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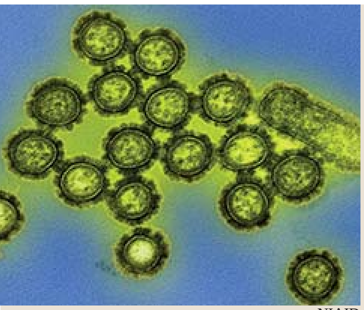
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The DoD Global, Laboratory-based, Influenza Surveillance Program: Summary for the 2013–2014 Influenza Season

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This report for the 2013–2014 influenza season summarizes the results of influenza surveillance carried out by the DoD Global, Laboratory-based, Influenza Surveillance Program, which is managed by the U.S. Air Force School of Aerospace Medicine Epidemiology Consult Service and Epidemiology Laboratory at Wright-Patterson Air Force Base, OH. Sentinel sites submitted 3,903 specimens for clinical diagnostic testing and 1,163 (29.8%) were positive for influenza virus. The predominant influenza subtype was influenza A(H1N1)pdm09, identified in 79.2% of all influenza-positive specimens. The other most common subtypes were influenza A(H3N2) (10.5%) and influenza B (10.1%). In August 2014, a human case of influenza A(H3N2) variant was identified in a patient with a history of exposure to swine. Adjusted vaccine effectiveness (VE) was calculated among 1,016 military dependents and retirees in the U.S. and was found to be 44.8% for all vaccine types. Uncertainties and other limitations associated with estimating VE are discussed.

Influenza surveillance has a high degree of military and public health importance. The influenza virus routinely mutates (i.e., genetic shift and drift) with the demonstrated potential to cause grave morbidity and mortality across the globe in a short period of time. Military members and their families are highly mobile and may reside where novel strains emerge. Additionally, military members may serve in environments (e.g., close quarters, intensive recruit training) that are well suited for the spread of respiratory pathogens. Although the threat from influenza has long been recognized (e.g., the 1918–1919 influenza pandemic killed 50 million to 100 million individuals), the first influenza vaccine was formulated and administered to U.S. troops in 1943 with a 70% vaccine effectiveness. In 1945, the vaccine was licensed for use in the U.S. However, 2 years later, the vaccine failed and researchers learned a valuable lesson: Influenza strains change. The first influenza surveillance program was formalized in 1947 after this realization.[1]

In 1976, the Air Force Armstrong Laboratory at Brooks Air Force Base, San Antonio, TX, began building a global influenza surveillance network to monitor influenza activity in the Air Force. In 1997, the program (formerly known as "Project Gargle") expanded to become a Department of Defense (DoD) program. Today, the Armed Forces Health Surveillance Branch, DoD Global Emerging Infections Surveillance and Response System (GEIS), funds the DoD Global, Laboratory-based, Influenza Surveillance Program, which is managed by the U.S. Air Force School of Aerospace Medicine (USAFSAM) Epidemiology Consult Service and Epidemiology Laboratory at Wright-Patterson AFB, OH. For more detailed history of the program's development, please refer to the Technical Report on Program Methods for the 2012–2013 Influenza Season.[2] Operational goals of the program are to prevent influenza infections and reduce morbidity and mortality, thus protecting U.S. forces. This protection is accomplished by identifying outbreaks, determining the incidence of influenza-like illness (ILI) among sentinel sites, identifying and isolating circulating influenza viruses, conducting vaccine effectiveness studies, and promptly detecting new variants or subtypes of influenza viruses for possible inclusion into the next year's influenza vaccine.

The DoD Global, Laboratory-based, Influenza Surveillance Program is a year-round sentinel surveillance program that works in collaboration with 91 sentinel sites and eight partner laboratories worldwide. The program requests each sentinel site to submit between six and 10 respiratory specimens a week, accompanied with patient questionnaires, from patients who meet the ILI case definition.[2] The preferred specimen is a nasal wash. However, the laboratory is also validated to accept nasopharyngeal swabs. Nasal wash specimens are preferred due to the volume (3 mL) of viable specimen that better supports the various tests performed.

Sentinel sites in the U.S. European Command area of responsibility, Hawaii, and Camp Lemonnier (Djibouti) may submit specimens to alternate laboratories through their existing surveillance programs (Assistant Secretary of Defense Health Affairs Memo: Sentinel Sites for the 2013–2014 Influenza Surveillance Program, 31 May 2013). Of the 91 sentinel sites, 82 are expected to submit specimens to the USAFSAM laboratory, while the other nine participate by sending specimens to alternate laboratories. Of the 82 sites expected to submit to USAFSAM, 76 (92.7%) sites submitted specimens for testing (routine diagnostic testing and sequencing) during the 2013–2014 influenza season. This report excludes data from specimens originally tested at Landstuhl Regional Medical Center (LRMC) in Germany. Sentinel site participation and performance vary by location and season. Although sentinel sites are required to participate, 100% participation continues to be an issue despite the training/education provided by the program.

METHODS

Laboratory testing

For the 2013–2014 influenza season (29 September 2013 through 27 September 2014), the USAFSAM laboratory tested all incoming specimens using reverse transcriptase polymerase chain reaction (RT-PCR) and viral culture. If RT-PCR was negative for influenza virus A and B, the specimen was then tested on the BioFire FilmArray® platform, which can detect up to 20 viral and bacterial respiratory pathogens. In addition to this routine testing, a portion of the positive influenza specimens was genetically sequenced to identify antigenic drift and adjust for it in the next season's vaccine selection (see the Editorial Comment). This was performed by amplifying the hemagglutinin (HA) gene using RT-PCR, then sequencing bidirectionally using dye terminator, Sanger-based methods.

Vaccine effectiveness

End-of-season vaccine effectiveness (VE) estimates were calculated for DoD-dependent beneficiaries, including retired service members. A case-test negative methodology was used, with a case defined as an individual who tested positive for influenza virus A or B on RT-PCR, culture, or FilmArray, and a control defined as an individual with a negative test for influenza virus A or B. To concentrate on specimens collected during peak influenza season, a 10% influenza positive threshold was used. Weeks 48–18 (23 November 2013 through 3 May 2014) had at least a 10% positivity rate. Thus, respiratory specimens from this time frame were included in this analysis. Vaccine data were obtained through the Air Force Complete Immunization Tracking Application (AFCITA), Defense Manpower Data Center (DMDC), and self-reported surveys. An individual was considered vaccinated if the immunization occurred at least 14 days prior to specimen collection. VE was calculated using multivariable logistic regression in SAS 9.3. Crude and adjusted odds ratios (ORs and AORs) were calculated for each group and for each vaccine, and VE was assessed using (1 – AOR) x 100. For example, for all dependents:

$$\text{OR} = \frac{(\text{No. of vaccinated cases}) \times (\text{No. of unvaccinated controls})}{(\text{No. of vaccinated controls}) \times (\text{No. of unvaccinated cases})} = \frac{99 \times 381}{225 \times 310} = 0.54$$

$$\text{VE} = (1 - \text{AOR}) \times 100 = 0.46 \times 100 = 46\%$$

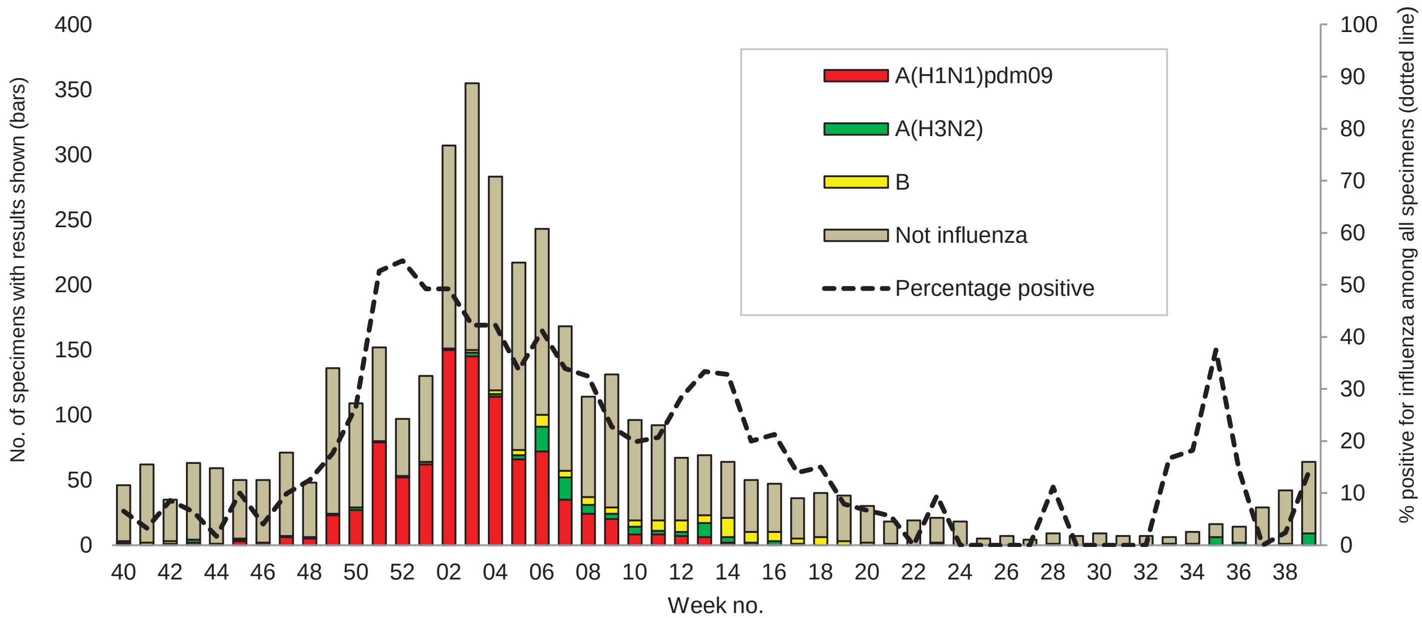
An influenza subtype–specific analysis was not performed because the season was predominated by influenza A(H1N1)pdm09 (approximately 80%), which drives the VE estimate. Models were adjusted for age, gender, location, and specimen collection date. Statistically significant results were identified in all dependents and in adults/retirees. Analysis was not performed on service members because they are a highly vaccinated population and a test negative control methodology has proven unsuccessful in previous studies. A methodology using healthy negative controls is being explored for future studies and analyses.

RESULTS

Viral surveillance

The 2013–2014 influenza season had moderate influenza activity, with influenza A(H1N1)pdm09 (79.2%, n=921) being the predominant strain. Activity peaked during Weeks 51 and 52 (15–28 December 2013) when more than 50% of respiratory specimens tested positive for influenza **(Figure)**. The USAFSAM Epidemiology Laboratory Service processed 4,155 respiratory specimens during the 2013–2014 influenza surveillance season. Of the 4,155 specimens submitted for surveillance, 3,903 (93.9%)

FIGURE. Numbers and percentage of influenza-positive specimens,[a] by week, 2013–2014 surveillance season



[a]Two influenza A (not subtyped) (Weeks 4 and 9) and one influenza A(H3N2)v (Week 34) specimens were excluded from the stacked graph due to small numbers but do contribute to percentage positive.

were submitted for routine testing (i.e., clinical diagnostic detection), which includes RT-PCR and viral culture (and possibly FilmArray), while 252 (6.1%) specimens were submitted for sequence analysis only. Of the specimens submitted for routine testing from 85 locations, 29.8% (n=1,163) were positive for influenza **(Table 1)**. Other respiratory pathogens were detected in 38.4% (n=1,485) of specimens, and less than 1% (n=33) were not tested for various reasons. Flu specimens testing negative for influenza A and B on RT-PCR underwent additional testing via the FilmArray panel. These results can be found in the 2013–2014 USAFSAM Influenza Surveillance Report.[3] Demographic information on the patient sources of those specimens submitted for routine testing can be found in **Table 2.**

Variant influenza virus

On 22 August 2014, a human case of influenza A(H3N2) variant in a military dependent at Wright-Patterson AFB was confirmed by the Centers for Disease Control and Prevention (CDC). The patient reported exposure to swine at a county fair prior to illness onset and presented with ILI symptoms on 19 August 2014. The patient's parents and sibling were also ill but were not tested for influenza. The patient was prescribed Tamiflu® and recovered. Sequencing conducted by USAFSAM determined that the HA and neuraminidase genes were of swine H3N2 origin, yet the matrix gene was of human H1N1pdm09 origin. This was the second human case of influenza A(H3N2)v reported in the U.S. in 2014, following 309 cases in 2012 and 19 in 2013. Most of these were associated with prolonged exposure to pigs at agricultural fairs, and evidence of widespread human-to-human transmission has not emerged.

Vaccine effectiveness

Influenza VE was calculated for 1,016 military dependents and retired service members (409 cases and 607 controls) who suffered from ILI and were located in the continental U.S. at the time of specimen collection. Among the cases and controls, approximately 9.7% and 22.2%, respectively, were vaccinated with the current season's influenza vaccine (17.3% vaccinated overall). Estimates were provided for all vaccine types (overall), live attenuated influenza vaccine (LAIV), and inactivated influenza vaccine (IIV) for each beneficiary group (all dependents, adults/retirees, and children [less than 18 years of age]) **(Table 3)**. VE estimates were higher for IIV for the all dependents group, with the highest being reported in the adults/retirees group (66% (95% CI, 45%–79%)). The VE estimate for all dependents, all vaccine types (overall) was 44.8% (95% CI, 25.5%–59.1%), which indicates moderate protection against medically attended, laboratory-confirmed influenza infection for the 2013–2014 year.

EDITORIAL COMMENT

After the 2009 influenza pandemic, the 2013–2014 season was the first where the predominant circulating virus was influenza

TABLE 1. Influenza subtypes identified during the 2013–2014 influenza season

Influenza virus	Frequency	%
A(H1N1)pdm09[a]	921	79.2
A(H3N2)	122	10.5
A(H3N2)v	1	0.1
A/Not subtyped	2	0.2
B[b]	117	10.1
Total	1,163	100.0

[a]Eight influenza A(H1N1)pdm09 viruses were identified as co-infections with a non-influenza pathogen.

[b]One influenza B was identified as a co-infection with a non-influenza pathogen.

TABLE 2. Demographic data for sources of specimens and results of routine testing, 2013–2014 influenza season

	Influenza A	Influenza B	No pathogen detected	Other respiratory pathogen	Total
Total	1,046	117	1,222	1,485	3,870
Gender					
Male	598	68	673	817	2,156
Female	446	48	543	657	1,694
Missing	2	1	6	11	20
Beneficiary					
Service member	436	25	526	418	1,405
Cadet/recruit	22	.	60	67	149
Adult	256	28	292	216	792
Retiree	74	10	95	58	237
Child	255	53	242	715	1,265
Other	3	1	7	11	22
Service					
Air Force	685	63	794	972	2,514
Army	220	30	232	274	756
Navy	82	12	123	153	370
Coast Guard	18	.	9	26	53
Marine Corps	20	3	31	37	91
Other	21	9	33	23	86
Command					
Central	17	6	18	17	58
Northern	921	72	1,122	1,359	3,474
Pacific	108	39	82	109	338
Age (years)					
0–5	111	15	107	541	774
6–9	64	17	39	98	218
10–17	80	21	97	76	274
18–24	127	5	263	223	618
25–44	486	31	505	391	1,413
45–64	161	25	147	118	451
65+	15	2	58	27	102
Unknown	2	1	6	11	20

TABLE 3. DoD Global, Laboratory-based, Influenza Surveillance Program end-of-year vaccine effectiveness, 23 November 2013 (Week 48) through 3 May 2014 (Week 18)

Beneficiary status[a]	Vaccine type	Cases n (%)	Controls n (%)	Crude OR	Adjusted OR	VE adjusted % (95% CI)
All dependents	Overall	409 (24)	607 (37)	0.54	0.55	44.8 (25.5, 59.1)
	LAIV	47 (11)	74 (12)	0.77	0.82	18.5 (-25.3, 47.0)
	IIV	52 (13)	151 (25)	0.42	0.44	56.2 (36.3, 69.8)
	Unvaccinated	310 (76)	381 (63)	Ref	Ref	Ref
Adults/ retirees	Overall	242 (23)	306 (40)	0.44	0.43	56.6 (35.1, 71.1)
	LAIV	23 (10)	27 (9)	0.83	0.76	23.5 (-46.3, 60.0)
	IIV	32 (13)	96 (31)	0.33	0.34	66.0 (45.1, 79.0)
	Unvaccinated	187 (77)	183 (60)	Ref	Ref	Ref
Children	Overall	167 (26)	301 (34)	0.69	0.72	27.8 (-12.7, 53.8)
	LAIV	24 (14)	47 (16)	0.80	0.80	19.6 (-43.0, 54.8)
	IIV	20 (12)	55 (18)	0.58	0.63	36.9 (-13.7, 64.9)
	Unvaccinated	123 (74)	198 (66)	Ref	Ref	Ref

OR, odds ratio; VE, vaccine effectiveness; LAIV, live attenuated influenza vaccine (LAIV4); IIV, inactivated influenza vaccine (IIV3, IIV4, ccIIV3)

[a]Dependents include any individual treated at a military treatment facility who is not a service member (child, spouse, retiree, etc.).

Notes:
1. For individuals less than 9 years of age, two vaccinations are recommended; for this study, this age group was handled the same as the older age groups with respect to vaccination (a subject was considered vaccinated if one influenza vaccination was received at least 14 days prior to specimen collection date).
2. VE was calculated using multivariable logistic regression with adjustment for age, gender, location, and time period.
3. n (%) represents the number and percentage of vaccinated individuals from each "overall" population.

A(H1N1)pdm09. However, influenza B viruses became predominant later in the season (**Figure 1**). Influenza activity most commonly peaks in January or February, and ILI among DoD beneficiaries during the 2013–2014 season aligned with this timing. Year-round influenza surveillance is vital. As with the 2009 pandemic, the aforementioned variant influenza A(H3N2) virus was detected during the "off-peak" season. Although influenza viruses can circulate among swine year-round, most outbreaks occur in the fall and winter, similar to influenza outbreaks in humans.

