FEBRUARY 2013

Volume 20
Number 2

MSMR

MEDICAL SURVEILLANCE MONTHLY REPORT

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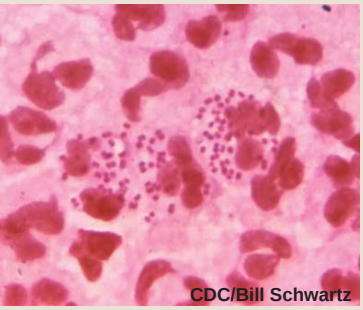
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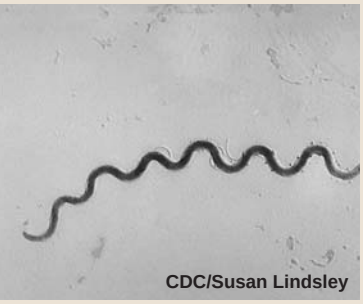
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Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
FEB 2013		**00-00-2013 to 00-00-2013**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Medical Surveillance Monthly Report (MSMR). Volume 20, Number 2. February 2013	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **Armed Forces Health Surveillance Center,11800 Tech Road, Suite 220 (MCAF-CS),Silver Spring,MD,20904**	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**Same as Report (SAR)**	**32**	

Editorial

The Changing Landscape of Controlling Sexually Transmitted Infections in the U.S. Military

Joel C. Gaydos, MD, MPH (COL, USA, Ret.); Kelly T. McKee, Jr., MD, MPH (COL, USA, Ret.); Charlotte A. Gaydos, MS, MPH, DrPH

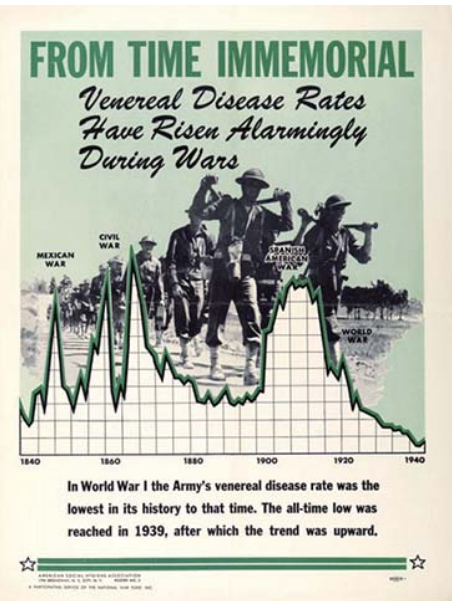
Evolving personnel policies, advancing medical research, innovations in laboratory science, a new vaccine, and the capacity of microorganisms to adapt to their human hosts' defenses have changed the clinical and public health practice of venereology in the U.S. military over the last 25 years. Since the end of World War II, many barriers that prevented women from training in military schools and performing military jobs have been removed, and the numbers of women in the U.S. Armed Forces have increased substantially.[1] In 2012, the 214,098 women in uniform constituted 14.6 percent of the active duty U.S. military, with even higher percentages in the Reserves (19.5%) and the National Guard (15.5%).[2]

As the uniformed services adjusted to the increases in women in the 1990s, medical researchers recognized that the traditional focus on the sexually transmitted diseases (STDs) syphilis and gonorrhea had to be broadened to include *Chlamydia trachomatis* (CT) and human papillomavirus (HPV) infections, both of which were highly prevalent and often caused serious sequelae.[3-9] The need to identify these mostly silent infections and to intervene to prevent complications like pelvic inflammatory disease (PID), chronic pelvic pain, ectopic pregnancies, infertility, and cervical cancer prompted a shift in terminology from "STDs" to sexually transmitted infections (STIs).[9-10]

Fortunately, rapid advances in medical laboratory technology led to the availability of molecular amplification tests that greatly improved sensitivity for detecting STI agents and offered practitioners a wide selection of sample types, to include urine, cervical swabs, vaginal swabs and penile swabs.[11] These tests were extremely useful in conventional clinical settings, but proved especially valuable as an efficient and economical way to identify people with silent CT infections through population-based screening in sexually active populations.[12-14] Since the serious sequelae occurred in women and the presumption prevailed that infected men would tend to be symptomatic, initial emphasis was placed on screening asymptomatic women.[4,15,16] In order to implement population-based screening of service members, military public health practitioners had to confront the problems of securing funding and identifying locations where screening could be efficiently and economically conducted with minimal disruption of critical military activities.

Over time, with the focus on screening women, the Navy, Air Force, Marine Corps and Coast Guard adopted the recommendation of the now defunct Armed Forces Epidemiological Board and initiated mass screening at basic training sites as part of their trainee health care programs.[17] The Army chose not to conduct a population-based program to inform, test and treat soldiers during basic training. Rather, the Army opted to initiate screening of new female members sometime in their first year of service after basic and advanced training had occurred. This policy was associated with higher rates of PID in the Army, compared to the Navy, and the identification of large numbers of women soldiers infected with CT soon after reporting for duty in Korea, a critical overseas location.[18,19] Recently, the Army designated advanced training sites as the locations for initially screening military women for CT.

In 2006 the U.S. Food and Drug Administration (FDA) licensed a human papillomavirus quadrivalent vaccine (HPV4) to protect against HPV strains 6, 11, 16 and 18, which are responsible for 70 percent of cervical cancers and 80 percent of genital warts.[20] Uptake of the HPV vaccine has been less than hoped for, not only in the civilian community but also in the military community, where the vaccine is not required but is offered without charge.[20] Several researchers, including some in the U.S. military, have found that the early impact of the quadrivalent HPV vaccine in preventing genital warts has been very encouraging, suggesting that the vaccine should be given to those needing



it as early as possible in service members' military careers.[20]

Determining the opportune times and places to test for CT and to administer the six-month, 3-dose HPV vaccine series are challenges that can be overcome with timely epidemiologic data and sound administrative policies. Surveillance for CT infections and for PID and other sequelae are ongoing and should inform military public health practitioners on the effectiveness of the service screening programs. Serological studies to assess HPV immunity in new military members and in those who have not completed the full HPV vaccine regimen are underway. Additionally, the occurrence of genital warts in military members will be monitored to assess vaccine effectiveness.

