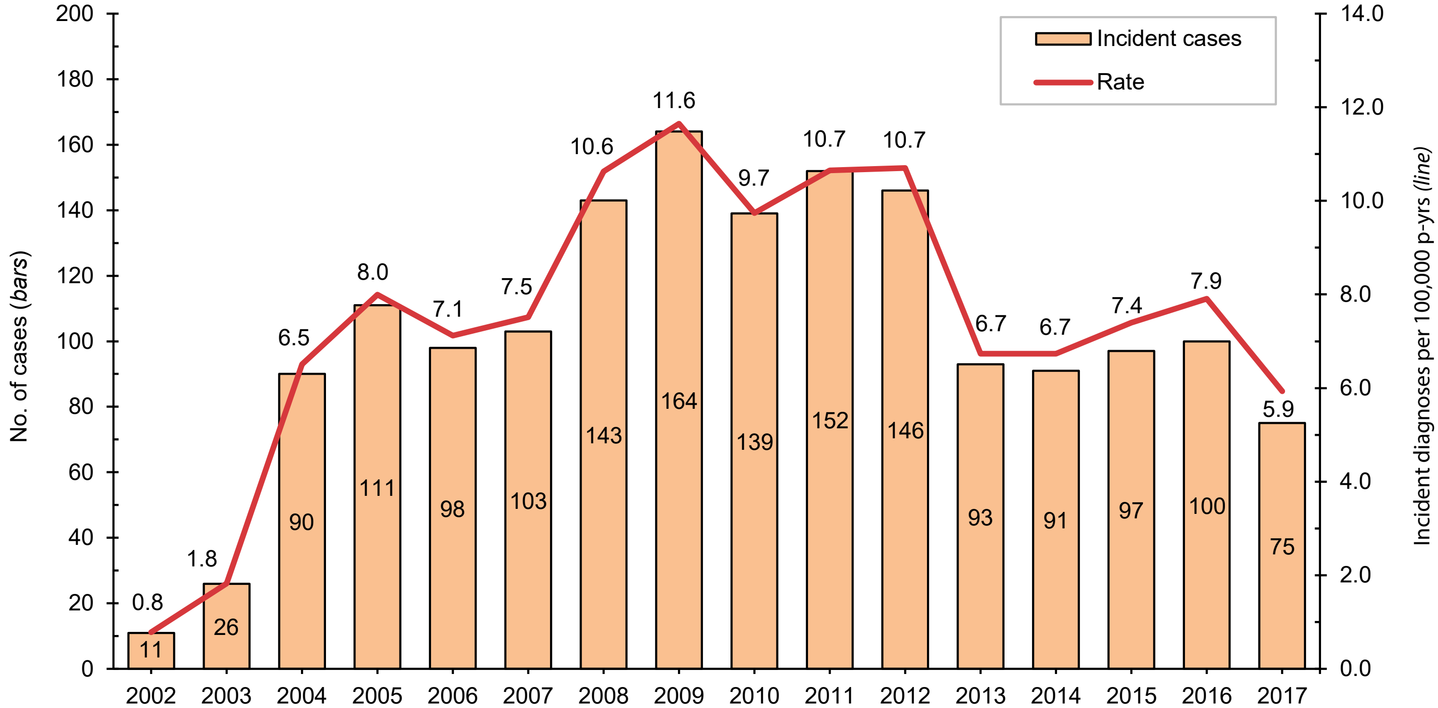
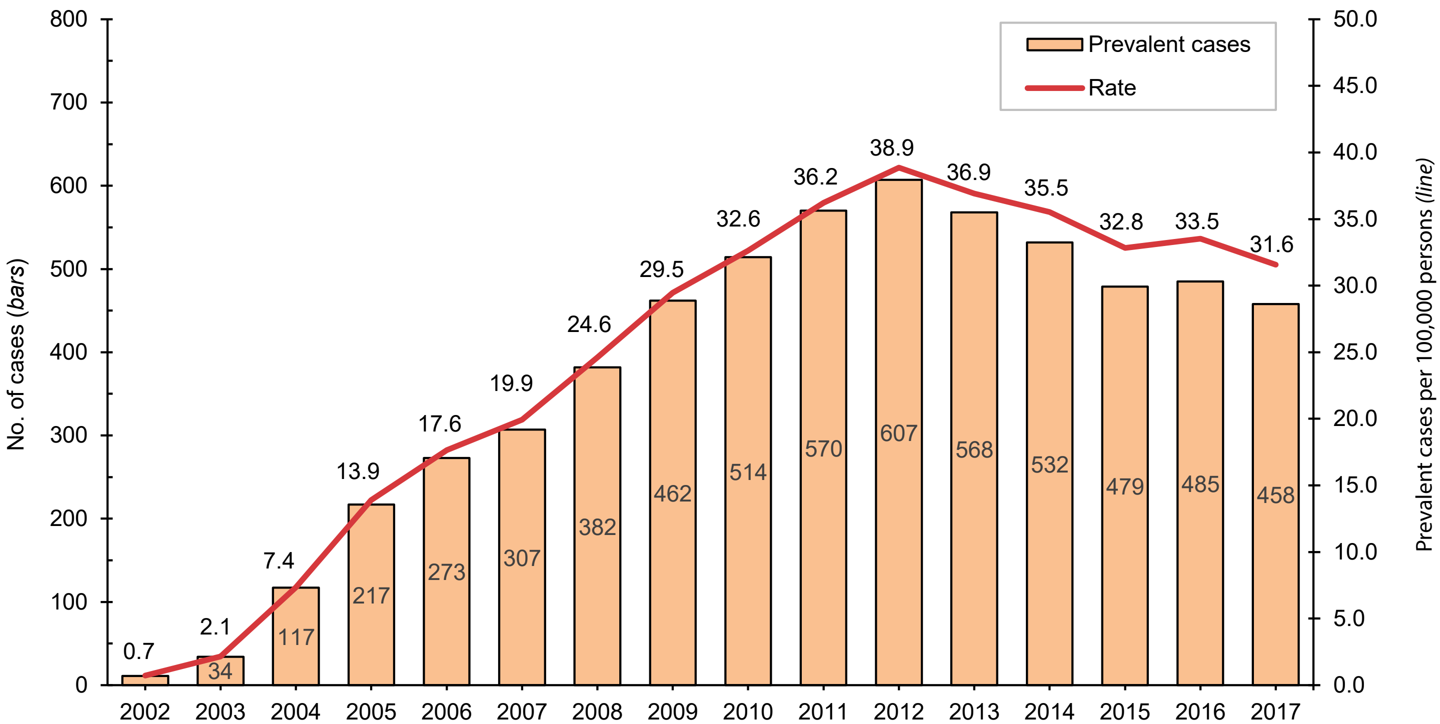