The use of observational data to calculate VE always introduces bias. Thus, statistical adjustment of the estimates should be made to reduce confounding. Display of the crude and adjusted estimates can help show the degree of confounding, and presenting only a crude estimate would be improper because the value has an even weaker causal interpretation.[4] One of the more concerning limitations of this study is the accuracy of an individual's vaccination status. Two sources of electronic immunization data (AFCITA and DMDC) and a self-reported questionnaire were used to help determine the vaccine status. It is easier to determine true vaccination status when using electronic data sources. If a patient did not have an electronic vaccine record, the questionnaire was reviewed to determine vaccination status. Those records with inconclusive vaccination data were assigned to an unknown category and excluded from analysis (n=462 for study population). Categorization of those with an unknown vaccine status to an unvaccinated group could positively or negatively impact the VE estimate based on the outcome of those individuals. The use of electronic immunization data sources minimizes recall bias, but this bias is still a threat to internal validity.

There is less concern about misclassification of the outcome of influenza testing because RT-PCR influenza testing was used. The test used has 100% sensitivity and 99.3% specificity, which reinforce the accuracy of the identification of a true positive, but these test characteristics were calculated under ideal conditions, and real-world usage includes specimen collection outside of a research setting and delays in testing associated with shipping and handling.

Influenza VE estimates vary by season, circulating subtype, vaccine type, and population studied. Vaccine mismatch due to antigenic drift can negatively affect VE. VE among military dependents and retired service members was lower than that of the general population, reported by the CDC (62% [53–69]); however, because the CDC conducted an A(H1N1)pdm09-specific analysis, these analyses are not directly comparable.

Development of a universal influenza vaccine could protect against a broad range of influenza strains as opposed to the current influenza vaccines that protect against three to four strains. Currently, scientists are working on a universal vaccine, but for the time being, the current vaccine is still the best means to prevent influenza. Good personal hygiene practices (e.g., washing hands, practicing coughing etiquette, and keeping distance from others when ill) will help decrease the spread of influenza.

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Correlation Between Antimicrobial Resistance in *Escherichia coli* Infections in Hospitalized Patients and Rates of Inpatient Prescriptions for Selected Antimicrobial Agents, Department of Defense Hospitals, 2010–2014

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During the past decade, increasing prevalence of antimicrobial resistance in *Escherichia coli* has complicated treatment of infections. Several studies have shown significant correlations between levels of susceptibility and levels of prescription use for preferred antimicrobials; however, most of these studies were conducted outside the U.S. and are outdated. This analysis aimed to identify inpatient *E. coli* infection trends and correlations between prescriptions and antimicrobial resistance observed among hospitalized Department of Defense beneficiaries during 2010–2014. A descending trend was observed for *E. coli* infection incidence during 2010–2013, with an upward trend noted during the last year of the study. Despite quarterly fluctuations, descending trends were noted among prescription rates and stable trends were observed for resistance rates throughout the study period. A statistically significant moderate and positive correlation (r=0.53; p=0.01) was noted between levels of ciprofloxacin prescriptions and ciprofloxacin resistance for *E. coli* isolates. Stewardship programs are encouraged to monitor this relationship.

The incidence of community-acquired *Escherichia coli* extra-intestinal infections ranges from 6 million to 8 million cases of uncomplicated cystitis to 127,500 cases of sepsis per year in the U.S.[1] Urinary tract infections (UTIs) caused by *E. coli* have been one of the most common extraintestinal infections reported in women.[1] Routine surveillance of infections in the Department of Defense (DoD) beneficiary population identifies *E. coli* as the most common cause of bacterial infections (unpublished data).

Broad and long-term use of antimicrobials has accelerated the emergence of antimicrobial resistance (AMR). Each year in the U.S., antimicrobial-resistant bacteria account for about 2 million infections and 23,000 deaths. Currently, AMR is recognized as a growing global threat that costs the U.S. healthcare system up to $34 billion annually.[2]

During the past decade, the increasing prevalence of AMR in *E. coli* has complicated treatment of these common infections. Fluoroquinolones, trimethoprim-containing products, and penicillins are among the preferred antimicrobials in the treatment of uncomplicated UTIs.[3,4] Among *E. coli* UTIs, several studies have shown decreasing susceptibility to these drugs, especially ciprofloxacin.[5–7] In addition, these decreases in susceptibility have been correlated with increased use of fluoroquinolones.[5,8–11] Unfortunately, the majority of previous studies were conducted outside the U.S., are outdated (1994–2004), and lack recent investigations into the correlation between *E. coli* resistance and antimicrobial use. In addition, two articles published more recently (2014–2015) that investigated correlations between ciprofloxacin prescriptions and resistance have found conflicting results; one study did not establish a correlation between use of fluoroquinolones and resistance to ciprofloxacin among *E. coli* isolates, while the other study reported a statistically significant and strong correlation (r=0.943, p=0.01) between ciprofloxacin prescriptions and resistance among inpatient *E. coli* infections.[12,13] Because *E. coli* infections are among the most frequently occurring infectious diseases in the U.S., this study examines the relationship between rates of inpatient prescriptions for selected antimicrobial agents and AMR in *E. coli* infections among hospitalized DoD beneficiaries during 2010–2014.

METHODS

Positive cultures for *E. coli* among inpatient DoD beneficiaries were identified from Health Level 7 (HL7)-formatted microbiology data that originated from fixed military treatment facilities (MTFs) during 2010–2014. BacLink and WHONET software programs,[14] developed by the World Health Organization to aid in the identification and analysis of multidrug-resistant organisms, were used to identify and organize antibiotic susceptibilities within microbiology records. From the microbiology records, *E. coli* infections were classified as inpatient by using the Medical Expense and Performance Reporting System code, with "A" indicating inpatient data. A unique infection was defined as the first positive *E. coli* culture per person per 30 days. Infection rates were calculated as the number of *E. coli* infections per 1,000 inpatient encounters per quarter.

Patient demographics were described by using variables within the HL7-formatted microbiology records. The TRICARE region was defined by the region of the servicing MTF, identified by the requesting Defense Medical Information System (DMIS) identification number. Age was defined as patient age at the date of microbiology record using date of birth. Sponsor service (Air Force, Army, Marine Corps, and Navy) and beneficiary status (Active Duty, Recruit, Retired, Family Member, and Other) were identified by the patient category code. The Family Member beneficiary category included family members of active duty service members and retirees; all other family members and beneficiaries (including National Guard members, reservists, and civilians) were given the beneficiary category designation of Other.

Prescriptions were counted for all admissions by using the inpatient HL7-formatted pharmacy databases from 2010–2014. The databases were queried for all inpatient prescriptions for sulfonamides (specifically trimethoprim/sulfamethoxazole), fluoroquinolones, and penicillins during the surveillance period. Trimethoprim/sulfamethoxazole was removed from analysis due to low counts of prescriptions available in the data. Fluoroquinolones of interest included levofloxacin, ciprofloxacin, ofloxacin, and moxifloxacin. Penicillins of interest included ampicillin, piperacillin/tazobactam, amoxicillin, nafcillin, oxacillin, penicillin G, penicillin V, and ticarcillin. Standard Inpatient Data Record data were used to confirm inpatient pharmacy records if the pharmacy transaction date was between the admission and discharge date. A unique prescription represents the first prescription per antimicrobial class per person for each inpatient encounter. Inpatient rate of prescribing was calculated as the total number of inpatient prescriptions for antimicrobials in a quarter per 1,000 admissions in a quarter.

The Johns Hopkins Antibiotic (ABX) Guide was used as a reference for the selection of antimicrobials recommended for treatment of *E. coli* infection and inclusion in this study.[15] Resistance data from microbiology records were compiled for antimicrobials recommended for treatment of an *E. coli* infection. Only antimicrobials with susceptibility testing for at least 30 isolates per quarter were included. Resistance rates were calculated as the percentage resistant to the antimicrobial of interest among all *E. coli* isolates tested for that drug during each quarter.

Spearman's correlation was used to test for significant ($p<0.05$) correlations between antimicrobial prescriptions and resistance. Correlations between antimicrobial prescriptions and resistance were evaluated for both the individual drug (e.g., levofloxacin, ciprofloxacin, ampicillin) and the drug class (e.g., fluoroquinolones and penicillins).

RESULTS

During 2010–2014, there were 8,516 inpatient *E. coli* infections reported in the DoD beneficiary population. Inpatient *E. coli* infections were most common among females, persons aged 65 years or older, Army beneficiaries, family members, and beneficiaries in the West TRICARE region **(Table 1)**. In the first 4 years of surveillance, a descending trend in quarterly incidence rates of *E. coli* infections was observed, with an upward trend noted during the last year of the study. The average inpatient incidence rate for *E. coli* infections was 6.8 per 1,000 inpatient encounters per quarter and rates ranged from 5.8 in Q2 2013 to 9.0 in Q4 2014 **(Figure 1)**. For the surveillance period, the quarterly incidence rate rose 25% from 7.2 in Q1 2010 to 9.0 in Q4 2014, although this was not a statistically significant change.

TABLE 1. Demographic characteristics of inpatients with *Escherichia coli* infections, Department of Defense hospitals, 2010–2014

	No.	%
Gender		
Female	4,820	56.6
Male	3,696	43.4
Age (years)		
0–17	617	7.3
18–24	829	9.7
25–34	922	10.8
35–44	580	6.8
45–64	1,989	23.4
65+	3,579	42.0
Service		
Air Force	1,759	20.7
Army	3,191	37.5
Marine Corps	576	6.8
Navy	1,809	21.2
Other	1,181	13.9
Beneficiary type		
Active duty	1,059	12.4
Family members	4,400	51.7
Other	1,269	14.9
Recruit	23	0.3
Retired	1,765	20.7
TRICARE region		
Alaska	144	1.7
North	2,221	26.1
OCONUS	516	6.1
South	2,347	27.6
West	3,288	38.6

Ampicillin, levofloxacin, piperacillin/tazobactam, and ciprofloxacin were the most commonly prescribed antimicrobials identified in the inpatient DoD beneficiary population. **Figure 2** shows the quarterly rates of prescriptions of these antimicrobials in the inpatient setting. Overall, a descending trend in prescription rates was noted for the four antimicrobial agents. Ampicillin was the most commonly prescribed with an average rate of 55.4 prescriptions per 1,000 inpatient encounters, followed by levofloxacin (44.1), and piperacillin/tazobactam (34.9). Levofloxacin had the largest change in prescription rate from Q1 2010 to Q4 2014 with a decrease of 27%, while ampicillin and ciprofloxacin each had a 17% decrease, none of which was statistically significant. Prescription rates for ofloxacin, moxifloxacin, amoxicillin, nafcillin, oxacillin, penicillin G, penicillin V, and ticarcillin were negligible (average rate for each drug was less than 5 per 1,000 inpatient encounters, except for amoxicillin which had an average rate of 15 per 1,000 inpatient encounters) and thus were not included in further analyses.

Figure 3 shows rates of *E. coli* resistance to the most commonly prescribed antimicrobials. Overall, stable trends were observed for levofloxacin, piperacillin/tazobactam, and ciprofloxacin, with minimal quarterly fluctuations during 2010–2014. Ampicillin showed the highest resistance rates with an average rate of 52.1, followed by ciprofloxacin (30.2), and levofloxacin (29.1). Ampicillin showed the most quarterly fluctuations; the resistance rate trended upward from the beginning of 2010, peaked in Q1 2012 (58% resistant),

FIGURE 1. Quarterly incidence rates of inpatient *Escherichia coli* infections, Department of Defense hospitals, 2010–2014

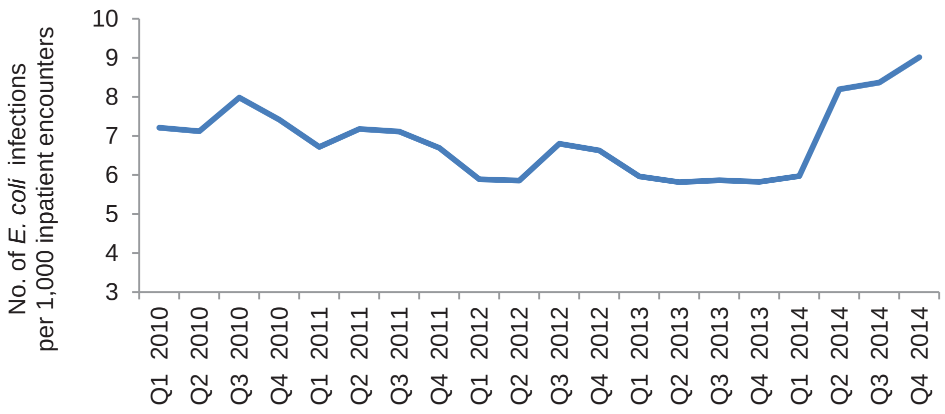


FIGURE 2. Quarterly incidence rates of all inpatient prescriptions of antimicrobials most commonly used for *Escherichia coli* infections, Department of Defense hospitals, 2010–2014

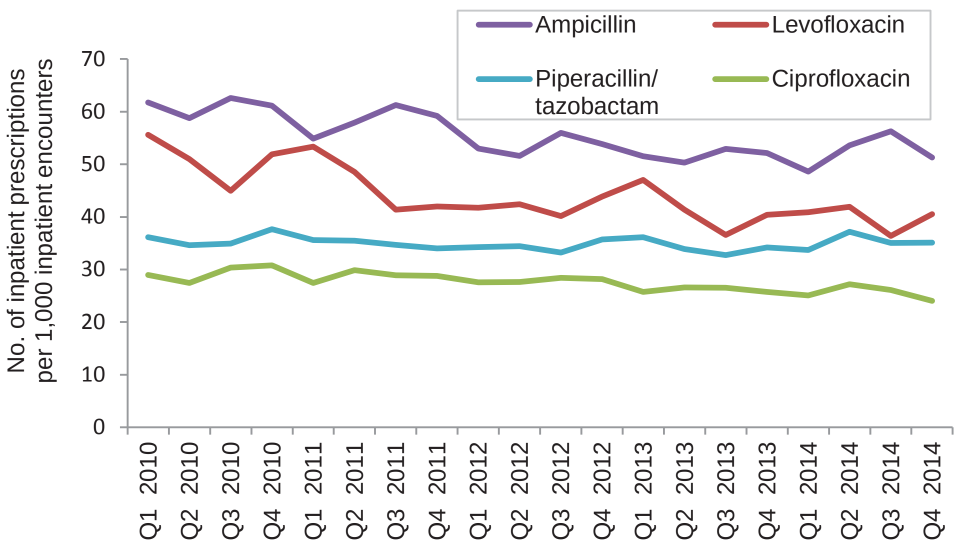
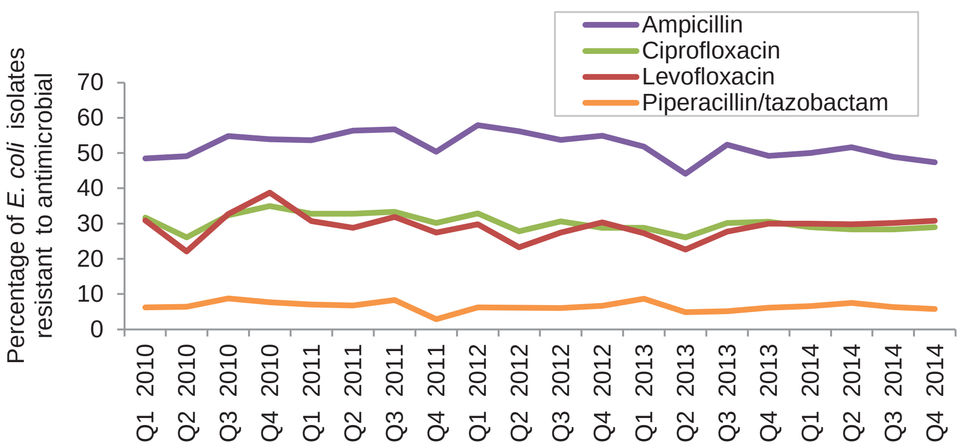


FIGURE 3. Quarterly inpatient *Escherichia coli* antimicrobial resistance rates, Department of Defense hospitals, 2010–2014



and then continued on a downward slope through the remainder of 2014. The largest change in resistance rate was noted for ciprofloxacin, for which the rate declined 9% from Q1 2010 to Q4 2014. However, this change was not statistically significant; isolates of *E. coli* would have needed to show a decrease in ciprofloxacin resistance rate to 20% or less in Q4 2014 to be statistically significant.

Spearman's correlations were used to examine the strength of the association between the rate of antimicrobials prescribed and the rate of AMR *E. coli*. **Table 2** shows correlation statistics for observed quarterly rates of prescription of antimicrobials and the corresponding quarterly rates of AMR *E. coli*. A statistically significant correlation was observed for the rate of ciprofloxacin prescription and level of ciprofloxacin resistance ($p=0.01$) with a moderate positive correlation coefficient ($r=0.53$). Additionally, statistically significant correlations were observed for the rate of ampicillin prescription and level of ciprofloxacin resistance ($p=0.03$) and the rate of penicillin prescription and level of fluoroquinolone resistance ($p=0.04$). However, weak positive correlation coefficients ($r=0.49$ and $r=0.46$, respectively) were indicated for both associations. **Figure 4** shows a point for each quarterly ciprofloxacin prescription rate and the corresponding percentage of *E. coli* resistance per quarter for ciprofloxacin. As indicated by the correlation coefficient, the rate of ciprofloxacin prescription is moderately and positively correlated with the level of ciprofloxacin resistance, suggesting that higher rates of ciprofloxacin prescriptions are associated with higher rates of ciprofloxacin resistance.