Two recent developments, one much more daunting than the other, require immediate attention. These are the repeal of the "Don't Ask, Don't Tell" policy (DADT)[21] and the declining susceptibility of *Neisseria gonorrhoeae* to existing antibiotics, in conjunction with a paucity of new antimicrobials on the horizon.[22-23]

The DADT policy, in place from 1993 to 2011, allowed gay men, lesbians and bisexuals to remain in the military services as long as they kept their sexual orientation secret. Concerns about revealing their secrets may have caused some service members to seek medical care outside the Military Health System (MHS).[24] With the repeal of DADT, these service members can now use the MHS without fear of discovery. The challenge to the MHS is to ensure that clinical providers and public health workers have the skills to address the needs of gays, lesbians and bisexuals. Useful information for health professionals can be found on the website of the U.S. Navy Sexual Health and Responsibility Program (SHARP).[25] Additionally, military infectious diseases and preventive medicine specialists have engaged the Centers for Disease Control and Prevention, Atlanta, GA, and the New England Sylvie Ratelle STD/HIV Prevention Training Center (http://www.ratelleptc.org/) to provide web-based continuing medical education sessions for military medical personnel as early as spring of this year. These sessions will cover STI diagnosis, treatment and control for all Department of Defense (DoD) beneficiaries.

Most concerning is the progressive acquisition of resistance to available antimicrobial agents by *N. gonorrhoeae*.[22,23,26] *N. gonorrhoeae* isolates resistant to the cephalosporins, the last remaining class of effective antimicrobials and the only antibiotics recommended for gonorrhea treatment, have been reported in Asia and Europe and, most recently, in North America.[22,23] New antibiotics are urgently needed but few are in the pipeline leading to FDA licensure.

The DoD must join with civilian public health agencies in aggressively promoting awareness, bolstering surveillance and laboratory capabilities, and ensuring that appropriate treatment regimens are universally applied. DoD surveillance systems must contribute useful and timely data and information on STIs among DoD health care beneficiaries. Additionally, U.S. military public health workers must collaborate with health care workers of host nation countries where U.S. forces are stationed to develop robust laboratory and surveillance systems.

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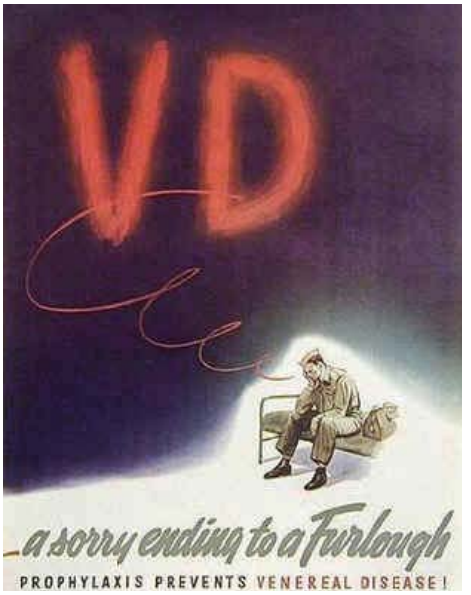

The views expressed are those of the authors and should not be construed to be the official positions of their affiliated organizations.

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Sexually Transmitted Infections, Active Component, U.S. Armed Forces, 2000-2012

This report summarizes incidence rates of the five most commonly diagnosed sexually transmitted infections (STIs) among active component service members of the U.S. Armed Forces during 2000 to 2012. Human papillomavirus (HPV) infections were the most common, followed in decreasing order of frequency by infections associated with chlamydia, herpes simplex virus, gonorrhea, and syphilis. Compared to their counterparts, women, younger service members, soldiers, and enlisted members had higher incidence rates of each STI. Rates tended to be lower among married personnel. Rates of chlamydia, HPV, and gonorrhea diagnoses were notably higher among women during 2006 to 2008 but rates of the latter two infections have since declined sharply. The relatively recent introduction of STI screening among young service women and the HPV vaccine are discussed.

Of the 63 infectious diseases of public health or operational importance that the Department of Defense requires health officials to report for surveillance purposes, the three most common are sexually transmitted infections (STIs) caused by bacteria.[1] These are STIs due to *Chlamydia trachomatis, Neisseria gonorhoeae,* and *Treponema pallidum*, the respective causative agents of chlamydial genital infections, gonorrhea, and syphilis. Two other, common, non-reportable STIs have viral etiologies: infections with human papillomavirus (HPV) and genital herpes simplex virus (HSV).

Sexually transmitted infections have historically been of concern to the U.S. Armed Forces because of their relatively high incidence, adverse impact on service members' availability and ability to perform their duties, and potential for serious medical sequelae if untreated. In the pre-antibiotic era, there were no satisfactory treatments for the three bacterial infections. The viral infections are not curable with antibiotics; however, suppression of recurrent herpes manifestations is attainable, and there is a vaccine to prevent infection with four of the most common HPV serotypes **(Table 1)**.

This article summarizes incident cases and incidence rates of these five STIs among active component military members during the years 2000 to 2012.