FIGURE 2. Number of prevalent cases and annual lifetime prevalence rates of metabolic syndrome, active component, U.S. Armed Forces, 2002–2017



unknown. However, several potential reasons for the low coding rate of MetS in the civilian health system have been posited. Some healthcare providers may think that the MetS is not a meaningful concept and thus lacks clinical utility.[11,40] In addition, it is possible that lack of or limited reimbursement for MetS by some commercial insurers may lead healthcare providers to focus on using diagnostic codes that can receive reimbursement (e.g., diabetes, hypertension).[41] Low frequency of coding also may be due to concern regarding the impact of the use of the MetS diagnostic code on life insurance policies and health insurance portability.[42] Additionally, limited coding time during clinic appointments may be devoted to other more urgent clinical conditions.[43,44]

It is important to note that, because diagnostic codes from inpatient and outpatient medical records were used as proxies for incident and prevalent cases, the validity of the current results depends upon the accuracy of a physician-assigned diagnosis of MetS. Furthermore, the pattern of, and trends in, prevalence and incidence rates reported here may be due, to an unknown degree, to variations in coding practices. Validation of ICD-9/ICD-10 diagnostic codes for MetS using ATP III criteria modified for the MHS electronic health record data available (e.g., self-reported height and weight) is needed to establish the level of agreement between the two methods for identifying this condition.

Another limitation of the current analysis is related to the implementation of MHS GENESIS, the new electronic health record for the Military Health System. For 2017, medical data from sites that were using MHS GENESIS are not available in DMSS. These sites include Naval Hospital Oak Harbor, Naval Hospital Bremerton, Air Force Medical Services Fairchild, and Madigan Army Medical Center. Therefore, medical encounter and person-time data for individuals seeking care at one of these facilities during 2017 were not included in the analysis.

MetS has obvious effects on accession into and retention in the military, most notably with respect to maintenance of flight status or the requirements of other special missions. Additional significant impacts of MetS on force readiness are based on administrative discharges for failure to meet weight standards, non-deployability due to type 2 diabetes diagnosis requiring medication, and increased potential for cardiovascular disease in deployed environments.[45-47] Future investigations of the incidence and prevalence of MetS among active component service members should employ a fuller range of available administrative data including the diagnostic codes for the individual components of MetS, codes pertaining to the biologic thresholds for these components, and documentation of prescription medication used to treat these component conditions.

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