EDITORIAL COMMENT

Several studies conducted between 1994 and 2005 showed moderate to high positive correlations between fluoroquinolone prescription rates and *E. coli* resistance to these antimicrobials. This report identified three statistically significant weak to moderate correlations at $p<0.05$. Levels of ciprofloxacin prescriptions and ciprofloxacin resistance were moderately

TABLE 2. Inpatient correlation between antimicrobial use and resistance, Department of Defense hospitals, 2010–2014

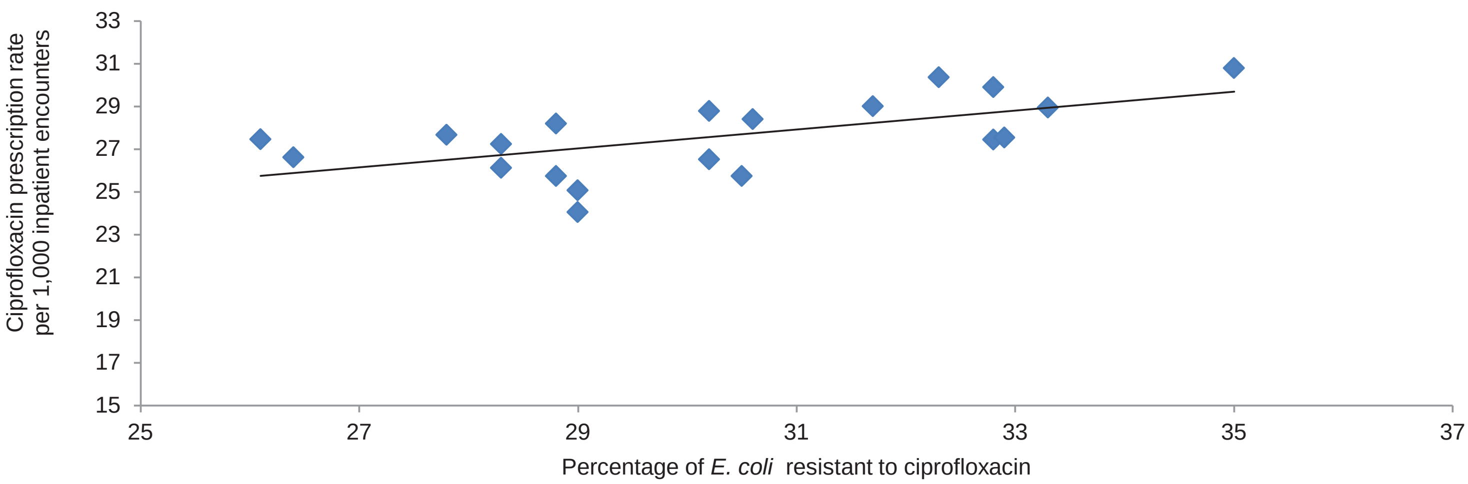
Prescription	*Escherichia coli* resistance	Spearman's correlation coefficients (95% CI)	*p*-value
Ciprofloxacin	Ciprofloxacin	0.53 (0.10, 0.78)	0.01
Ampicillin	Ciprofloxacin	0.49 (0.05, 0.76)	0.03
Penicillins	Fluoroquinolones	0.46 (0.004, 0.74)	0.04
Fluoroquinolones	Ciprofloxacin	0.32 (-0.15, 0.66)	0.17
Fluoroquinolones	Fluoroquinolones	0.31 (-0.16, 0.66)	0.19
Ampicillin	Ampicillin	0.26 (-0.21, 0.63)	0.28
Levofloxacin	Ciprofloxacin	0.23 (-0.24, 0.61)	0.34
Penicillins	Penicillins	0.16 (-0.30, 0.56)	0.50
Levofloxacin	Levofloxacin	0.15 (-0.31, 0.55)	0.53
Piperacillin/tazobactam	Ciprofloxacin	0.14 (-0.32, 0.55)	0.55

associated; levels of ampicillin prescriptions and ciprofloxacin resistance were weakly associated; and levels of penicillin prescriptions and fluoroquinolone resistance were weakly associated.[16] The moderate correlation coefficient suggests that higher levels of prescription rates are associated with higher levels of resistance. The lack of statistically significant changes over the surveillance period, irrespective of the quarterly fluctuations, for both ciprofloxacin prescription rates and ciprofloxacin resistance rates supports the moderate effect observed. A ciprofloxacin resistance rate of 20% or less was required in Q4 2014 to denote a statistically significant change during the surveillance period.[17] Similarly, the overall change in the prescription rates for ciprofloxacin from Q1 2010 to Q4 2014 was not statistically significant (p=0.49). It is possible that a threshold of change in prescription rates is required to have an impact on the incidence of resistance; if so, the overall change in prescription rates seen in this study would fail to influence resistance. Hsu et al. also noted fewer significant correlations between antimicrobial prescription and subsequent resistance in Singapore Hospitals between 2006 and 2008 when compared to studies published using data from the previous decade.[6,7,9,11]

There were limitations to this study. HL7-formatted data are generated from the Composite Health Care System at fixed MTFs. These data sources are limited in that they do not include data from healthcare services provided in the inpatient setting outside of the Military Health System (MHS), in shipboard facilities, or at in-theater facilities. The absence of such data could produce an underestimate of the infection burden among hospitalized MHS beneficiaries; however, given the beneficiary population studied, this limitation would likely have minimal impact on the findings and conclusions. In particular, the MHS beneficiaries who receive health care at shipboard and in-theater facilities are almost exclusively active duty personnel. Military personnel are primarily male and are much younger and healthier than the beneficiaries who are typically affected by *E. coli* infections and admitted to military hospitals. Additionally, it is possible that physicians sometimes chose to treat infections presumptively without culturing. Such practices would result in underestimates of the true burden of *E. coli* infections and AMR reported for hospitalized DoD beneficiaries.

The use of microbiology data for analysis of AMR is limited by the practice of

FIGURE 4. Inpatient correlation between ciprofloxacin prescriptions and *Escherichia coli* resistance to ciprofloxacin, Department of Defense hospitals, 2010–2014



cascade reporting. MHS laboratories participate in cascade reporting, a practice in which a laboratory might test an isolate against an extensive panel of antibiotics, but report results only for the antibiotics included on the facility's preferred formulary list. This practice is performed to varying degrees at DoD MTFs and is used as an effort to guide decisions on effective, but cost efficient, treatment. Thus, a complete picture of the susceptibility patterns for isolates may not be known and thus may affect trends of antimicrobial resistance observed within the DoD.

In conclusion, *E. coli* infections remain a common occurrence among hospitalized DoD beneficiaries. This study represents the first major examination of the association between prescription rates and recent AMR trends among hospitalized DoD beneficiaries. Although not statistically significant, descending trends were noted among prescription rates and stable trends were observed for resistance rates throughout the study period. However, a statistically significant moderate relationship was observed between rates of ciprofloxacin prescriptions and rates of *E. coli* resistant to ciprofloxacin in this analysis. Continued surveillance of prescription practices and AMR is needed to monitor trends in such relationships. In addition, enhanced antimicrobial stewardship programs should be established within the DoD to ensure treatment guidelines for *E. coli* promote prudent and judicious antimicrobial use to refrain from propagating further AMR.

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Brief Report

The Epidemiology of Herpes Simplex Virus Type 2 Infections in a Large Cohort of HIV-infected Patients, 2006–2014

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Worldwide genital herpes simplex virus type 2 (HSV-2) is a common infection.[1] HSV-2 infection is associated with a 2- to 4-fold increase in HIV acquisition.[2–4] In some countries with high rates of HSV-2 infection, as much as 50% of incident HIV infections are associated with pre-existing HSV-2 infection.[3] There is also evidence that patients with HSV-2 and HIV co-infection may be more likely to transmit HIV to uninfected partners.[5] Therefore, there is a clear link between these two viral infections worthy of detailed analysis. During the past several decades, notable shifts in HSV-2 infection rates have been observed in the general population.[6–9] In the U.S., there was a significant rise in HSV-2 seroprevalence during the 1980s and 1990s, showing an overall 30% increase and reaching a rate of 21.9% in the general population between 1988 and 1994.[7] However, rates decreased to 17% between 1999 and 2004 and overall rates declined further to 15.7% between 2005 and 2010.[6,9] It is unclear whether similar changes have occurred within the HIV-infected population. The epidemiology of HSV-2 infection within the military HIV-infected population is relatively understudied.[10] This report evaluates the epidemiology of HSV-2 infection within the U.S. Military HIV Natural History Study (NHS), a longitudinal study of a cohort of HIV-infected participants from all branches of service within the Department of Defense (DoD) and other healthcare beneficiaries of the Military Health System (MHS).

METHODS

Study population and definitions

The NHS follows a cohort of HIV-infected DoD beneficiaries (active duty service members, retirees, and dependents) **(Table 1)**. Patients enrolled in the NHS have visits scheduled every 6 months at one of six military treatment facilities. During these visits, subjects undergo blood draws (for study specific and clinical tests), are evaluated by research personnel, and undergo examination by an HIV specialist. In 2006, serologic testing for HSV-2 was introduced as a study-specific test. This analysis included subjects with HSV-2 testing performed during and after 2006. The subjects were defined as those having prevalent HSV-2 infection if the results on initial testing were positive. All participants with initial negative HSV-2 tests subsequently confirmed positive on testing were considered incident cases.

Laboratory testing

Serologic testing was performed using BioRad Bioplex 2200 HSV1/2 ELISA, Wampole HSV1/2 ELISA, or Quest Diagnostics HerpeSelect HSV1/2 ELISA, depending on clinic location and date of testing.

Statistics

Descriptive statistics are used to describe the population. HSV-2 prevalence was defined by a positive HSV-2 antibody result at the time of initial testing. Incidence rates were calculated using the number of newly positive HSV-2 antibody tests and the number of person-years (p-yrs) of follow-up in each calendar year. Participants' person-time was counted from the date of first negative HSV-2 test to the date of the first positive HSV-2 test, or until follow-up was censored due to death, loss to follow-up, or the end of each calendar year. Poisson regression analysis was used to test for trends in rates.

RESULTS

HSV-2 prevalence

Of the 5,925 participants ever enrolled in the NHS, 2,178 (37%) subjects had HSV-2 testing performed after 2006 **(Figure 1)**. The 2,178 subjects tested were predominantly male (94%), African American (43%), Caucasian (39%), and Hispanic/Other (17%), with a median age of 37.3 years (Inter Quartile Range [IQR]: 27.7–45.0) **(Table 1)**. Of those tested for HSV-2 after 2006, a total of 981 of 2,178 (45%) were positive at the time of their initial tests. The proportions of those tested for HSV-2 who were positive on their initial tests markedly varied from year to year (range: 33% in 2010 to 49% in 2006–2007) **(Figure 2)**. African American study participants had a greater burden of disease, compared with Caucasians (53% vs. 33%, p<.0001) and Hispanic/Other (53% vs. 17%, p<.0001) **(Figure 2)**.

HSV-2 incidence

A total of 974 subjects whose initial HSV-2 tests were negative contributed 4,052.4 p-yrs of follow-up time to the

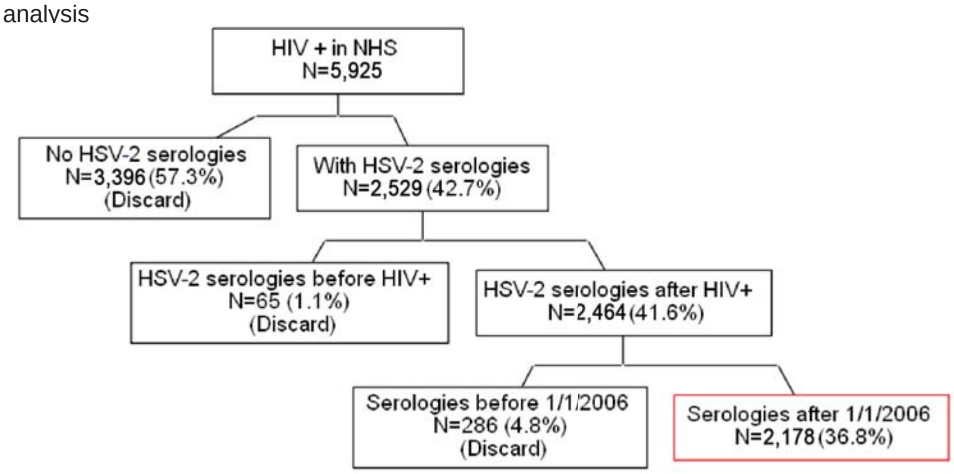
TABLE. Baseline demographic characteristics of subjects enrolled in the U.S. Military HIV Natural History Study (NHS)

	Total NHS N=5,925	Total patient population, incidence analysis N=974	Total patient population, prevalence analysis N=2,178
Gender			
Male	5,383 (90.85)	936 (96.10)	2,046 (93.94)
Female	542 (9.15)	38 (3.90)	132 (6.06)
Race/ethnicity			
Caucasian	2,494 (42.09)	447 (45.89)	859 (39.44)
African American	2,604 (43.95)	329 (33.78)	941 (43.20)
Hispanic	535 (9.03)	121 (12.42)	231 (10.61)
Asian	140 (2.36)	44 (4.52)	65 (2.98)
Native American	33 (0.56)	5 (0.51)	12 (0.55)
Other	107 (1.81)	28 (2.87)	67 (3.08)
Missing	12 (0.20)		3 (0.14)
Service			
Army	1,675 (28.27)	136 (13.96)	505 (23.19)
Navy	1,899 (32.05)	484 (49.69)	926 (42.52)
Air Force	1,787 (30.16)	237 (24.33)	498 (22.87)
Marine Corps	358 (6.04)	84 (8.62)	174 (7.99)
Other[a]	184 (3.11)	32 (3.29)	70 (3.21)
Missing	22 (0.37)	1 (0.10)	5 (0.23)
Duty status			
Active duty	2,701 (45.59)	574 (58.93)	1,081 (49.63)
Retired length of service	905 (15.27)	237 (24.33)	599 (27.50)
Retired medically	1,687 (28.47)	112 (11.50)	338 (15.52)
Dependent	460 (7.76)	28 (2.87)	87 (3.99)
Other[b]	150 (2.53)	23 (2.36)	70 (3.21)
Missing	22 (0.37)		3 (0.14)

[a]Coast Guard, Public Health Service, National Guard/Reserve, foreign military

[b]Reserves inactive duty, honorable discharge

FIGURE 1. Flow chart of patient inclusion for herpes simplex virus type 2 (HSV-2) prevalence analysis

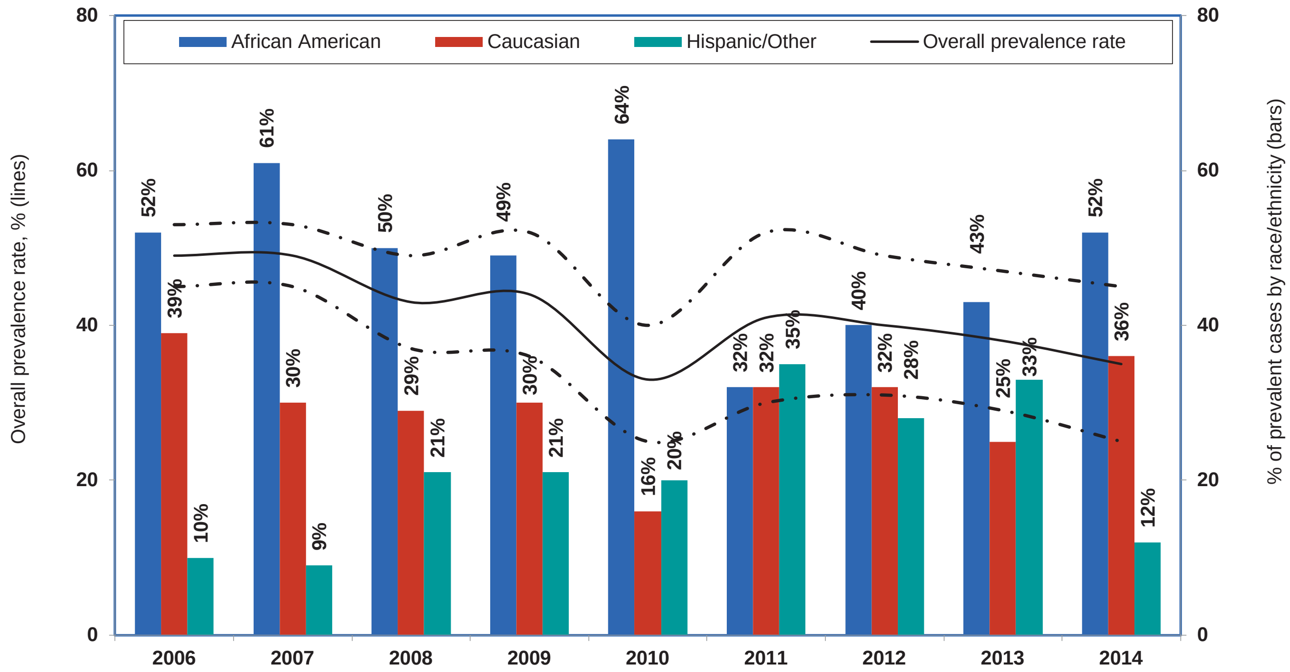


incidence analysis **(Figure 3)**. The median number of HSV-2 tests per person was 4 (IQR: 2–6). During follow-up, 188 participants developed incident HSV-2 infection (97.3% males; 43.1% African American, 37.2% Caucasian, and 19.7% Hispanic/Other; median age 30.6 years [IQR: 25.0–39.3]). The overall incidence of HSV-2 was 4.64 per 100 p-yrs of follow-up (95% CI: 4.00, 5.35) **(Figure 4)**. Incidence rates did not demonstrate statistically significant variation during the study period. During calendar years 2006–2010, rates were 5.00 per 100 p-yrs (95% CI: 4.11, 6.01); in 2011–2014, incidence was similar at 4.19 per 100 p-yrs ([95% CI: 3.30, 5.24, p=0.24]). The overall incidence of HSV-2 was higher among African Americans, compared with Caucasians (6.45 per 100 p-yrs; [95% CI: 5.12, 8.01] vs. 3.46 per 100 p-yrs; [95% CI: 2.70, 4.38], p=0.0001) but was similar to the rates observed among Hispanic/Other (6.45 per 100 p-yrs; [95% CI: 5.12, 8.01] vs. 4.77 per 100 p-yrs [95% CI: 3.36, 6.58]; p=0.12) **(Figure 4).**

EDITORIAL COMMENT

This study represents the first analysis of HSV-2 infections within a cross-section of the HIV-infected population receiving care from the MHS. These data show that the prevalence of HSV-2 infection in the NHS was lower than rates reported from other contemporary U.S. cohorts, where the reported rate range was 58%–60%.[11,12] Gender differences in the composition of the cohorts could partially explain these differences, given that female gender is a known risk factor for HSV-2 infections.[6,7,13] Males comprised 94% of the NHS population who underwent HSV-2 testing in comparison to 77%–84% of subjects enrolled in other similar studies.[11,12] Differences in sociobehavioral factors may also account for lower rates in the NHS. NHS participants are well educated (at a minimum they have a high school degree or equivalent) and have unrestricted access to health care and counseling. These favorable sociobehavioral factors have been associated with lower rates of sexually transmitted infections.[7,14] Ethnic

FIGURE 2. Prevalence of herpes simplex virus type 2 (HSV-2) in the U.S. Military HIV Natural History Study, by race/ethnicity



	2006	2007	2008	2009	2010	2011	2012	2013	2014
No. of HSV-2 tests performed	668	582	233	166	135	76	118	106	94
No. of HSV-2 positive	326	287	100	73	44	31	47	40	33
Overall prevalence rate	49%	49%	43%	44%	33%	41%	40%	38%	35%
95% CI upper boundary	53%	53%	49%	52%	40%	52%	49%	47%	45%
95% CI lower boundary	45%	45%	37%	36%	25%	30%	31%	29%	25%

Note: The solid and dotted lines represent the local linear robust fit smoothing line and the pointwise 95% CI, respectively, for incident HSV-2. The shaded bars represent percentage of prevalent cases by race/ethnicity.