METHODS

The surveillance period was the 13-year interval from 1 January 2000 through 31 December 2012. The surveillance population consisted of all active component service members who served at any time during the period. Diagnoses of STIs were derived from medical administrative data and reports of notifiable medical events routinely provided to the Armed Forces Health Surveillance Center (AFHSC) and maintained in the Defense Medical Surveillance System (DMSS) for surveillance purposes. For each service member, the number of days in active military service was ascertained and then aggregated into a total for all service members in each calendar year and expressed as person-years of service. Person-years were then used as the denominators for the calculation of incidence rates.

For surveillance purposes, an incident case of chlamydia or gonorrhea was defined by case-defining diagnostic codes **(Table 2)** in either the first or second diagnostic position of a record of an outpatient

TABLE 1. Summary of characteristics of sexually transmitted infections (STIs) described in this report

Name of STI	Rank order of incidence in SMs	Type of causative microbe	Infection curable with antibiotics	Suppressive antivirals useful	Examples of major complications	Vaccine available
Human papillomavirus (HPV)	1	Virus	No	No	Cancer of cervix, penis, anus, throat; genital warts	Yes
Chlamydia	2	Bacterium	Yes	.	PID, ectopic pregancy, infertility	No
Genital herpes simplex virus (HSV)	3	Virus	No	Yes	Genital sores, infection of newborn babies	No
Acute gonorrhea	4	Bacterium	Yes	.	PID, ectopic pregancy, infertility, joint and blood infection	No
Syphilis	5	Bacterium	Yes	.	Damage to brain, blood vessels, bones, joints	No

SM = Service members
PID = Pelvic inflammatory disease

encounter or in a notifiable disease report. Codes for chronic gonorrhea infections were excluded. An individual could be counted as having a second (or subsequent) case only if there were more than 30 days between the dates of encounters in which the diagnoses were recorded.

Incident cases of HSV and HPV were defined by the presence of the requisite ICD-9 codes in either the first or second diagnostic position of a record of an outpatient encounter; an individual could be an incident case of HSV or HPV only once during the surveillance period. Individuals who had diagnoses of HSV or HPV infections prior to the surveillance period were excluded from the analysis as were their associated person-times in the calculations of incidence rates for these diagnoses.

An incident case of syphilis was defined by the presence of the requisite ICD-9 code in either the first or second diagnostic positions of a record of an outpatient encounter, or in one of the first three diagnostic positions of a record of hospitalization, or by a notifiable disease report. An individual could be counted as having a second (or subsequent) case only if there were more than 365 days between the dates of the encounters in which the diagnoses were recorded. Individuals with syphilis diagnoses prior to the surveillance period were excluded. Incidence of syphilis by four different types (congenital, primary and secondary, latent, and late syphilis) was also analyzed. An individual with a diagnosis of one type could not be counted in the other types; priority was given in the order indicated in parentheses above.

TABLE 2. International Classification of Diseases, 9th Revision (ICD-9-CM) codes used to identify cases of STI in electronic health care records

Name of STI	ICD-9-CM codes
Human papillomavirus (HPV)	078.1, 079.4, 795.05, 795.09, 795.15, 796.75, 796.79
Chlamydia	099.41, 099.5
Genital herpes simplex virus (HSV)	054.1
Acute gonorrhea	098.0x, 098.1x, 098.4x, 098.8x
Syphilis, all types	All of those below
Congenital syphilis	090.x
Primary and secondary syphilis	091.x
Latent syphilis	092.x
Late syphilis	093.x, 094.x, 095.x, 096.x, 097.x

FIGURE 1. Incidence rates of human papillomavirus infections, by gender, active component, 2000-2012

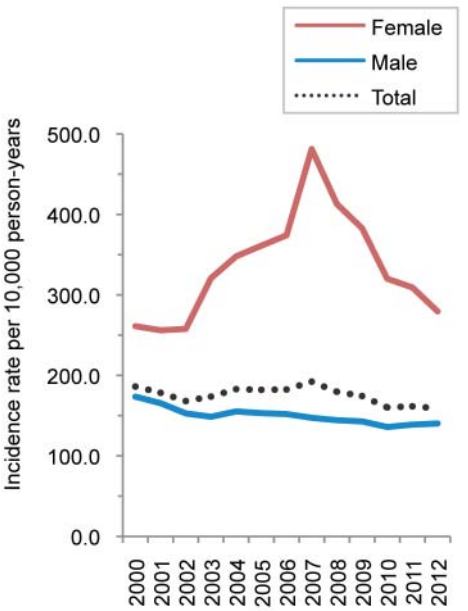
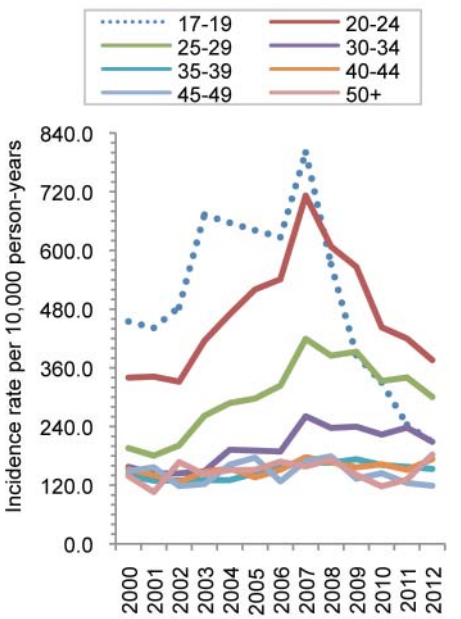


FIGURE 2. Incidence rates of human papillomavirus infections among females, by age group, active component, 2000-2012



RESULTS

During the surveillance period, the number of incident diagnoses of HPV infection in active component service members was greater than any other single STI and 53 percent higher than the total number of diagnoses of chlamydia, the next most frequently diagnosed STI **(Table 3)**. Although the number of incident diagnoses of each STI was greater in men than women, the incidence rates for each STI were markedly higher among women than men. Except for HSV, incidence rates of STIs were highest among the two youngest age groups and declined with increasing age. The rate of HPV infections was lower, but the rates of all other STIs were higher, among black, non-Hispanic than any other racial-ethnic group members. Among members of specified racial-ethnic groups, the HPV infection rates of white, non-Hispanic members were highest. Among service members with known homes of record, STI rates were highest among those from the Southern region of the United States except for HPV infection, for which rates were slightly higher for the Western and Midwestern regions. For most of the STIs, rates tended to be highest among members of the Army, enlisted service members, and those with lower levels of educational achievement. HPV incidence rates again showed a different pattern. By Service, the highest rate of HPV diagnoses was among members of the Coast Guard, and the differences in rates by educational level and rank were slight. For those with known marital status, the clearest difference was that married service members had the lowest incidence rates for all five STIs **(Table 3)**. Results by each STI are described below.

Human papillomavirus infections

The incidence rate of diagnoses of HPV among all active component service

TABLE 3. Incident cases and incidence rates of sexually transmitted infections among active component service members, 2000-2012

	Human papillomavirus		Chlamydia		Genital herpes simplex virus		Gonorrhea		Syphilis (all types)	
	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
Total (2000-2012)	304,021	175.5	198,274	107.3	41,108	22.4	41,713	22.6	5,764	3.1
Service										
Army	102,590	163.0	98,467	148.0	16,203	24.6	24,447	36.8	2,756	4.1
Navy	69,812	164.5	29,665	65.7	9,387	21.0	6,890	15.3	1,416	3.1
Air Force	85,622	212.4	53,464	121.8	10,663	24.5	6,270	14.3	996	2.3
Marine Corps	35,603	155.5	15,601	64.9	3,766	15.7	3,787	15.7	468	1.9
Coast Guard	10,394	221.9	1,077	21.0	1,089	21.4	319	6.2	128	2.5
Sex										
Male	224,040	150.1	110,812	70.2	23,212	14.8	30,310	19.2	4,660	3.0
Female	79,981	333.9	87,462	326.6	17,896	68.5	11,403	42.6	1,104	4.1
Age group										
17-19	30,292	230.9	31,017	232.9	3,421	25.7	5,742	43.1	486	3.6
20-24	130,987	226.0	112,037	183.6	16,569	27.3	22,149	36.3	2,125	3.5
25-29	66,766	178.5	37,126	91.1	9,970	24.7	8,492	20.8	1,308	3.2
30-34	31,485	126.1	11,475	42.3	5,190	19.4	3,052	11.3	724	2.7
35-39	23,265	107.5	4,671	20.2	3,492	15.3	1,528	6.6	613	2.7
40-44	13,770	112.2	1,593	12.1	1,800	13.8	590	4.5	343	2.6
45-49	5,381	122.1	302	6.4	519	11.1	134	2.8	117	2.5
50+	2,075	141.6	53	3.4	147	9.4	26	1.7	48	3.1
Race/ethnicity										
American Indian/Alaskan Native	1,524	73.3	1,870	83.9	206	9.3	246	11.0	34	1.5
Asian/Pacific Islander	9,976	146.7	6,429	89.1	887	12.4	851	11.8	161	2.2
Black, non-Hispanic	40,040	132.8	77,718	244.9	12,070	38.6	25,238	79.5	2,342	7.4
Hispanic	31,211	175.3	22,448	118.3	4,367	23.2	3,413	18.0	661	3.5
Other	8,988	244.5	5,321	136.0	1,047	26.9	652	16.7	139	3.6
White, non-Hispanic	203,896	188.4	79,835	68.9	21,411	18.6	10,350	8.9	2,238	1.9
Unknown	8,386	187.3	4,653	96.8	1,120	23.5	963	20.0	189	3.9
Home of record										
Midwest	49,439	179.4	27,332	93.0	6,058	20.8	5,154	17.5	806	2.7
Northeast	33,891	165.3	21,048	96.6	4,642	21.5	4,639	21.3	645	3.0
South	107,863	169.0	90,957	133.9	16,859	25.1	22,865	33.7	2,677	3.9
West	59,620	180.0	32,290	91.3	6,948	19.8	4,965	14.0	832	2.4
Territory	1,917	142.8	1,393	98.3	311	22.1	251	17.7	59	4.2
Unknown	51,291	190.6	25,254	87.5	6,290	22.0	3,839	13.3	745	2.6
Rank										
Enlisted	256,616	176.6	192,511	124.6	36,468	23.8	40,600	26.3	5,322	3.4
Officers	47,405	169.8	5,763	19.1	4,640	15.5	1,113	3.7	442	1.5
Educational level										
No high school	1,851	160.7	1,314	108.6	242	20.1	375	31.0	75	6.2
High school	217,990	178.3	174,556	134.6	30,508	23.7	36,623	28.2	4,464	3.4
Some college	24,372	162.5	10,587	65.0	3,855	24.0	2,229	13.7	464	2.8
College	49,602	168.3	7,636	23.9	5,310	16.8	1,426	4.5	592	1.9
Unknown	10,206	190.2	4,181	74.2	1,193	21.3	1,060	18.8	169	3.0
Marital status										
Single	155,512	213.5	126,931	166.0	20,207	26.6	26,796	35.0	3,103	4.1
Married	134,319	143.5	59,690	59.3	17,334	17.4	12,888	12.8	2,359	2.3
Other	13,665	207.0	11,324	154.0	3,505	48.8	1,956	26.6	296	4.0
Unknown	525	264.3	329	160.2	62	30.4	73	35.6	6	2.9

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

members reached 159.1 cases per 10,000 person-years (p-yrs) in 2012, the lowest rate of the entire surveillance period. Incidence rates among male service members slowly declined during the surveillance period, from a high of 173.6 cases per 10,000 p-yrs in 2000 to a low of 135.9 cases per 10,000 p-yrs in 2010 **(Figure 1)**. Rates among women steadily rose to a peak of 481.2 per 10,000 p-yrs in 2007 but sharply declined thereafter by 42 percent to a rate of 279.5 per 10,000 p-yrs in 2012. Most of the recent fall in women's rates was associated with dramatic declines in the rates for women in the youngest age groups after they peaked in 2007 **(Figure 2)**.