FIGURE 3. Flow chart of patient inclusion for herpes simplex virus type 2 (HSV-2) incidence analysis

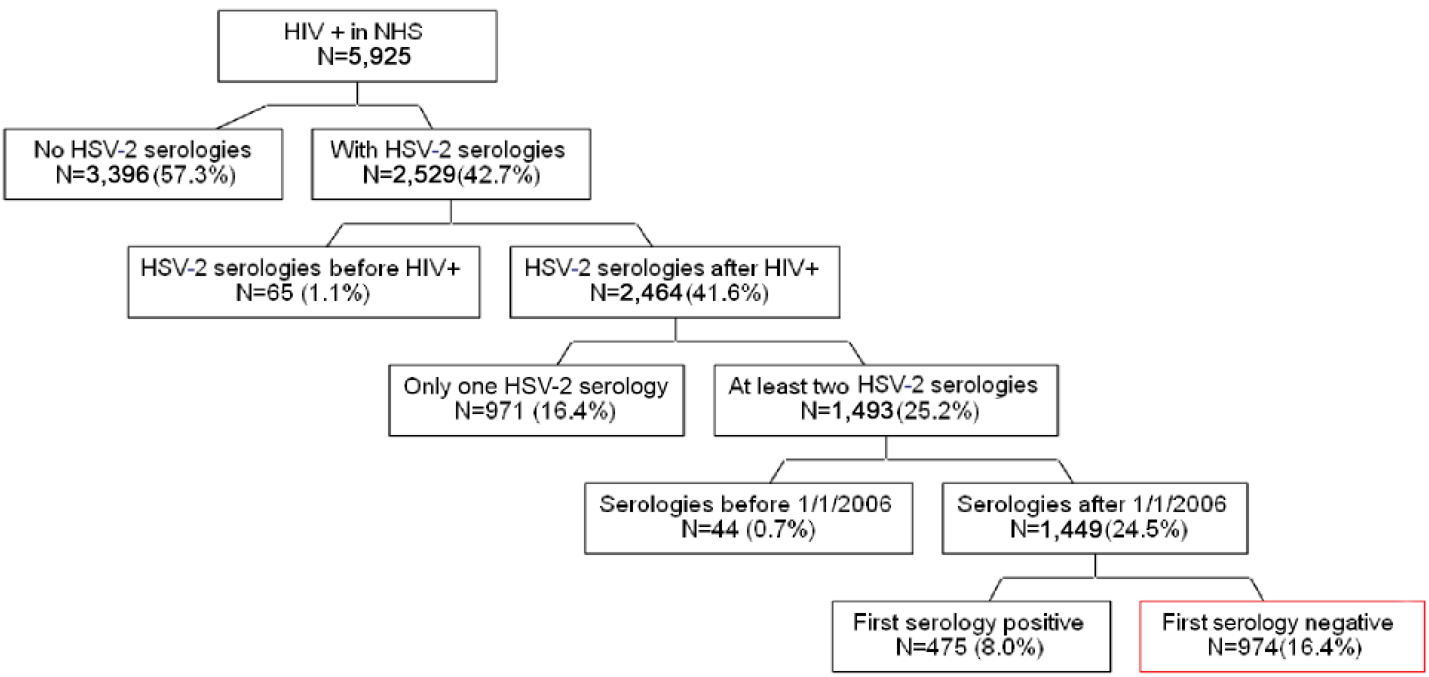
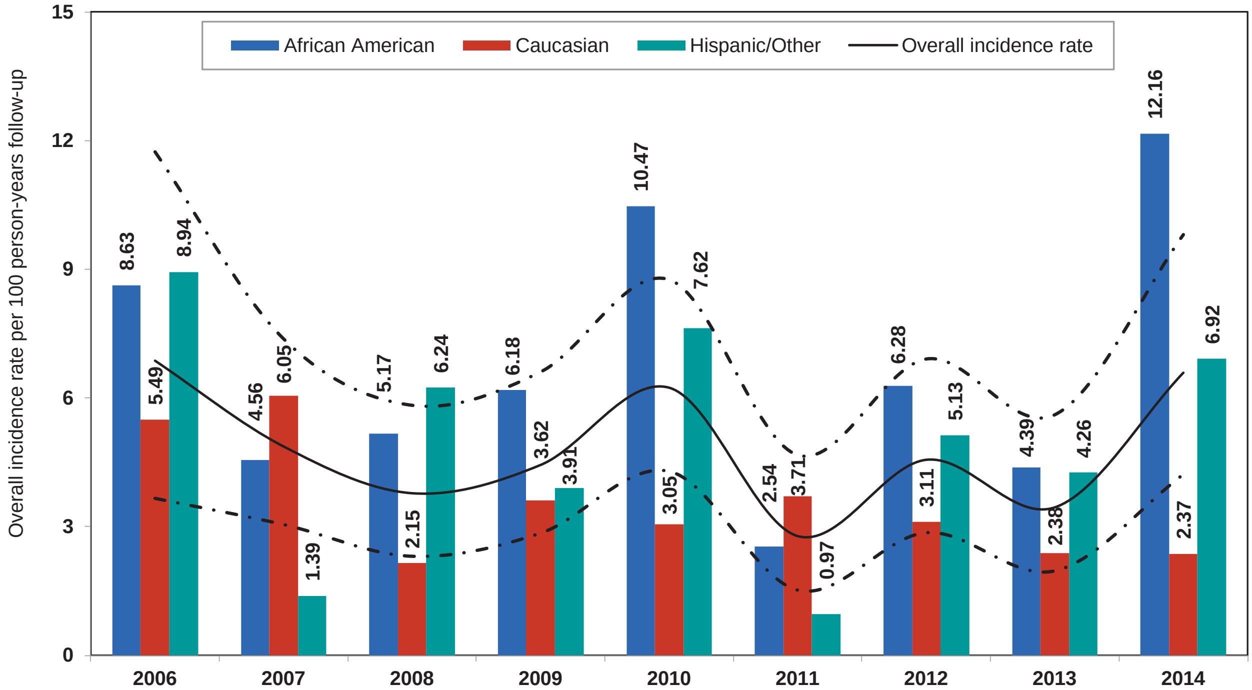


FIGURE 4. Incident herpes simplex virus type 2 (HSV-2) infection in the U.S. Military HIV Natural History Study, by race/ethnicity



	2006	2007	2008	2009	2010	2011	2012	2013	2014
No. of HSV-2 tests performed	372	553	604	605	607	550	555	518	467
No. of HSV-2 positive	13	22	20	24	33	14	22	16	24
Person-years follow-up	189.29	451.53	529.51	540.18	529.18	502.8	482.33	463.54	364.04
Overall incidence rate	6.87	4.87	3.78	4.44	6.24	2.78	4.56	3.45	6.59
95% CI upper boundary	11.74	7.38	5.83	6.61	8.76	4.67	6.91	5.61	9.81
95% CI lower boundary	3.66	3.05	2.31	2.85	4.29	1.52	2.86	1.97	4.22

Note: The solid and dotted lines represent the local linear robust fit smoothing line and the pointwise 95% CI, respectively, for incident HSV-2. The shaded bars represent incident rates by ethnicity.

differences observed in the NHS are similar to those previously reported, with African Americans being disproportionately affected.[11,12] The incidence of HSV-2 infection ranged from 2.78 to 6.87 per 100 p-yrs during the study period but did not demonstrate statistically significant variation from year to year due to overlapping confidence intervals. These rates are lower than those observed in a study of HIV-infected adolescents (8.50 per 100 p-yrs of follow-up),[15] and are similar to the rates observed in the HIV-infected Air Force cohort [incidence rate 5.7 per 100 p-yrs of follow-up (95% CI: 4.76–5.37)].[10] Overall, the younger age of the adolescent HIV-infected cohort may account for this higher incidence rate. Additionally, the method used may slightly overestimate person-time and thus underestimate incidence rates. A limitation was that a single testing platform was not used throughout the study period. However, the platforms utilized have similar sensitivities and specificities and good percentages of agreement.[16]

In conclusion, this study represents an initial analysis of HSV-2 infections within a unique population of DoD beneficiary HIV-infected patients. The prevalence of HSV-2 infections in the NHS is lower than previously reported. African Americans appear to bear a disproportionate burden of HSV-2 infections. Annual rates of incident HSV-2 infections remained stable during the study period.

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Medical Surveillance Monthly Report (MSMR) invites readers to submit topics for consideration as the basis for future *MSMR* reports. The *MSMR* editorial staff will review suggested topics for feasibility and compatibility with the journal's health surveillance goals. As is the case with most of the analyses and reports produced by Armed Forces Health Surveillance Branch staff, studies that would take advantage of the healthcare and personnel data contained in the Defense Medical Surveillance System (DMSS) would be the most plausible types. For each promising topic, Armed Forces Health Surveillance Branch staff members will design and carry out the data analysis, interpret the results, and write a manuscript to report on the study. This invitation represents a willingness to consider good ideas from anyone who shares the *MSMR*'s objective to publish evidence-based reports on subjects relevant to the health, safety, and well-being of military service members and other beneficiaries of the Military Health System (MHS).

In addition, *MSMR* encourages the submission for publication of reports on evidence-based estimates of the incidence, distribution, impact, or trends of illness and injuries among members of the U.S. Armed Forces and other beneficiaries of the MHS. Instructions for authors can be found on the *MSMR* page of the Armed Forces Health Surveillance Branch website: www.afhsc.mil/msmr/Instructions.

Please email your article ideas and suggestions to the *MSMR* editorial staff at: dha.ncr.health-surv.mbx.afhs-msmr@mail.mil.

Update: Heat Injuries, Active Component, U.S. Army, Navy, Air Force, and Marine Corps, 2015

The incidence rate of heat stroke among active component members of the U.S. Army, Navy, Air Force, and Marine Corps in 2015 was higher than rates in the previous 4 years. Incidence rates of heat stroke were higher among males, those younger than 20 years of age, Asian/Pacific Islanders, Marine Corps and Army members, and service members in combat-specific occupations, compared to their respective counterparts. More service members were treated for "other heat injuries" in 2015 (n=1,933) than in either of the previous 2 years. The incidence rate of "other heat injuries" was higher among females than males and rates were highest among service members younger than 20 years of age, among Army and Marine Corps members, among recruit trainees, and among service members in combat-specific occupations. During 2011–2015, 720 diagnoses of heat injuries were documented among service members serving in Iraq/Afghanistan; 6.9% (n=50) of those diagnoses were for heat stroke.

Heat-related injuries are a significant threat to the health and operational effectiveness of military members and their units.[1,2] Over many decades, lessons learned during training and operations in hot environments as well as the findings of numerous research studies have resulted in doctrine, equipment, and preventive measures that can significantly reduce the adverse health effects of military activities in heat.[1–3] Although numerous effective countermeasures are available, physical exertion in hot environments still causes hundreds of injuries—some life threatening—among U.S. military members each year.[4,5]

In the U.S. Military Health System (MHS), the most serious heat-related injuries are considered notifiable medical events. Since 31 July 2009, a notifiable case of heat stroke (ICD-9: 992.0) has been defined as a "severe heat stress injury, specifically including injury to the central nervous system, characterized by central nervous system dysfunction and often accompanied by heat injury to other organs and tissue."[6,7] Notifiable cases of heat injuries other than heat stroke include "moderate to severe heat injuries associated with strenuous exercise and environmental heat stress…that require medical intervention or result in lost duty time." All heat injuries that require medical intervention or result in lost duty are reportable. Cases that do not require medical intervention or result in lost duty time are not reportable.[6,7]

This report summarizes not only reportable medical events of heat injuries but also heat injury–related hospitalizations and ambulatory visits among active component members of the U.S. Army, Navy, Air Force, and Marine Corps during 2015, and compares them to the previous 4 years. Episodes of heat stroke and "other heat injuries" are summarized separately; for this analysis, "other heat injuries" includes heat exhaustion and "unspecified effects of heat."

METHODS

The surveillance period was 1 January 2011 through 31 December 2015. The surveillance population included all individuals who served in the active components of the Army, Navy, Air Force, or Marine Corps at any time during the surveillance period. Coast Guard members were not included in this year's annual update because of missing data for 2015. The Defense Medical Surveillance System (DMSS) maintains electronic records of all actively serving U.S. military members' hospitalizations and ambulatory visits in U.S. military and civilian (contracted/purchased care through the MHS) medical facilities worldwide; the DMSS also maintains records of medical encounters of service members deployed to Southwest Asia/Middle East (as documented in the Theater Medical Data Store [TMDS]). Because heat injuries represent a threat to the health of individual service members and to military training and operations, the Armed Forces require expeditious reporting of these reportable medical events through one of the service-specific electronic reporting systems; these reports are routinely transmitted and incorporated into the DMSS.

For this analysis, DMSS was searched to identify all records of medical encounters and notifiable medical event reports that included primary (first-listed) or secondary (second-listed) diagnoses of heat stroke (ICD-9: 992.0; ICD-10: T67.0) or "other heat injury" (heat exhaustion [ICD-9: 992.3–992.5; ICD-10: T67.3–T67.5] and "unspecified effects of heat" [ICD-9: 992.9; ICD-10: T67.9]).

This report summarizes numbers of individuals affected by documented heat injuries (i.e., incident cases) during each calendar year. To estimate numbers of incident cases per year, each individual who was affected by a heat injury event (one or more) during a year accounted for one incident case during the respective year. To classify the severity of incident cases per year, those that were associated with any heat stroke diagnosis were classified as heat stroke cases; all others were classified as "other heat injury" cases.

For surveillance purposes, a "recruit trainee" was defined as an active component service member (grades E1–E4) who was assigned to one of the Services' recruit training locations (per the individual's initial military personnel record). For this report, each service member was considered a recruit trainee for the period of time corresponding to the usual length of recruit training in his or her service. Recruit trainees were considered a separate category of enlisted service members in summaries of heat injuries by military grade overall.

Records of medical evacuations from the U.S. Central Command (CENTCOM) area of responsibility (AOR) (i.e., Iraq, Afghanistan) to a medical treatment facility outside the CENTCOM AOR were analyzed separately. Evacuations were considered case-defining if affected service members had at least one inpatient or outpatient heat injury medical encounter in a permanent military medical facility in the U.S. or Europe from 5 days before to 10 days after their evacuation dates.

TABLE 1. Incident cases[a] and incidence rates[b] of heat injury, active component members, U.S. Army, Navy, Air Force, and Marine Corps, 2015

	Heat stroke		Other heat injury		Total heat injury diagnoses	
	No.	Rate[b]	No.	Rate[b]	No.	Rate[b]
Total	417	0.32	1,933	1.49	2,350	1.81
Sex						
Male	384	0.35	1,625	1.48	2,009	1.83
Female	33	0.16	308	1.54	341	1.70
Age (years)						
< 20	64	0.73	450	5.12	514	5.85
20–24	186	0.45	830	1.99	1,016	2.43
25–29	93	0.30	388	1.26	481	1.57
30–34	46	0.22	136	0.65	182	0.87
35–39	20	0.14	74	0.51	94	0.65
40+	8	0.06	55	0.41	63	0.47
Race/ethnicity						
White, non-Hispanic	234	0.30	1,154	1.48	1,388	1.79
Black, non-Hispanic	59	0.27	351	1.63	410	1.91
Hispanic	65	0.41	249	1.56	314	1.97
Asian/Pacific Islander	30	0.51	109	1.87	139	2.39
Other/unknown	29	0.32	70	0.77	99	1.09
Service						
Army	256	0.53	1,173	2.41	1,429	2.93
Navy	25	0.08	107	0.33	132	0.41
Air Force	10	0.03	174	0.57	184	0.60
Marine Corps	126	0.68	479	2.60	605	3.29
Military status						
Recruit	20	0.76	248	9.45	268	10.21
Enlisted	322	0.31	1,528	1.46	1,850	1.77
Officer	75	0.32	157	0.68	232	1.01
Military occupation						
Combat-specific	168	0.95	615	3.47	783	4.42
Armor/motor transport	8	0.17	55	1.20	63	1.37
Pilot/air crew	0	0.00	22	0.44	22	0.44
Repair/engineering	44	0.11	278	0.72	322	0.83
Communications/intelligence	54	0.19	309	1.08	363	1.27
Health care	33	0.28	103	0.87	136	1.16
Other	110	0.46	551	2.32	661	2.79
Home of record[c]						
Midwest	80	0.35	363	1.58	443	1.93
Northeast	57	0.35	219	1.33	276	1.68
South	158	0.29	855	1.59	1,013	1.88
West	101	0.34	449	1.52	550	1.86
Other/unknown	21	0.29	47	0.64	68	0.93

[a]One case per person per year.
[b]Number of cases per 1,000 person-years
[c]As self-reported at time of entry into service

RESULTS

In 2015, there were 417 incident cases of heat stroke and 1,933 incident cases of "other heat injury" among active component service members **(Table 1)**. The overall crude incidence rates of heat stroke and "other heat injury" were 0.32 and 1.49 per 1,000 person-years (p-yrs), respectively.

The annual incidence rate (unadjusted) of cases of heat stroke in 2015 was higher than the rates in any of the previous 4 years **(Figure 1)**. There were more heat stroke–related ambulatory visits in 2015 than in 2014 but comparable numbers of reportable events and hospitalizations. The annual incidence rate (unadjusted) of cases of "other heat injury" was 18% higher in 2015 than in 2014 due to an increase in reportable events and ambulatory visits **(Figure 2)**.

In 2015, subgroup-specific incidence rates of heat stroke were highest among males and service members younger than 20 years of age, Asian/Pacific Islanders, Marine Corps and Army members, recruit trainees, and those in combat-specific occupations **(Table 1)**. Heat stroke rates in the Marine Corps were 28% higher than in the Army; Army rates were more than 6-fold those in the Navy and 17-fold those in the Air Force; the rate among females was more than 50% lower than the rate among males. There were only 20 cases of heat stroke among recruit trainees, but their incidence rate was more

FIGURE 1. Incident cases and incidence rates of heat stroke by source of report and year of diagnosis, active component members, U.S. Army, Navy, Air Force, and Marine Corps, 2011–2015

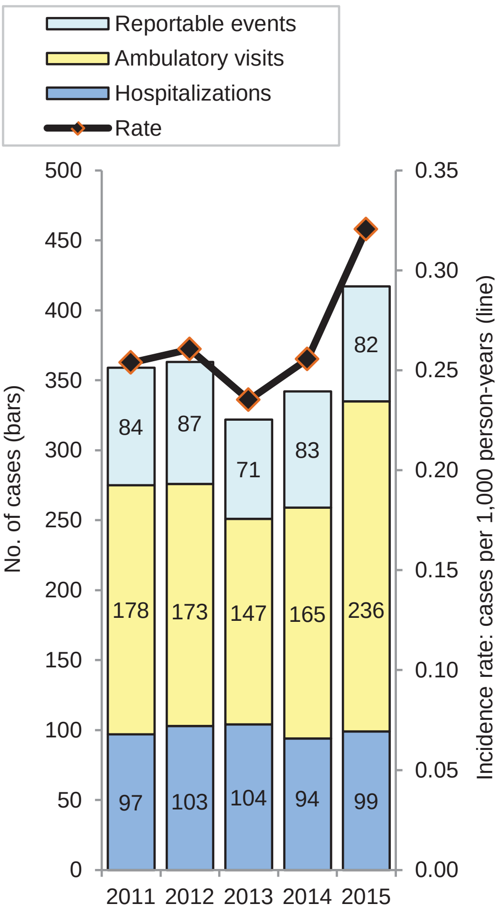


FIGURE 2. Incident cases and incidence rates of "other heat injury" by source of report and year of diagnosis, active component members, U.S. Army, Navy, Air Force, and Marine Corps, 2011–2015

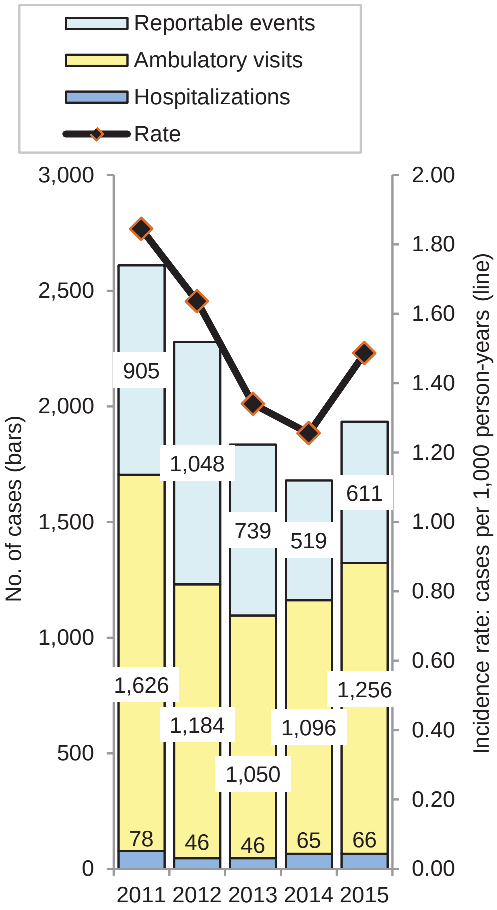


TABLE 2. Numbers of heat injuries[a] by location of diagnosis/report, active component members, U.S. Army, Navy, Air Force, and Marine Corps, 2011–2015

Location of diagnosis	No.	% total
Fort Bragg, NC	1,502	12.4
Fort Benning, GA	1,399	11.5
Fort Jackson, SC	1,164	9.6
MCB Camp Lejeune/ Cherry Point, NC	665	5.5
Fort Campbell, KY	551	4.5
MCRD Parris Island/ Beaufort, SC	482	4.0
Fort Polk, LA	403	3.3
MCB Camp Pendleton, CA	287	2.4
Fort Hood, TX	272	2.2
MCB Quantico, VA	270	2.2
NMC San Diego, CA	252	2.1
Fort Stewart, GA	246	2.0
Okinawa, Japan	225	1.9
JBSA-Lackland AFB, TX	178	1.5
Fort Sill, OK	150	1.2
All other locations	4,092	33.7
Total	12,138	100.0

[a]One heat injury per person per 60 days

MCRD, Marine Corps Recruit Depot; MCB, Marine Corps Base; NMC, Naval Medical Center; JBSA, Joint Base San Antonio

than twice that of other enlisted members and officers.

In contrast to the heat stroke findings, the crude incidence rate of "other heat injuries" was higher among females than males **(Table 1)**. In 2015, subgroup-specific incidence rates of "other heat injuries" were highest by far among service members younger than 20 years of age, among Army and Marine Corps members, among recruit trainees, and among service members in combat-specific occupations.

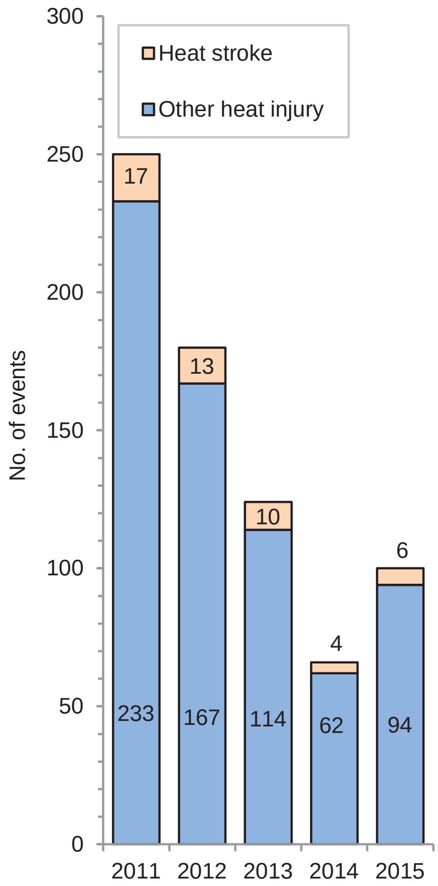
Heat injuries by location

During the 5-year surveillance period, 12,138 heat-related injuries were diagnosed at more than 250 military installations and geographic locations worldwide. Three Army installations accounted for about one-third of all heat injuries during the period (Fort Bragg, NC [n=1,502]; Fort Benning, GA [n=1,399]; and Fort Jackson, SC [n=1,164]); four other installations accounted for an additional 17% of heat injury events (Marine Corps Base Camp Lejeune/Cherry Point, NC [n=665]; Fort Campbell, KY [n=551]; Marine Corps Recruit Depot Parris Island/Beaufort, SC [n=482]; and Fort Polk, LA [n=403]). Of the 10 installations with the most heat injury events, the majority are located in the southeastern U.S. **(Table 2)**.

Heat injuries in Iraq and Afghanistan

During the 5-year surveillance period, 720 heat injuries were diagnosed and treated in Iraq and Afghanistan **(Figure 3)**. Of these, 6.9% (n=50) were diagnosed as heat stroke. The numbers of heat injuries in Iraq and Afghanistan increased 52% in 2015 relative to 2014. Prior to 2015, the number of heat injuries had decreased every year since 2011. Deployed service members who were affected by heat injuries were most frequently male (n=580; 80.6%); white, non-Hispanic (n=425: 59.0%); aged 20–24 years (n=345; 47.9%); in the Army (n=420; 58.3%); enlisted (n=689; 95.7%); and in repair/engineering (n=214; 29.7%) or combat-specific (n=191; 26.5%) occupations **(data not shown)**. During the surveillance period, 11 service members were medically evacuated for heat injuries from Iraq or Afghanistan; 45% of the evacuations (n=5) took place in either July or August.

FIGURE 3. Numbers of heat injuries[a] reported from Iraq/Afghanistan, 2011–2015



[a]One per person per 60 days.

EDITORIAL COMMENT

This annual update of heat injuries in the active components of the Army, Navy, Air Force, and Marine Corps documented that the annual incidence rates of diagnoses of heat stroke, after a period of relative stability, increased in 2015. The incidence rates of diagnoses of other heat injuries declined by nearly one-third during the first 4 years of the surveillance period but increased about 18% from 2014 to 2015. The separate analysis of heat injuries diagnosed and treated in Iraq and Afghanistan during the surveillance period showed a 52% increase in the number of heat injuries in 2015 relative to 2014. However, the overall decrease in the annual numbers of incident cases of heat injuries during the entire surveillance period is consistent with the declining numbers of U.S. forces in those two countries in the past 5 years.

The results of this update should be interpreted with consideration of its limitations. Similar heat-related clinical illnesses are likely managed differently and reported with different diagnostic codes at different locations and in different clinical settings. Such differences undermine the validity of direct comparisons of rates of nominal heat stroke and "other heat injury" events across locations and settings. Also, heat injuries during training exercises and deployments that are treated in field medical facilities are not completely ascertained as cases for this report. It should also be noted that the guidelines for mandatory reporting of heat injuries (renamed "heat illness") were modified in the 2012 revision of the guidelines for reportable medical events.[6,7] It is possible that the numbers of reports of heat injuries might have been affected by the change in guidelines. To compensate for such possible variation in reporting, the analysis for this update, as in previous years, included cases identified in DMSS records of ambulatory care and hospitalizations utilizing a consistent set of ICD-9 codes for the entire surveillance period. The data indicate that a sizable proportion of cases identified through DMSS records did not prompt mandatory reports through the reporting system. The shift from ICD-9 to ICD-10 coding that occurred in the last quarter of 2015 presented another potential limitation. A hypothetical concern was that the use of the new coding system might affect the completeness and/or accuracy of recording the diagnoses of interest. However, the straightforward nature of the ICD-9 to ICD-10 code translation for the diagnoses of interest likely limits this source of error.

In spite of its limitations, this report documents that heat injuries are still a significant threat to the health of U.S. military members and the effectiveness of military operations. Of all military members, the youngest and most inexperienced Marines and soldiers (particularly those training at installations in the southeastern U.S.) are at highest risk of heat injuries—including heat stroke, exertional hyponatremia, and exertional rhabdomyolysis (see the other articles in this issue of the *MSMR*).

Commanders, small unit leaders, training cadre, and supporting medical personnel (particularly at recruit training centers and installations with large combat troop populations) must ensure that military members whom they supervise and support are informed regarding risks, preventive countermeasures (e.g., water consumption), early signs and symptoms, and first-responder actions related to heat injuries.[1–3] Leaders should be aware of the dangers of insufficient hydration on the one hand and excessive water intake on the other; they must have detailed knowledge of, and rigidly enforce countermeasures against, all types of heat injuries.

Policies, guidance, and other information related to heat injury prevention and treatment among U.S. military members are available online at: http://phc.amedd.army.mil/topics/discond/hipss/Pages/HeatinjuryPrevention.aspx and http://www.marines.mil/Portals/59/Publications/MCO%206200.1E%20W%20CH%201.pdf

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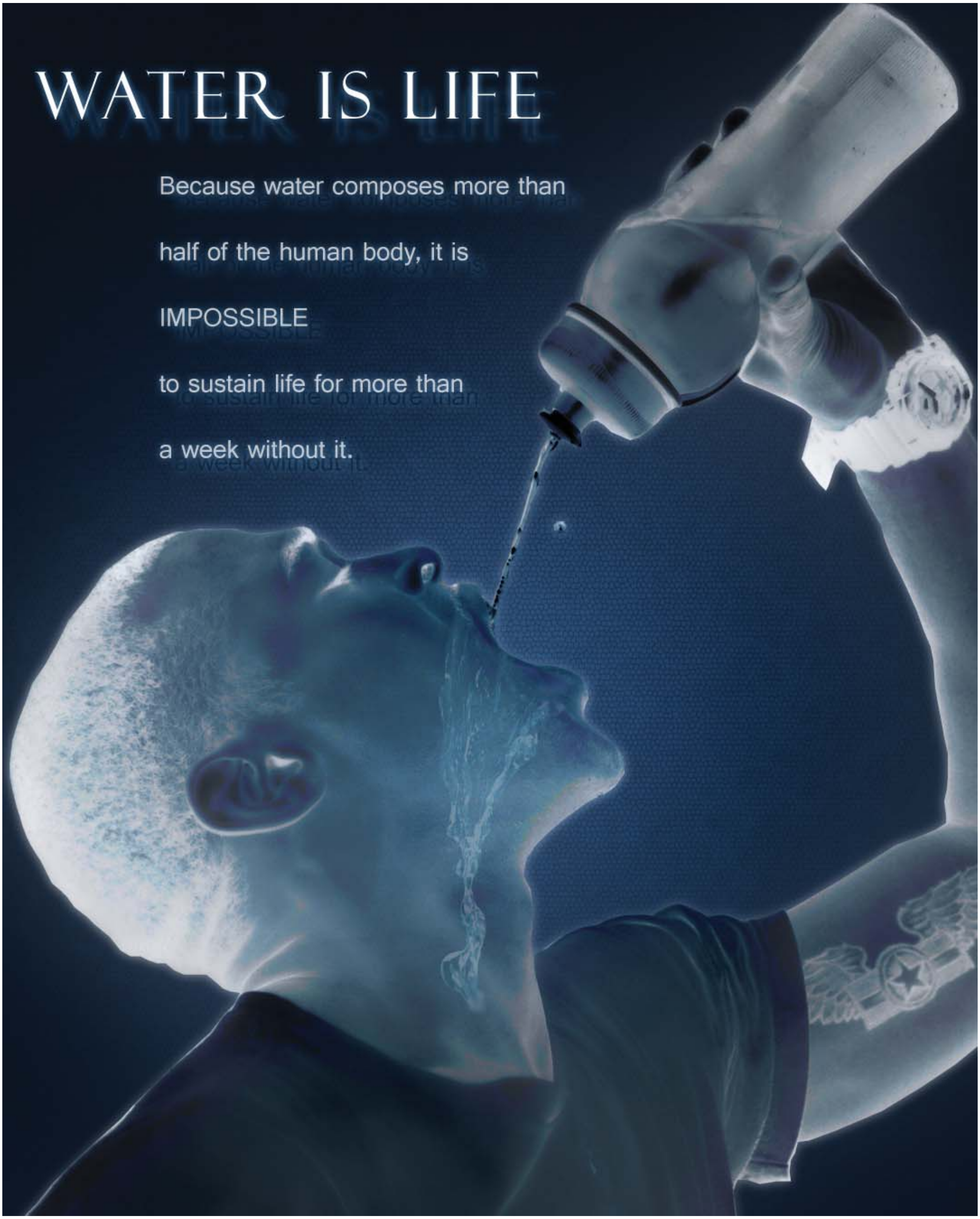

WATER IS LIFE
Because water composes more than
half of the human body, it is
IMPOSSIBLE
to sustain life for more than
a week without it.

Update: Exertional Rhabdomyolysis, Active Component, U.S. Army, Navy, Air Force, and Marine Corps, 2011–2015

Among active component members of the U.S. Army, Navy, Air Force, and Marine Corps in 2015, there were 456 incident episodes of rhabdomyolysis likely due to physical exertion or heat stress ("exertional rhabdomyolysis"). Annual rates of incident diagnoses of exertional rhabdomyolysis increased 17% between 2014 and 2015. In 2015, the highest incidence rates occurred in service members who were male; younger than 20 years of age; black, non-Hispanic; members of the Marine Corps and Army; recruit trainees; and in combat-specific occupations. Most cases of exertional rhabdomyolysis were diagnosed at installations that support basic combat/recruit training or major ground combat units of the Army or Marine Corps. Medical care providers should consider exertional rhabdomyolysis in the differential diagnosis when service members (particularly recruits) present with muscular pain and swelling, limited range of motion, or the excretion of dark urine (e.g., myoglobinuria) after strenuous physical activity, particularly in hot, humid weather.

Rhabdomyolysis refers to the rapid breakdown of skeletal muscle cells, a process most often recognized by the appearance in the urine of brown-colored myoglobin following its release from damaged muscle cells into the bloodstream. Myoglobin is toxic to the tubular cells of the kidney and can induce renal failure. In U.S. military members, rhabdomyolysis is a significant threat during physical exertion, particularly under heat stress. Each year, the *MSMR* summarizes numbers, rates, trends, risk factors, and locations of occurrences of exertional heat injuries, including exertional rhabdomyolysis. This report includes the data for the years 2011–2015. More detailed information about the definition, causes, and prevention of exertional rhabdomyolysis can be found in previous issues of the *MSMR*.[1]

METHODS

The surveillance period was 1 January 2011 through 31 December 2015. The surveillance population included all individuals who served in an active component of the U.S. Army, Navy, Air Force, or Marine Corps at any time during the surveillance period. The Defense Medical Surveillance System (DMSS) maintains electronic records of all actively serving U.S. military members' hospitalizations and ambulatory visits in U.S. military and civilian (contracted or purchased care through the Military Health System) medical facilities worldwide. The DMSS also maintains records of medical encounters of service members deployed to Southwest Asia/Middle East (as documented in the Theater Medical Data Store).

For this analysis, the DMSS was searched for records of healthcare encounters (inpatient or outpatient) associated with diagnoses related to the occurrence of exertional rhabdomyolysis. For surveillance purposes, a case of "exertional rhabdomyolysis" was defined as a hospitalization or ambulatory visit with a discharge diagnosis in any position of either "rhabdomyolysis" (ICD-9: 728.88; ICD-10: M62.82) or "myoglobinuria" (ICD-9: 791.3; ICD-10: R82.1) plus a diagnosis in any position of one of the following: "volume depletion (dehydration)" (ICD-9: 276.5x; ICD-10: E86.0, E86.1, E86.9), "effects of heat" (ICD-9: 992.0–992.9; ICD-10: T67.0–T67.9), "effects of thirst (deprivation of water)" (ICD-9: 994.3; ICD-10: T73.1), "exhaustion due to exposure" (ICD-9: 994.4; ICD-10: T73.2), or "exhaustion due to excessive exertion (overexertion)" (ICD-9: 994.5; ICD-10: T73.3). Each individual could be included as a case only once per calendar year.