Chlamydia trachomatis infections

During the surveillance period, rates of diagnosis of *Chlamydia trachomatis*

infection among service women generally ranged between four to five times those among men. Annual rates among men were relatively stable, but the rates among women widely fluctuated. Women's rates peaked in 2008 (406.7 per 10,000 p-yrs) but fell by 18 percent to 332.6 per 10,000 p-yrs in 2012 **(Figure 3)**. Most of the variations in rates among women were attributable to fluctuations within the two youngest age groups **(Figure 4)**.

Genital herpes simplex infections

Incidence rates of genital herpes infections were relatively stable during the surveillance period. Rates among female service members ranged from a high of 79.6 per 10,000 p-yrs in 2001 to 62.8 per 10,000 p-yrs in 2010. Men's rates were highest in 2004 (15.6 per 10,000 p-yrs) and lowest in 2000 (12.4 per 10,000 p-yrs) **(Figure 5)**. Among women, rates were consistently highest among the youngest aged (17-19 years) women and progressively declined with increasing age. Male service members' rates, however, were highest in those aged 25-29, followed closely by age groups 20-24 and then 30-34. The rates among the youngest males (ages 17-19) were lower than among all other age groups except for service men 45 and older **(data not shown)**. Incidence rates of diagnoses of genital herpes among service members with marital status of "other" were markedly higher than among those who were categorized as "single" and "married" **(Figure 6)**.

Acute gonorrhea infections

During the surveillance period annual incidence rates of gonorrhea for all service members were relatively stable, ranging from 28.4 per 10,000 p-yrs in 2001 to 19.1 per 10,000 p-yrs in 2011. Annual rates among women were consistently two to

FIGURE 3. Incidence rates of *Chlamydia trachomatis* infections, by gender, active component, 2000-2012

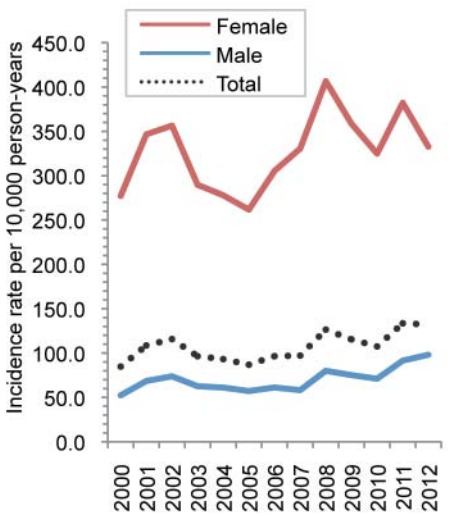


FIGURE 4. Incidence rates of *Chlamydia trachomatis* infections among females, by age group, active component, 2000-2012

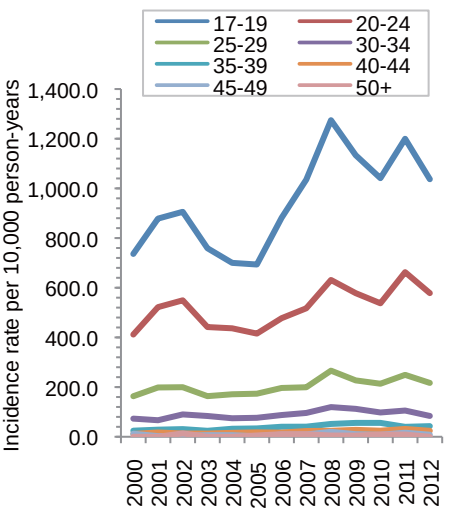


FIGURE 5. Incidence rates of genital herpes simplex virus infections, by gender, active component, 2000-2012

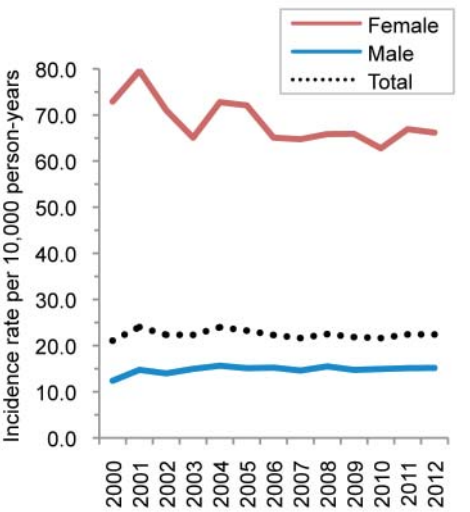


FIGURE 6. Incidence rates of genital herpes simplex virus infections, by marital status, active component, 2000-2012

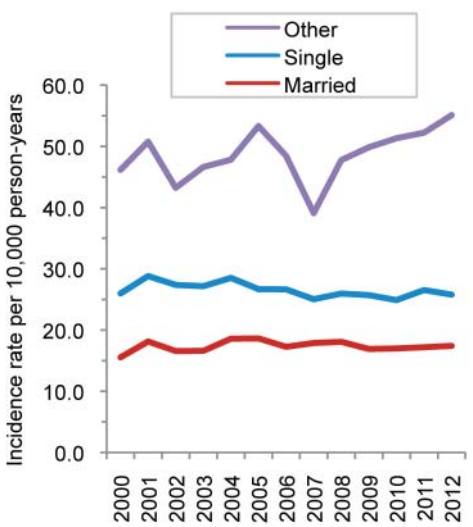


FIGURE 7. Incidence rates of acute gonorrhea infections, by gender, active component, 2000-2012