To exclude cases of rhabdomyolysis that were secondary to traumatic injuries, intoxications, or adverse drug reactions, medical encounters with diagnoses in any position of "injury, poisoning, toxic effects" (ICD-9: 800–999), except "sprains and strains of joints and adjacent muscles" (ICD-9: 840–848; ICD-10: S43, S53, S63, S73, S83, S93) were not considered indicative of "exertional rhabdomyolysis." Because the treatment facilities of the Military Health System transitioned to the use of ICD-10 codes on 1 October 2015, every record of an encounter with a diagnosis of "rhabdomyolysis" (ICD-10 code: M62.82) or "myoglobinuria" (ICD-10 code: R82.1) during the last quarter of 2015 was individually examined for the presence of exclusionary diagnoses described above.

For surveillance purposes, a "recruit trainee" was defined as an active component member in an enlisted grade of E1–E4 who was assigned to one of the Services' recruit training locations (per the individual's initial military personnel record). For this report, each service member was considered a recruit trainee for the period of time corresponding to the usual length of recruit training in his or her service. Recruit trainees were considered a separate category of enlisted service members in summaries of rhabdomyolysis cases by military grade overall.

Records of medical evacuations from the U.S. Central Command (CENTCOM) area of responsibility (AOR) (e.g., Iraq, Afghanistan) to a medical treatment facility outside the CENTCOM AOR were analyzed separately. Evacuations were considered case-defining if affected service members met the above criteria in a permanent military medical facility in the U.S. or Europe from 5 days before to 10 days after their evacuation dates.

RESULTS

In 2015, there were 456 incident diagnoses of rhabdomyolysis likely associated with physical exertion and/or heat stress ("exertional rhabdomyolysis") **(Table 1)**. The crude incidence rate was 35.1 per 100,000 person-years (p-yrs).

In 2015, relative to their respective counterparts, the highest incidence rates of exertional rhabdomyolysis affected service members who were male; younger than 20 years of age; and black, non-Hispanic **(Table 1)**. Compared to other race/ethnicity groups, the incidence rate of exertional rhabdomyolysis among black, non-Hispanics was highest overall during the period and in every year except 2013 when the highest rate occurred in Asian/Pacific Islanders **(data not shown)**. Subgroup-specific incidence rates were highest among service members in the Marine Corps and Army, and those in combat-specific occupations. Of note, incidence rates among recruit trainees were more than five times those among other enlisted members and officers, even though the trainees accounted for only 9.6% of all cases in 2015.

The annual rates of exertional rhabdomyolysis decreased slightly over the course of the first 3 years of the surveillance period. Annual rates of incident diagnoses of exertional rhabdomyolysis then increased 26% between 2013 and 2015, with the greatest change occurring between 2014 and 2015 (17%). **(Figure 1)**.

In 2015, 78% of all service members who were diagnosed with exertional rhabdomyolysis were in either the Army (n=219) or the Marine Corps (n=138) **(Table 1)**. Annual incidence rates were much higher in the Marine Corps than any of the other services during every year of the surveillance period **(Figure 2)**. The annual incidence rates in the Marine Corps and the Army increased during 2014–2015, but rates in the Air Force and Navy remained relatively stable. During the 5-year surveillance period, most cases (70%) occurred during May–September **(Figure 3)**.

TABLE 1. Incident cases and incidence rates[a] of exertional rhabdomyolysis, active component, U.S. Army, Navy, Air Force, and Marine Corps, 2015

	Hospitalizations		Ambulatory visits		Total	
	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
Total	197	15.1	259	19.9	456	35.1
Gender						
Male	185	16.8	238	21.6	423	38.4
Female	12	6.0	21	10.5	33	16.5
Age (years)						
<20	30	27.9	57	53.0	87	80.9
20–24	54	12.7	93	21.8	147	34.5
25–29	64	21.3	54	18.0	118	39.3
30–34	25	12.2	30	14.7	55	26.9
35–39	17	12.1	15	10.7	32	22.9
40+	7	5.7	10	8.2	17	13.9
Race/ethnicity						
White, non-Hispanic	95	12.2	124	15.9	219	28.2
Black, non-Hispanic	57	26.5	72	33.5	129	60.1
Hispanic	25	15.7	38	23.8	63	39.5
Asian/Pacific Islander	12	20.6	17	29.2	29	49.8
Other/unknown	8	8.8	8	8.8	16	17.6
Service						
Army	108	22.2	111	22.8	219	44.9
Navy	18	5.6	20	6.2	38	11.8
Air Force	25	8.1	36	11.7	61	19.9
Marine Corps	46	25.0	92	50.0	138	75.0
Military status						
Recruit	11	41.9	33	125.8	44	167.7
Enlisted	152	14.6	195	18.7	347	33.2
Officer	34	14.7	31	13.4	65	28.2
Military occupation						
Combat-specific	58	32.7	65	36.7	123	69.4
Armor/motor transport	5	10.9	5	10.9	10	21.8
Pilot/air crew	4	8.0	1	2.0	5	10.0
Repair/engineering	34	8.8	39	10.1	73	18.9
Communications/intelligence	29	10.2	36	12.6	65	22.8
Health care	16	13.6	15	12.7	31	26.3
Other	51	21.5	98	41.3	149	62.9
Home of record[b]						
Midwest	34	14.8	37	16.1	71	31.0
Northeast	25	15.2	34	20.7	59	35.9
South	86	16.0	126	23.4	212	39.4
West	47	15.9	53	17.9	100	33.8
Other/unknown	4	5.6	9	12.7	13	18.4

[a]Number of cases per 100,000 person-years

[b]As self-reported at time of entry into service

Rhabdomyolysis by location

During the 5-year surveillance period, the medical treatment facilities at nine installations diagnosed at least 50 cases each and, together, about half (51%) of all diagnosed cases **(Table 2)**. Of these installations, three provide support to recruit/basic combat training centers (Marine Corps Recruit Depot [MCRD] Parris Island/Beaufort, SC; Fort Benning, GA; and Joint Base San Antonio–Lackland, TX). In addition, six installations support large combat troop populations (Fort Bragg, NC; Marine Corps Base [MCB] Camp Pendleton, CA; MCB Camp Lejeune/Cherry Point, NC; Fort Shafter, HI; Fort Hood, TX; and Fort Campbell, KY). The most cases overall (together accounting for 25% of all cases) were diagnosed at Fort Bragg, NC (n=309) and MCRD Parris Island/Beaufort, SC (n=211).

FIGURE 1. Incident cases and incidence rates of exertional rhabdomyolysis by clinical setting, active component, U.S. Army, Navy, Air Force, and Marine Corps, 2011–2015

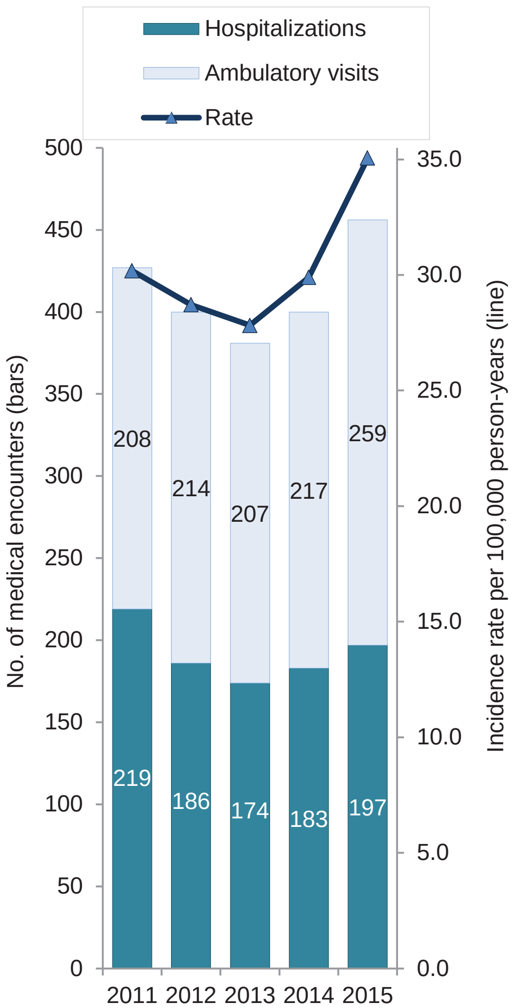


FIGURE 2. Incidence rates of exertional rhabdomyolysis by service, active component, U.S. Army, Navy, Air Force, and Marine Corps, 2011–2015

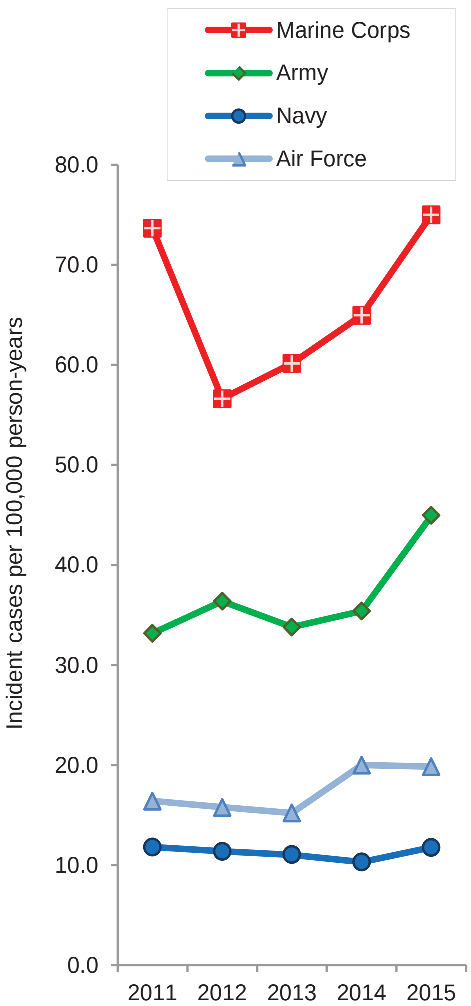


TABLE 2. Incident cases of exertional rhabdomyolysis by installation (with at least 30 cases during the period), active component, U.S. Army, Navy, Air Force, and Marine Corps, 2011–2015

Location of diagnosis	No.	% total
Fort Bragg, NC	309	15.0
MCRD Parris Island/ Beaufort, SC	211	10.2
MCB Camp Pendleton, CA	108	5.2
MCB Camp Lejeune/ Cherry Point, NC	95	4.6
Fort Shafter, HI	74	3.6
Fort Hood, TX	69	3.3
Fort Benning, GA	68	3.3
JBSA-Lackland, TX	59	2.9
Fort Campbell, KY	51	2.5
Fort Jackson, SC	40	1.9
Fort Stewart, GA	40	1.9
Fort Bliss, TX	37	1.8
Fort Belvoir, VA	37	1.8
NMC San Diego, CA	36	1.7
NMC Portsmouth, VA	30	1.5
Other locations	800	38.8
Total	2,064	100.0

MCRD, Marine Corps Recruit Depot; MCB, Marine Corps Base; JBSA, Joint Base San Antonio; NMC, Naval Medical Center

Rhabdomyolysis in Iraq and Afghanistan

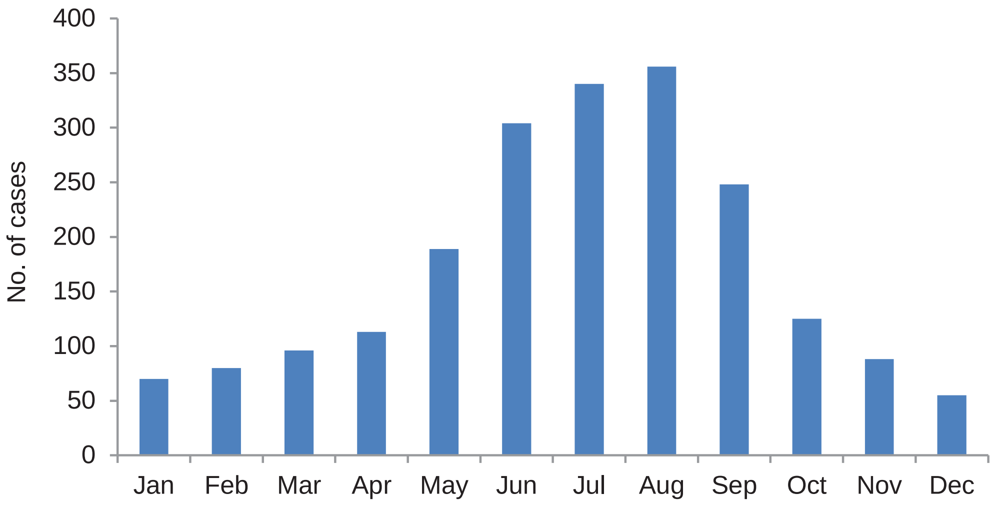
During the 5-year surveillance period, there were 17 incident cases of exertional rhabdomyolysis diagnosed and treated in Iraq/Afghanistan **(data not shown)**. Deployed service members who were affected by exertional rhabdomyolysis were most frequently male (n=16; 94.1%); white, or black, non-Hispanic (n=8; 47.1% and n=6; 35.3%, respectively); younger than 20 years of age (n=6; 35.3%); in the Army (n=12; 70.6%); enlisted (n=15; 88.2%); and in combat-specific occupations (n=11; 64.7%). Two active component service members were medically evacuated from Iraq/Afghanistan for exertional rhabdomyolysis; both occurred in September **(data not shown)**.

EDITORIAL COMMENT

This report documents a modest increase in the annual rates of diagnoses of exertional rhabdomyolysis among active component U.S. military members in 2015, compared to 2013 and 2014. Exertional rhabdomyolysis continued to occur most frequently from late spring through early fall at installations that support basic combat/recruit training or major Army or Marine Corps combat units.

The risks of heat injuries, including exertional rhabdomyolysis, are increased among individuals who suddenly increase overall levels of physical activity, recruits who are not physically fit when they begin training, and recruits from relatively cool and dry climates who may not be acclimated to the high heat and humidity at training camps in the summer.[2,3] Soldiers and Marines in combat units often conduct rigorous unit physical training, personal fitness training, and field training exercises regardless of weather conditions. Thus, it is not surprising that recruit camps

FIGURE 3. Incident cases of exertional rhabdomyolysis by month, active component members, U.S. Army, Navy, Air Force, and Marine Corps, 2011–2015



and installations with large ground combat units account for most of these cases.

The annual incidence rates in black, non-Hispanic service members were consistently higher than the rates among members of other race/ethnicity subgroups in 2015 and in previous years. This observation has been attributed, at least in part, to an increased risk of exertional rhabdomyolysis among individuals with sickle cell trait.[4-6] However, in 2013, the rate among Asian/Pacific Islanders was the highest of all race/ethnicity groups. Although the annual incidence rates for this group have been on the increase since 2009, the reasons for such a trend are unknown. Supervisors at all levels should assure that guidelines to prevent heat injuries are consistently implemented and should be vigilant for early signs of exertional heat injuries, including rhabdomyolysis, among all service members.

The findings of this report should be interpreted with consideration of its limitations. A diagnosis of "rhabdomyolysis" alone does not indicate the cause. Ascertainment of the probable causes of cases of exertional rhabdomyolysis was attempted by using a combination of ICD-9 and ICD-10 diagnostic codes related to rhabdomyolysis with additional codes indicative of the effects of exertion, heat, or dehydration. Furthermore, other codes were used to exclude cases of rhabdomyolysis that were secondary to trauma, intoxication, or adverse drug reactions. Another potential limitation is presented by the shift from ICD-9 to ICD-10 coding that took place in 2015. A hypothetical concern was that the use of the new coding system might affect the completeness and/or accuracy of recording the diagnoses of interest, including exclusionary diagnoses. However, the number of encounters that met the inclusion criteria for exertional rhabdomyolysis was relatively small (119 encounters representing 71 individuals) and permitted a case-by-case review of the diagnostic codes and application of exclusions. Although only 14% of the year's total of diagnoses of hyponatremia were captured with ICD-10 codes, use of these codes was restricted to the late fall and winter when the incidence of diagnoses associated with heat stress would be expected to be much lower than during the warmest months of the year.

The measures that are effective at preventing exertional heat injuries in general apply to the prevention of exertional rhabdomyolysis. In the military training setting, the intensity and duration of exercise and adherence to prescribed work-rest cycles during strenuous physical activities should be adapted not only to ambient weather conditions but also to the fitness levels of participants in strenuous activities. The physical activities of overweight and/or previously sedentary new recruits should increase gradually and be closely monitored. Water intake should comply with current guidelines and be closely supervised. Strenuous activities during relatively cool mornings following days of high heat stress should be particularly closely monitored; in the past, such situations have been associated with increased risk of exertional heat injuries (including rhabdomyolysis).[7] Commanders and supervisors at all levels should be aware of and alert for early signs of exertional heat injuries and should aggressively intervene when dangerous conditions, activities, or suspicious illnesses are detected.

Finally, medical care providers should consider exertional rhabdomyolysis in the differential diagnosis when service members (particularly recruits) present with muscular pain or swelling, limited range of motion, or the excretion of dark urine (possibly due to myoglobinuria) after strenuous physical activity, particularly in hot, humid weather.

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Update: Exertional Hyponatremia, Active Component, U.S. Army, Navy, Air Force, and Marine Corps, 2000–2015

From 2000 through 2015, there were 1,542 incident diagnoses of exertional hyponatremia among active component members of the U.S. Army, Navy, Air Force, and Marine Corps. Annual incidence rates rose sharply from 2008 through 2010 but then decreased by more than 50% from 2010 through 2013. In 2015, the number of cases (n=116) increased by approximately 20% from the previous year. The recent increase in rates overall reflects increased rates in the Army and the Marine Corps. Relative to their respective counterparts, crude incidence rates of exertional hyponatremia for the entire 16-year surveillance period were higher among females, those in the youngest age group, Marines, and recruit trainees. Service members (particularly recruit trainees) and their supervisors must be vigilant for early signs of heat-related illnesses and must be knowledgeable of the dangers of excessive water consumption and the prescribed limits for water intake during prolonged physical activity (e.g., field training exercises, personal fitness training, recreational activities) in hot, humid weather.

Exertional, or exercise-induced, hyponatremia is defined as a low concentration of sodium in the blood (i.e., serum sodium concentration below 135 mEq/L) occurring during or up to 24 hours after prolonged physical activity.[1] This condition can have serious and sometimes fatal clinical effects.[1,2] Risk factors associated with the development of exertional hyponatremia include excessive water consumption, excessive sodium losses in sweat, and inadequate sodium intake during prolonged physical exertion, particularly during heat stress.[2–5]

Acute hyponatremia creates an osmotic imbalance between fluids outside and inside of cells. The osmotic gradient causes water to flow from outside to inside the cells of various organs, including the lungs ("pulmonary edema") and brain ("cerebral edema"). Swelling of the brain increases intracranial pressure, which can decrease cerebral blood flow and disrupt brain function (e.g., hypotonic encephalopathy, seizures, coma). Without rapid and definitive treatment to relieve increasing intracranial pressure, the brain stem can herniate through the base of the skull and can compromise the life-sustaining functions that are controlled by the cardiorespiratory centers of the brain stem.[2–4]

In summer 1997, Army training centers reported five hospitalizations of soldiers for hyponatremia secondary to excessive water consumption during military training in hot weather—one case was fatal and several others required intensive medical care.[6] In April 1998, the U.S. Army Research Institute of Environmental Medicine, Natick, MA, revised the guidelines for fluid replacement during military training in heat. The new guidelines were designed to protect service members from not only heat injury, but also hyponatremia due to excessive water consumption. The guidelines limited fluid intake regardless of heat category or work level to no more than 1½ quarts hourly and 12 quarts daily.[7] There were fewer hospitalizations of soldiers for hyponatremia due to excessive water consumption during the year after compared to before implementation of the new guidelines.[7]

This report uses a surveillance case definition for "exertional hyponatremia" to estimate frequencies, rates, trends, geographic locations, and demographic and military characteristics of exertional hyponatremia cases among active component members of the U.S. Army, Navy, Air Force, or Marine Corps from 2000 through 2015.

METHODS

The surveillance period was 1 January 2000 through 31 December 2015. The surveillance population included all individuals who served in an active component of the U.S. Army, Navy, Air Force, or Marine Corps at any time during the surveillance period. Coast Guard members were not included in this year's annual update because of missing data for 2015. Diagnoses were ascertained from administrative records of medical encounters archived in the Defense Medical Surveillance System (DMSS), which contains electronic records of all actively serving U.S. military members' hospitalizations and ambulatory visits in U.S. military and civilian (contracted/purchased care through the Military Health System) medical facilities worldwide as well as records of medical encounters of service members deployed to Southwest Asia/Middle East (as documented in the Theater Medical Data Store [TMDS]).

For surveillance purposes, a case of exertional hyponatremia was defined as a hospitalization or ambulatory visit with a primary (first-listed) diagnosis of "hyposmolality and/or hyponatremia" (ICD-9: 276.1; ICD-10: E87.1) and no other illness or injury-specific diagnoses (ICD-9: 001–999) in any diagnostic position; or both a diagnosis of "hyposmolality and/or hyponatremia" (ICD-9: 276.1; ICD-10: E87.1) and at least one of the following within the first three diagnostic positions (dx1–dx3): "fluid overload" (ICD-9: 276.6; ICD-10: E87.70, E87.79), "alteration of consciousness" (ICD-9: 780.0x; ICD-10: R40.0, R40.1, R40.2), "convulsions" (ICD-9: 780.39; ICD-10: R56.9), "altered mental status" (ICD-9: 780.97; ICD-10: R41.82), "effects of heat/light" (ICD-9: 992.0–992.9; ICD-10: T67.0–T67.9), or "rhabdomyolysis" (ICD-9: 728.88; ICD-10: M62.82).

Medical encounters were not considered case-defining events if the associated records included diagnoses of alcohol/illicit drug abuse; psychosis, depression, or other major mental disorders; endocrine (e.g., pituitary, adrenal) disorders; kidney diseases; intestinal infectious diseases; cancers; major traumatic injuries; or complications of medical care in any diagnostic position. Because the treatment facilities of the Military Health System transitioned to the use of ICD-10 codes on 1 October 2015, every record of an encounter with a diagnosis of "hyposmolality and/or hyponatremia" (ICD-10: E87.1) during the last quarter of 2015 was individually examined for the presence of exclusionary diagnoses described above. Each individual could be included as a case only once per calendar year.

For surveillance purposes, a "recruit trainee" was defined as an active component member in an enlisted grade (E1–E4) who was assigned to one of the Services' recruit training locations (per the individual's initial military personnel record). For this report, each service member was considered a recruit trainee for the period of time corresponding to the usual length of recruit training in his/her service. Recruit trainees were considered a separate category of enlisted service members in summaries of exertional hyponatremia by military grade overall.

Records of medical evacuations from the U.S. Central Command (CENTCOM) area of responsibility (AOR) (e.g., Iraq, Afghanistan) to a medical treatment facility outside the CENTCOM AOR were analyzed separately. Evacuations were considered case defining if the affected service members met the above criteria in a permanent military medical facility in the U.S. or Europe from 5 days before to 10 days after their evacuation dates.

RESULTS

During 2000–2015, permanent medical facilities reported 1,542 incident diagnoses of exertional hyponatremia among active component members of the U.S. Army, Navy, Air Force, or Marine Corps (incidence rate: 7.0 cases per 100,000 person-years [p-yrs]) **(Table 1)**. In 2015, there were 116 incident diagnoses of exertional hyponatremia (incidence rate: 8.9 per 100,000 p-yrs) among active component members. Incidence rates of exertional hyponatremia peaked in 2010 (12.6 per 100,000 p-yrs) and then declined by more than 50% to 5.3 cases per 100,000 p-yrs in 2013 before increasing in 2014 and 2015 **(Figure 1)**.

In 2015, among the Services, the highest overall incidence rate was in the Marine Corps (20.1 per 100,000 p-yrs), although the Army had the most cases during the year (n=50) **(Table 1)**. During the 16-year surveillance period, the overall crude incidence rate was highest in the Marine Corps (15.1 per 100,000 p-yrs), intermediate in the Army and Air Force (6.8 and 5.7 per 100,000 p-yrs, respectively), and lowest in the Navy (4.1 per 100,000 p-yrs) **(Table 1, Figure 2)**. Incidence rates in the Army and the Marine Corps increased during 2014–2015, but rates in the Navy and Air Force remained relatively stable **(Figure 2)**.

In 2015, 80% of exertional hyponatremia cases (n=93) affected males, but the rate during the year was higher among females (11.5 per 100,000 p-yrs) than males (8.4 per 100,000 p-yrs) **(Table 1)**. Females also had higher overall incidence rates during the entire surveillance period.

TABLE 1. Incident cases and incidence rates of exertional hyponatremia, active component, U.S. Army, Navy, Air Force, and Marine Corps, 2000–2015

	2015		Total 2000–2015	
	No.	Rate[a]	No.	Rate[a]
Total	116	8.9	1,542	7.0
Sex				
Male	93	8.4	1,278	6.8
Female	23	11.5	264	8.2
Age (years)				
<20	17	19.3	218	13.9
20–24	42	10.1	483	6.7
25–29	19	6.2	278	5.6
30–34	14	6.7	166	5.0
35–39	8	5.5	171	6.3
40+	16	12.1	226	9.8
Race/ethnicity				
White, non-Hispanic	77	9.9	1,053	7.7
Black, non-Hispanic	9	4.2	188	4.9
Hispanic	17	10.7	151	6.5
Asian/Pacific Islander	6	10.3	65	7.2
Other/unknown	7	7.7	85	6.4
Service				
Army	50	10.3	558	6.8
Navy	13	4.0	226	4.1
Air Force	16	5.2	309	5.7
Marine Corps	37	20.1	449	15.1
Military status				
Recruit	14	53.4	138	29.9
Enlisted	72	6.9	1,110	6.2
Officer	30	13.0	294	8.1
Military occupation				
Combat-specific	26	14.7	243	8.5
Armor/motor transport	2	4.4	52	5.9
Pilot/air crew	3	6.0	44	5.2
Repair/engineering	21	5.4	279	4.3
Communications/intelligence	19	6.7	264	5.3
Health care	6	5.1	114	6.1
Other	39	16.5	546	13.2
Home of record[b]				
Midwest	21	9.2	256	7.1
Northeast	18	10.9	201	7.7
South	49	9.1	608	7.3
West	21	7.1	250	5.7
Territory	0	0.0	7	7.9
Unknown	7	9.9	220	7.4

[a]Number of cases per 100,000 person-years

[b]Self-reported at time of entry into service

FIGURE 1. Annual incident cases and incidence rates of exertional hyponatremia, active component, U.S. Army, Navy, Air Force, and Marine Corps, 2000–2015

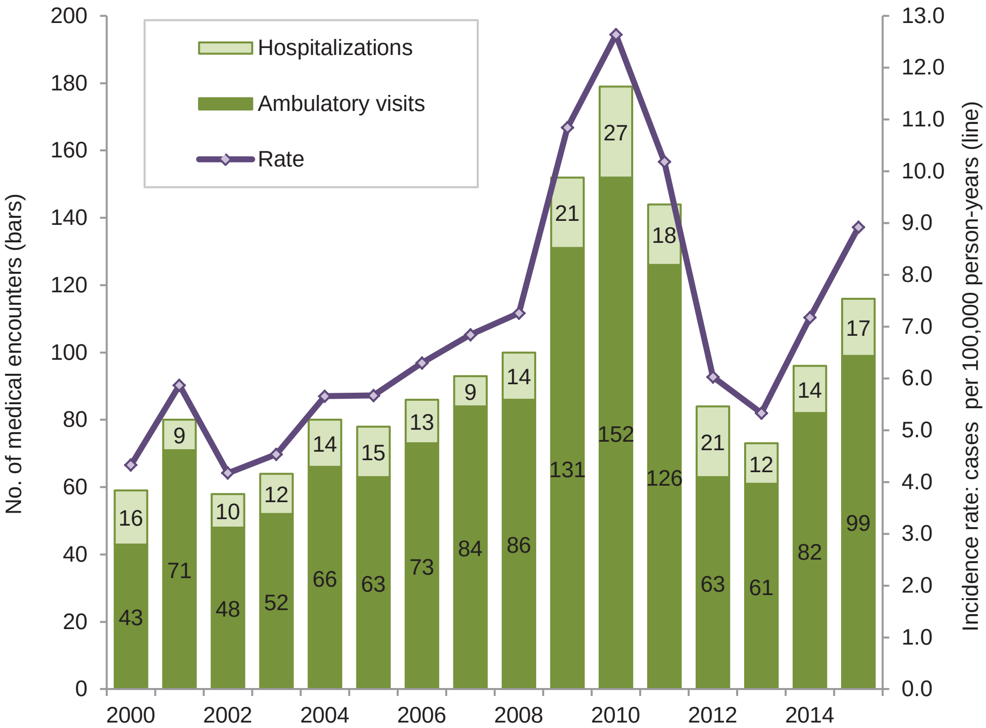
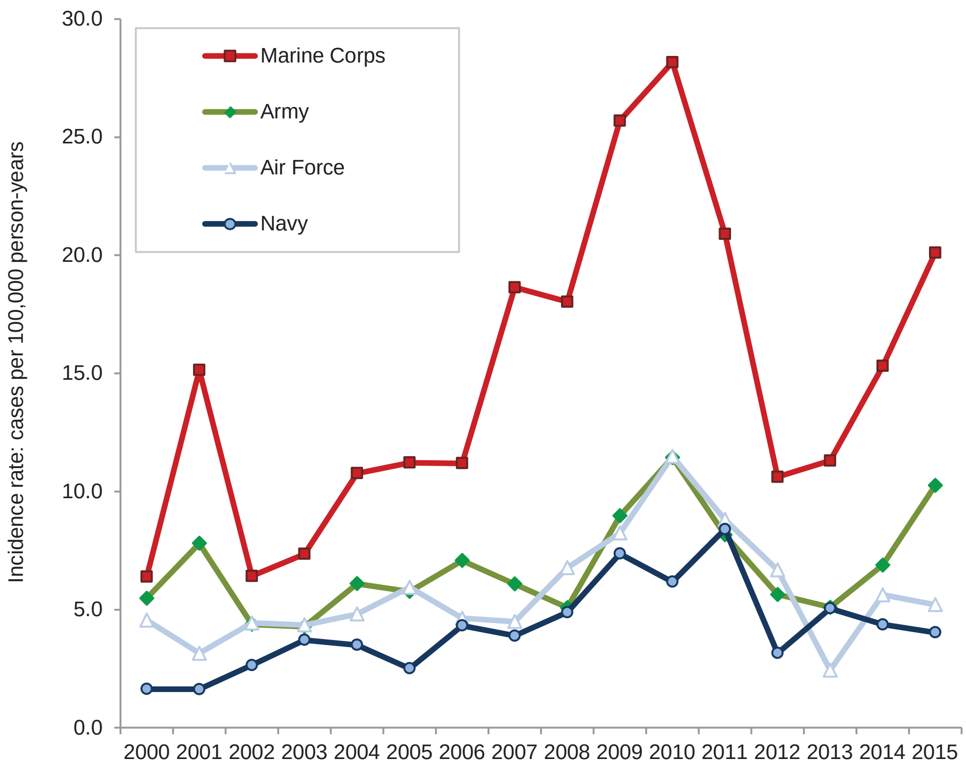


FIGURE 2. Annual incidence rates of exertional hyponatremia by service, active component, U.S. Army, Navy, Air Force, and Marine Corps, 2000–2015



In 2015 and during the surveillance period overall, the highest age group–specific incidence rates affected the youngest (less than 20 years of age) service members **(Table 1)**. Also, overall rates were higher among white, non-Hispanic than other racial/ethnic groups of service members. Rates among recruit trainees in 2015 and overall were more than triple the rates among other enlisted members and officers.

Exertional hyponatremia by location

During the 16-year surveillance period, exertional hyponatremia cases were diagnosed at U.S. military medical facilities at more than 200 locations; however, seven locations contributed 40 or more cases each and accounted for more than one-third of all cases **(Table 2)**. The location with the most cases overall was the Marine Corps Recruit Depot (MCRD) Parris Island/Beaufort, SC (n=216).

Exertional hyponatremia in Iraq and Afghanistan

From 2008 through 2015, a total of 85 cases of exertional hyponatremia were diagnosed and treated in Iraq and Afghanistan. Deployed service members who were affected by exertional hyponatremia were most frequently male (n=58; 68.2%), white, non-Hispanic (n=57; 67.1%), aged 20–24 years (n=30; 35.3%), in the Army (n=45; 52.9%), enlisted (n=69; 81.2%), and in repair/engineering (n=20; 23.5%) or communications/intelligence (n=19; 22.4%) occupations **(data not shown)**. During the entire surveillance period, six service members were medically evacuated from Iraq or Afghanistan for exertional hyponatremia **(data not shown)**.

EDITORIAL COMMENT

This report documents that, after a 3-year period of declining numbers and rates of exertional hyponatremia diagnoses among active component members of the U.S. Army, Navy, Air Force, or Marine Corps, numbers and rates of diagnoses increased slightly in 2014 and continued to increase in 2015.

The results of this report should be interpreted with consideration of several limitations. For example, there is not a diagnostic

TABLE 2. Incident cases of exertional hyponatremia by installation (with at least 25 cases during the period), active component, U.S. Army, Navy, Air Force, and Marine Corps, 2000–2015

Location of diagnosis	No.	%
MCRD Parris Island/ Beaufort, SC	216	14.0
Fort Benning, GA	108	7.0
JBSA-Lackland, TX	56	3.6
MCB Camp Lejeune/ Cherry Pt, NC	51	3.3
Fort Bragg, NC	50	3.2
Walter Reed NMMC, MD[a]	48	3.1
MCB Camp Pendleton, CA	44	2.9
NMC Portsmouth, VA	38	2.5
NMC San Diego, CA	38	2.5
MCB Quantico, VA	37	2.4
Fort Jackson, SC	34	2.2
Fort Leonard Wood, MO	27	1.8
Other locations	795	51.6
Total	1,542	100.0

[a]Walter Reed National Military Medical Center (NMMC) is a consolidation of National Naval Medical Center (Bethesda, MD) and Walter Reed Army Medical Center (Washington, DC). This number represents the sum of the two sites prior to the consolidation (November 2011) and the number reported at the consolidated location.

MCRD, Marine Corps Recruit Depot; JBSA, Joint Base San Antonio; MCB, Marine Corps Base; NMC, Naval Medical Center

code specific for "exertional hyponatremia." Thus, for surveillance purposes, cases of presumed exertional hyponatremia were ascertained from records of medical encounters that included diagnoses of "hyposmolality and/or hyponatremia," but not of other conditions (e.g., metabolic, renal, psychiatric, or iatrogenic disorders) that increase the risk of hyponatremia in the absence of physical exertion or heat stress. As such, the results of this analysis should be considered estimates of the actual incidence of symptomatic exertional hyponatremia from excessive water consumption among U.S. military members. The accuracy of estimated numbers, rates, trends, and correlates of risk depends on the completeness and/or accuracy of diagnoses that are reported on standardized records of relevant medical encounters. As a result, an increase in reporting of diagnoses indicative of exertional hyponatremia may reflect, at least in part, increasing awareness of, concern regarding, and aggressive management of incipient cases by military supervisors and primary healthcare providers. The shift from ICD-9 to ICD-10 coding that occurred during the last quarter of the surveillance period presented another potential limitation. A hypothetical concern was that the use of the new coding system might affect the completeness or accuracy of recording the diagnoses of interest, including exclusionary diagnoses. However, the number of encounters that met the inclusion criteria for exertional hyponatremia was relatively small (26 encounters representing 13 individuals) and permitted a case-by-case review of the diagnostic codes and application of exclusions. Although only 10% of the year's total of diagnoses of hyponatremia were captured with ICD-10 codes, use of those codes was limited to the late fall and winter when the incidence of diagnoses associated with heat stress would be expected to be much lower than during the warmest months of the year.

In the past, concerns about hyponatremia resulting from excessive water consumption were focused at training—particularly recruit training—installations. In this analysis, rates were relatively high among the youngest—hence, the most junior—service members, and the most cases were diagnosed at medical facilities that support large recruit training centers and large Army and Marine Corps combat units (e.g., MCRD Parris Island/Beaufort, SC; Fort Benning, GA; Camp Lejeune/Cherry Point, NC; Fort Bragg, NC). In many circumstances (e.g., recruit training, Ranger School), military trainees rigorously adhere to standardized training schedules—regardless of weather conditions. In hot and humid weather, commanders, supervisors, instructors, and medical support staff must be aware of and enforce guidelines for work-rest cycles and water consumption.