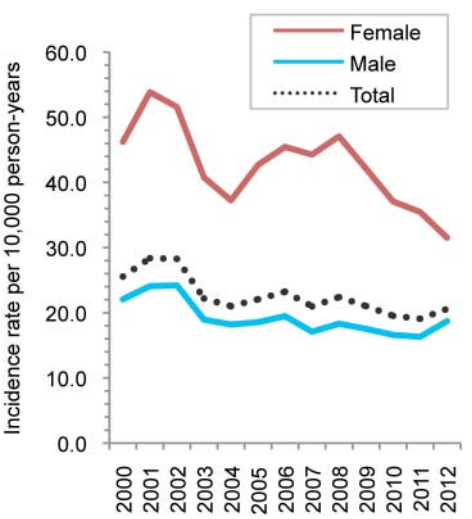
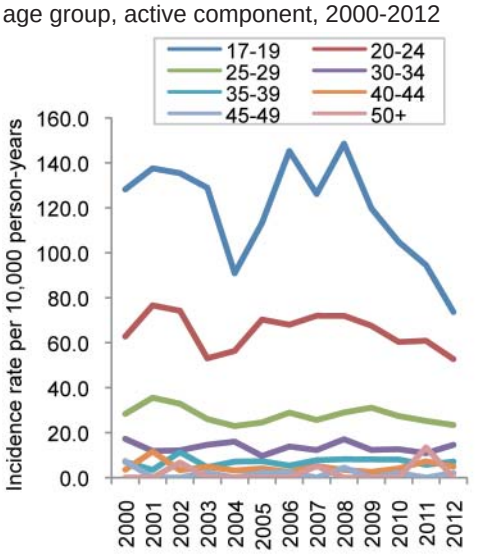


FIGURE 8. Incidence rates of acute gonorrhea infections among females, by age group, active component, 2000-2012



three times those among men except for 2012 when the ratio fell to 1.7 as the total rate for women reached the lowest level of the entire surveillance period **(Figure 7)**. The dramatic swings in annual rates among women were associated mainly with fluctuations in rates among the youngest age groups of women. Rates in 17-19 year old service women were sharply higher in the period 2006 to 2008, but declined dramatically since then to the lowest rate of the entire surveillance period in 2012 (73.7 per 10,000 p-yrs) **(Figure 8)**.

Syphilis

Total incidence rates for syphilis in the first two years of the surveillance period were almost double those of the rest of the period **(Figure 9)**. After 2001, overall annual rates of syphilis were relatively stable and averaged about 2.7 cases per 10,000 p-yrs. Annual incidence rates among women slowly declined and fell below those of men for the first time in 2010. The expanded analysis of syphilis incidence among the four different types found the following numbers of cases and total rates during the surveillance period: congenital (175 cases, rate 0.09 per 10,000 p-yrs), primary and secondary (2,563 cases, rate 1.39 per 10,000 p-yrs), latent (146 cases, rate 0.08 per 10,000 p-yrs), and late syphilis (2,733 cases, rate 1.48 per 10,000 p-yrs) **(Table 4)**. Of all cases of syphilis, 45.6 percent of diagnoses were for primary and

FIGURE 9. Incidence rates of syphilis (all types) by gender, active component, 2000-2012

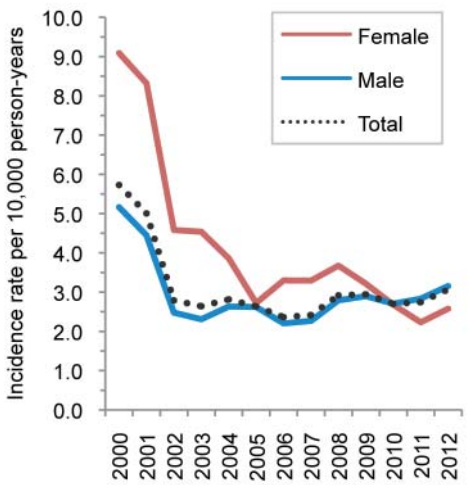


TABLE 4. Incident cases and incidence rates of four types of syphilis among active component service members, 2000-2012