Although there have been no deaths from hyponatremia reported among active duty service members since the late 1990s, other military populations have reported deaths due to exertional hyponatremia. For example, a well-conditioned and heat-adapted 20-year-old soldier in the South African National Defence Force died of exertional hyponatremia during a timed training march in 2014.[8] Service members and their supervisors must be knowledgeable of the dangers of excessive water consumption and the prescribed limits for water intake during prolonged physical activity (e.g., field training exercises, personal fitness training, recreational activities) in hot, humid weather. The current U.S. Military Fluid Replacement Guidelines can be found at: http://hprc-online.org/nutrition/files/current-u-s-military-fluid-replacement.

Women had relatively high rates of hyponatremia during the entire surveillance period; women may be at greater risk because of lower fluid requirements and longer periods of exposure to risk during some training exercises (e.g., land navigation courses, load-bearing marches).[5] Service members (particularly recruit trainees and women) and their supervisors must be vigilant for early signs of heat-related illnesses and intervene immediately and appropriately (but not excessively) in such cases.

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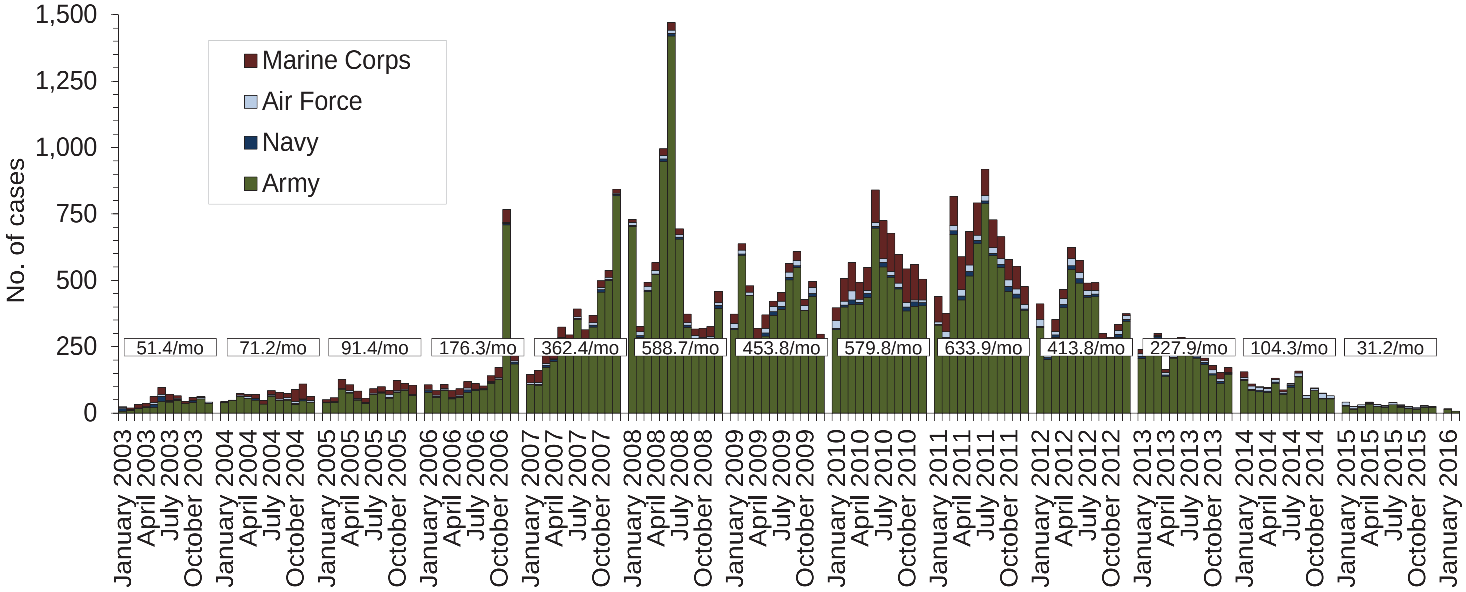
Deployment-related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003–February 2016 (data as of 25 March 2016)

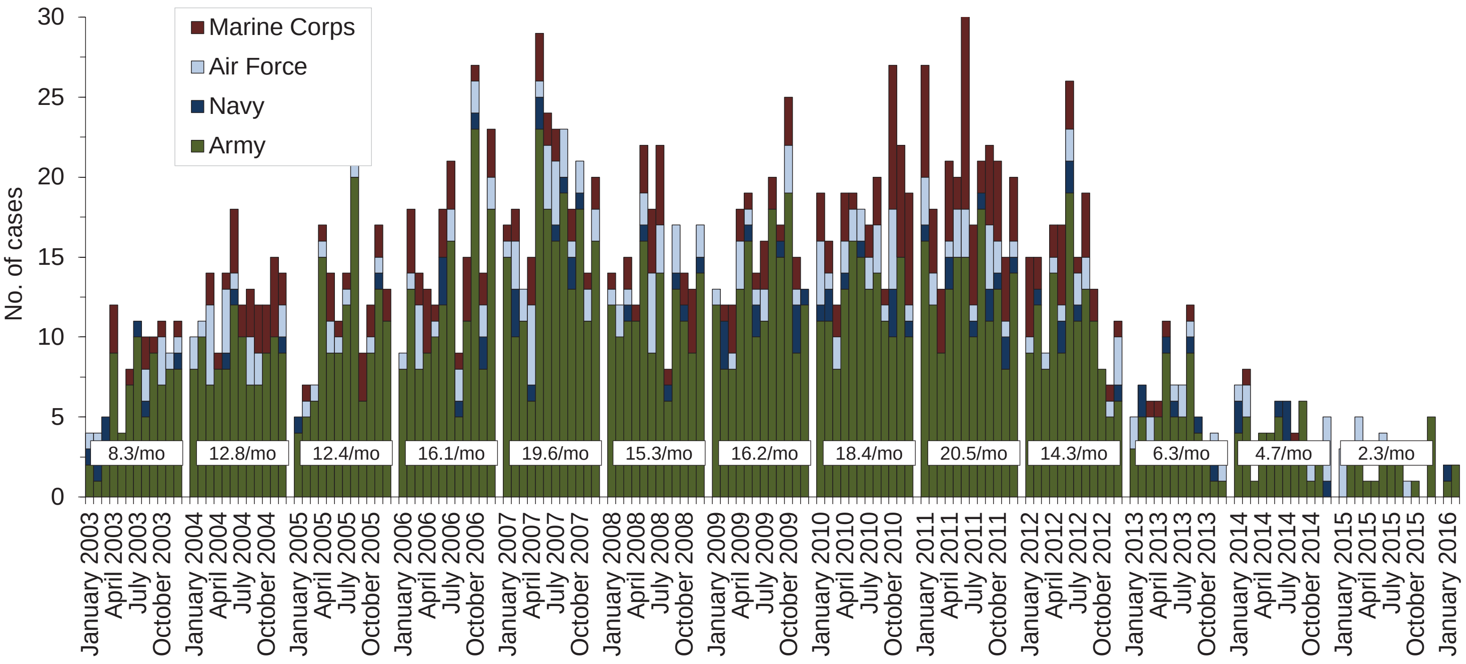
Traumatic brain injury (TBI) (ICD-9: 310.2, 800–801, 803–804, 850–854, 907.0, 950.1–950.3, 959.01, V15.5_1–9, V15.5_A–F, V15.52_0–9, V15.52_A–F, V15.59_1–9, V15.59_A–F)[a]



Reference: Armed Forces Health Surveillance Center. Deriving case counts from medical encounter data: considerations when interpreting health surveillance reports. *MSMR*. 2009;16(12):2–8.

[a]Indicator diagnosis (one per individual) during a hospitalization or ambulatory visit while deployed to/within 30 days of returning from deployment (includes in-theater medical encounters from the Theater Medical Data Store [TMDS] and excludes 4,677 deployers who had at least one TBI-related medical encounter any time prior to deployment).

Deep vein thrombophlebitis/pulmonary embolus (ICD-9: 415.1, 451.1, 451.81, 451.83, 451.89, 453.2, 453.40–453.42, and 453.8)[b]

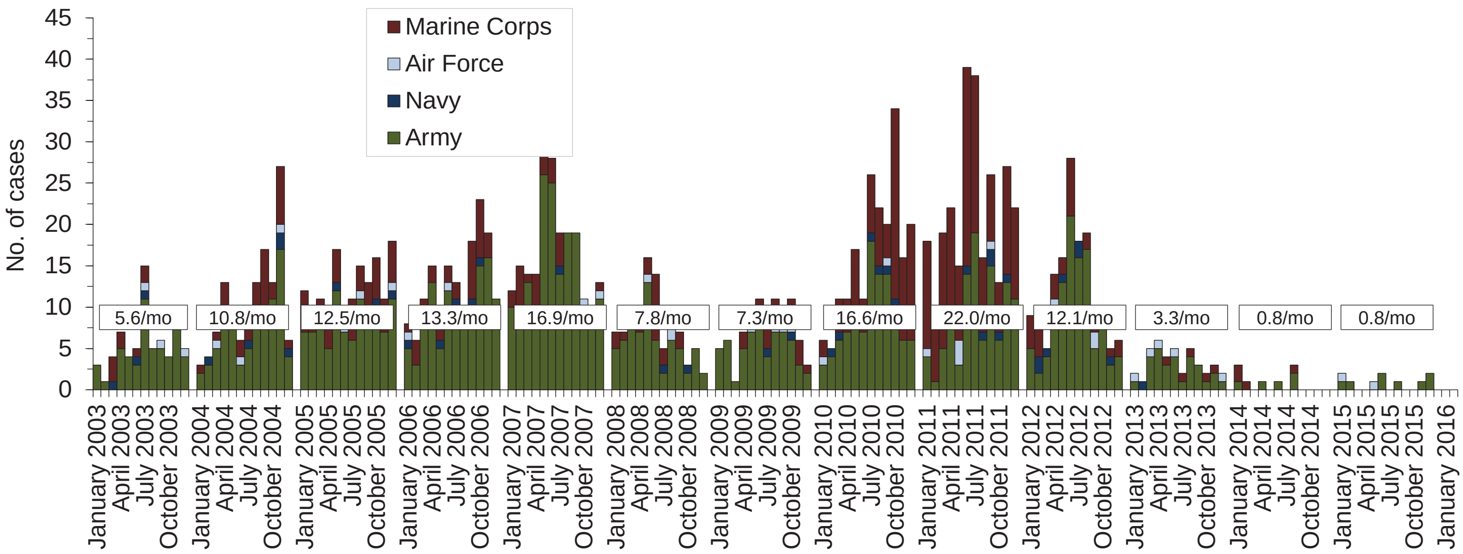


Reference: Isenbarger DW, Atwood JE, Scott PT, et al. Venous thromboembolism among United States soldiers deployed to Southwest Asia. *Thromb Res*. 2006;117(4):379–383.

[b]One diagnosis during a hospitalization or two or more ambulatory visits at least 7 days apart (one case per individual) while deployed to/within 90 days of returning from deployment.

Deployment-related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003–February 2016 (data as of 25 March 2016)

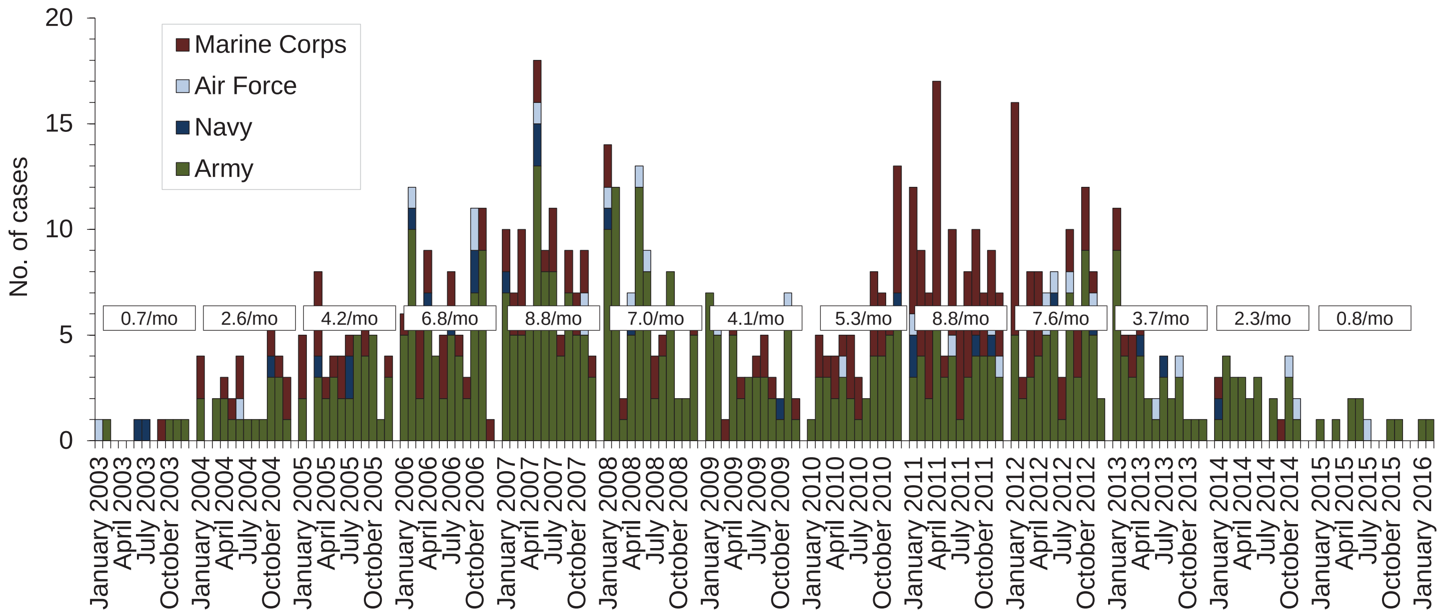
Amputations (ICD-9-CM: 887, 896, 897, V49.6 except V49.61–V49.62, V49.7 except V49.71–V49.72, PR 84.0–PR 84.1, except PR 84.01–PR 84.02 and PR 84.11)[a]



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: amputations. Amputations of lower and upper extremities, U.S. Armed Forces, 1990–2004. *MSMR*. 2005;11(1):2–6.

[a]Indicator diagnosis (one per individual) during a hospitalization while deployed to/within 365 days of returning from deployment

Heterotopic ossification (ICD-9: 728.12, 728.13, 728.19)[b]

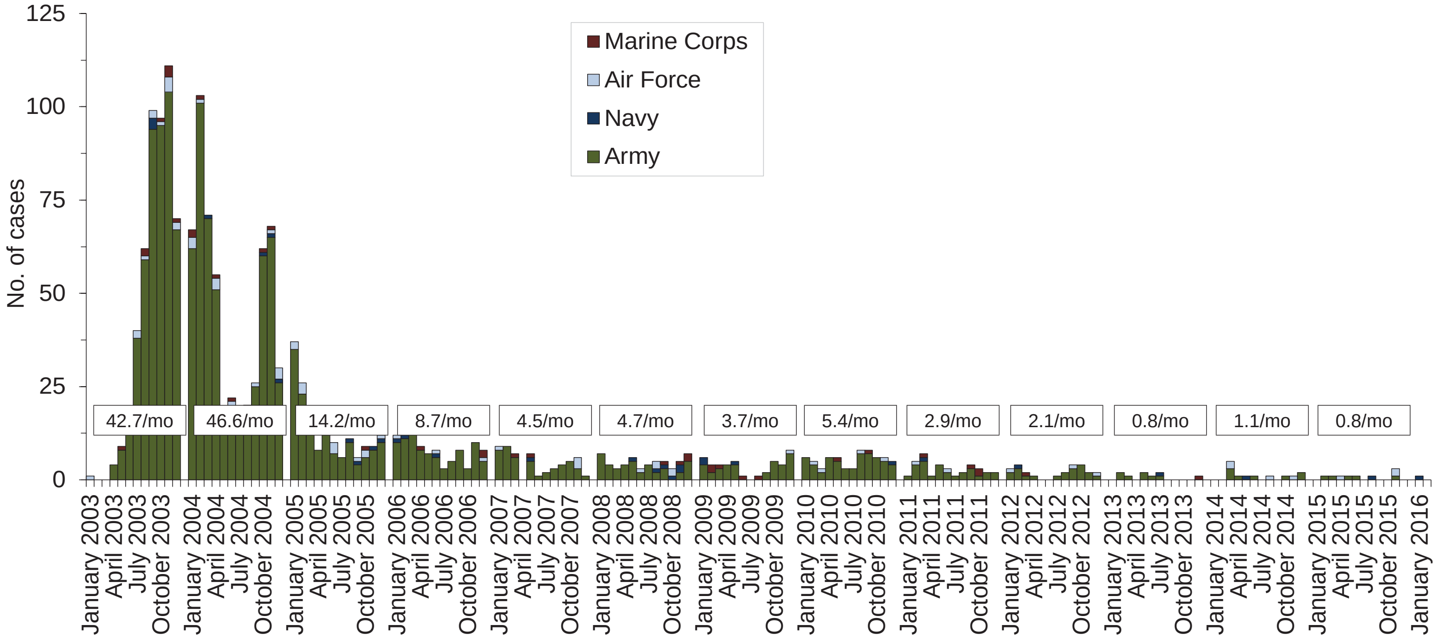


Reference: Army Medical Surveillance Activity. Heterotopic ossification, active components, U.S. Armed Forces, 2002–2007. *MSMR*. 2007;14(5):7–9.

[b]One diagnosis during a hospitalization or two or more ambulatory visits at least 7 days apart (one case per individual) while deployed to/within 365 days of returning from deployment

Deployment-related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003–February 2016 (data as of 25 March 2016)

Leishmaniasis (ICD-9: 085.0–085.9)[b]



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: leishmaniasis. Leishmaniasis among U.S. Armed Forces, January 2003–November 2004. *MSMR*. 2004;10(6):2–4.

[b]Indicator diagnosis (one per individual) during a hospitalization, ambulatory visit, and/or from a notifiable medical event during/after service in OEF/OIF/OND.

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