	Congenital syphilis		Primary and secondary syphilis		Latent syphilis		Late syphilis	
	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
Total (2000-2012)	175	0.09	2,563	1.39	146	0.08	2,733	1.48
Service								
Army	42	0.06	1,091	1.64	68	0.10	1,480	2.22
Navy	48	0.11	663	1.47	50	0.11	608	1.35
Air Force	51	0.12	508	1.16	18	0.04	401	0.91
Marine Corps	26	0.11	232	0.96	5	0.02	197	0.82
Coast Guard	8	0.16	69	1.35	5	0.10	47	0.92
Sex								
Male	143	0.09	2,091	1.32	125	0.08	2,170	1.37
Female	32	0.12	472	1.76	21	0.08	563	2.10
Age group								
17-19	11	0.08	235	1.76	9	0.07	225	1.69
20-24	74	0.12	970	1.59	55	0.09	1,007	1.65
25-29	35	0.09	593	1.46	36	0.09	598	1.47
30-34	13	0.05	336	1.24	20	0.07	319	1.18
35-39	23	0.10	259	1.12	13	0.06	297	1.28
40-44	12	0.09	130	0.99	8	0.06	181	1.38
45-49	7	0.15	35	0.74	4	0.08	66	1.40
50+	.	.	5	0.32	1	0.06	40	2.54
Race/ethnicity								
American Indian/ Alaskan Native	2	0.09	18	0.81	.	.	15	0.67
Asian/Pacific Islander	4	0.06	77	1.07	2	0.03	73	1.01
Black, non-Hispanic	44	0.14	1,077	3.39	59	0.19	1,073	3.38
Hispanic	16	0.08	273	1.44	17	0.09	342	1.80
Other	6	0.15	59	1.51	2	0.05	63	1.61
White, non-Hispanic	94	0.08	976	0.84	61	0.05	1,080	0.93
Unknown	9	0.19	83	1.73	5	0.10	87	1.81
Home of record								
Midwest	30	0.10	315	1.07	20	0.07	424	1.44
Northeast	18	0.08	277	1.27	18	0.08	320	1.47
South	70	0.10	1,202	1.77	76	0.11	1,246	1.83
West	20	0.06	392	1.11	20	0.06	376	1.06
Territory	.	.	24	1.69	.	.	35	2.47
Unknown	37	0.13	353	1.22	12	0.04	332	1.15
Rank								
Enlisted	160	0.10	2,359	1.53	137	0.09	2,527	1.64
Officers	15	0.05	204	0.67	9	0.03	206	0.68
Educational level								
No HighSchool	1	0.08	53	4.38	.	.	20	1.65
High School	130	0.10	1,974	1.52	125	0.10	2,121	1.64
Some College	19	0.12	204	1.25	7	0.04	224	1.37
College	21	0.07	260	0.81	12	0.04	280	0.88
Unknown	4	0.07	72	1.28	2	0.04	88	1.56
Marital status								
Single	77	0.10	1,477	1.93	93	0.12	1,368	1.79
Married	80	0.08	955	0.95	46	0.05	1,231	1.22
Other	18	0.24	129	1.75	7	0.10	130	1.77
Unknown	.	.	2	0.97	.	.	4	1.95

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

secondary (early) syphilis and 48.7 percent were for late syphilis, for a total of 94 percent. Rates of early syphilis were highest in the youngest age group and declined with advancing age. Rates of late syphilis diagnoses were highest in those aged 50 and over, but were lowest in those in the age groups encompassing ages 30-49 **(Table 4)**.

EDITORIAL COMMENT

During most of the 13-year surveillance period the incidence rates of the five STIs examined were relatively stable among male service members. Among female service members the incidence rates were stable for HSV, but the rates of infection with HPV, chlamydia, gonorrhea, and syphilis fluctuated considerably. Notably, HPV, gonorrhea, and syphilis rates among women trended steadily downward after 2008.

The peaking of incidence rates for HPV, chlamydia, and gonorrhea in the interval 2006 to 2008 was largely attributable to dramatic increases in rates among service women in the youngest age groups. It is likely that the implementation of the Services' screening programs for STIs among female service members as they entered active service and the subsequent annual screenings for women under age 26 played a major role in the detection of these three STIs. Because asymptomatic (silent) infection with HPV, chlamydia, and gonorrhea is common among sexually active women, the introduction of widespread screening would result in a surge in the numbers of infections diagnosed among young women. For chlamydia and gonorrhea, the early detection and curative treatment of these infections would likely, over time, contribute to a decline in incidence rates of these diagnoses as the prevalence of untreated infection in the population of young service women was driven downward.

In the case of HPV infection, because there is no treatment to eradicate the virus, it is plausible that the introduction of the HPV vaccine for women and girls in 2006 started to affect the rates of acquisition of HPV infection in subsequent years. Although the numbers of young women in the Armed Forces who have completed the HPV vaccine series have been relatively low,[2] it is likely that at least some young women had been immunized before entering military service. The analysis in this report is not able to clarify this conjecture, but other studies using serological evidence of vaccine receipt may shed light on the impact of vaccination prior to military service.

The observation that incidence rates of syphilis were dramatically higher in the first two years (2000-2001) of the surveillance period was unexpected. The incidence rule used in this analysis for each of the STIs excluded individuals who had been diagnosed with the respective STI before the year 2000 in order to focus on first-time detections of incident infections and to avoid attributing pre-2000 infections to the first year or two of the surveillance period. Because the incidence rates of syphilis after 2001 were stable and were about half the rates for 2000 and 2001, it seems likely that the attempt to exclude prevalent cases of syphilis failed. Most of the unexpectedly high rates in 2000 and 2001 were due to cases in Army service members. It is possible that the electronic records from the Army were incomplete prior to 2000, but this hypothesis will require future, further analysis.

This report has several limitations that should be considered when interpreting the results. Analyses were based on administrative records of medical encounters. Such records do not specify the laboratory tests (or specific results) or clinical criteria that were used to confirm STI diagnoses. In addition, diagnoses of STIs may be incorrectly coded; for example, STI-specific "rule out" diagnoses or vaccinations (e.g., HPV vaccination) may be reported with STI-specific diagnostic codes. Conversely, "true" STI cases may not be captured if coded in the medical record using symptom codes (e.g., urethritis) rather than STI-specific codes; this could contribute to underestimation of STI cases. In addition, the STI diagnoses reported here underestimate the actual numbers of diagnoses to the extent that affected service members are diagnosed and treated through non-reimbursed, non-military care providers (e.g., county health departments, family planning centers) or in deployed settings (e.g., overseas training exercises, combat operations, on-board ships) unless these encounters are reported via a notifiable medical event.

This analysis was based on incident diagnoses of STIs. For some STIs, the detection of prevalent infections may occur long after the subject infections were acquired. As a result, changes in incidence rates reflect, at least in part, temporal changes in case ascertainment (e.g., more aggressive screening). The lack of standard practices across the services and their installations regarding screening, testing, treatment, and reporting complicate interpretations of differences between services, military and demographic subgroups, and locations. Establishing screening, testing, treatment, and reporting standards across the Services and ensuring adherence would likely improve efforts to detect, characterize, and counter STI-related health threats to our military members.

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2. Maktabi H, Ludwig SL, Eick-Cost A, Yerubandi UD, Gaydos JC. Quadrivalent human papillomavirus vaccine initiation, coverage, and compliance among U.S. active component service women, 2006-2011. *MSMR*. 2012 May;19(5):16.

Predictive Value of Reportable Medical Events for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*

Neisseria gonorrhoeae (gonorrhea) and *Chlamydia trachomatis* (chlamydia) are notifiable diseases reported under the guidelines of the Armed Forces Reportable Medical Event Guidelines and Case Definitions. Records of clinical laboratory tests (Health Level 7) were used to calculate the sensitivity, specificity, and positive predictive value (PPV) of confirmed reportable medical events (RMEs) for gonorrhea and chlamydia. The sensitivity—which reflects the proportion of "true cases" identified by an RME—was 65 percent and 62 percent for gonorrhea and chlamydia, respectively. The specificity – the percentage of individuals with negative lab tests who did not have RMEs – was high (>98%) for both infections. The PPV – the percentage of people with an RME who have a positive test– was also relatively high (>80%) for both infections. Using confirmed RMEs alone to estimate incident cases of gonorrhea and chlamydia may underestimate the true disease burden.

Neisseria gonorrhoeae (gonorrhea) and *Chlamydia trachomatis* (chlamydia) are etiologic agents of common sexually transmitted infections (STIs). In the United States, gonorrhea and chlamydia are both infectious diseases designated as notifiable at the national level; i.e., every individual identified with an infection must be reported to local and state public health disease surveillance systems.[1] In the U.S. Military Health System, notifiable diseases are reported under the guidelines of the Armed Forces Reportable Medical Events Guidelines and Case Definitions.[2] Each Service implements its own reporting system, data collection, and quality assurance; collected data is integrated by the Armed Forces Health Surveillance Center into the Defense Medical Surveillance System for further reporting and analysis.[2]

Previously in the *MSMR*, the completeness and timeliness of reportable medical events (RMEs) was assessed through a comparison of RMEs to hospitalized and ambulatory encounters occurring in fixed U.S. military medical facilities with documented standardized records that include coded diagnoses (per the International Classification of Diseases, Ninth Revision [ICD-9-CM]).[3] The overall (Army, Navy, Air Force) completeness of gonorrhea and chlamydia RMEs for capturing medical encounters indicative of their respective infections was 45 percent for gonorrhea and 52 percent for chlamydia. The methods used for that *MSMR* article likely produced biased estimates of the actual completeness of reporting because administrative data may be incomplete in capturing true disease status (e.g., coding inaccuracies, rule-out diagnoses, non-specific diagnoses) – particularly for common infections such as gonorrhea and chlamydia.

Results from clinical laboratory testing provide a resource outside of administrative data to evaluate the completeness and timeliness of RMEs. The sensitivities and specificities of current nucleic acid tests (e.g., nucleic acid amplification tests [NAATs], DNA probes) for gonorrhea and chlamydia are high;[4-9] therefore, these laboratory results can be used as reliable indicators of disease status. This report summarizes the use of records of laboratory tests as gold standards to estimate the sensitivity, specificity, and positive predictive value of reportable medical events for gonorrhea and chlamydia.

METHODS

The surveillance period was 1 January 2010 through 31 December 2012. The surveillance population included all U.S. service members of the Army, Navy, Air Force, Marine Corps, and Coast Guard who served in the active component during the surveillance period.

Records of laboratory tests (Health Level 7 [HL7]) are routinely transmitted to the Armed Forces Health Surveillance Center and were utilized for this report. HL7 data includes only laboratory records generated at fixed military treatment facilities; therefore, laboratory tests performed at nonmilitary facilities (purchased care), at sea (shipboard), or during deployment to an operational theater were not included in this analysis.

Laboratory test names for gonorrhea and chlamydia were identified by searching the laboratory data of a sample of 200 reportable medical events categorized as "confirmed" for gonorrhea or chlamydia. A majority of these laboratory tests were nucleic acid tests (e.g., NAATs, DNA probe). Culture and immunoassay-based laboratory tests were a very small proportion of all laboratory tests, so they were excluded from the analysis. Laboratory test names indicating both gonorrhea and chlamydia were excluded because the results were not specific as to which disease was positive or negative.

The laboratory test names identified were then used to search the full HL7 dataset for all results for tests with those names; test results were classified into positive and negative. Laboratory test results that indicated the result was inconclusive (e.g., indeterminate, equivocal) or not performed (e.g., test not performed, rejected) were excluded from the analysis.

Although the Centers For Disease Control and Prevention 2010 STD treatment guidelines do not recommend follow-up tests to confirm clearance of infection (i.e.,"test of cure") for gonorrhea and chlamydia, some clinicians may order such tests approximately three weeks after treatment.[10,11] For this analysis, if more than one laboratory test result was reported within a 21-day period, only the first test was used in order to avoid capturing follow-up testing for the same infection. Furthermore, multiple tests may occur for the same episode of infection because of sampling from multiple sites (e.g., blood, urine, swabs), so only one laboratory test per individual per day was included. If an individual had discordant test results on a single day (i.e., a positive and a negative test) the positive test was prioritized and used for the analysis.

Relevant notifiable event reports from service-specific reporting systems (i.e., RMEs) were obtained from data routinely maintained in the Defense Medical Surveillance System (DMSS). Only reports for which the sender indicated that the diagnosis was "confirmed" were considered confirmed reportable medical events (RMEs).

The sensitivity, specificity, and positive predictive value (PPV) of confirmed reportable medical events for gonorrhea and chlamydia were calculated **(Table 1)**.[12,13] "Disease" status was considered positive or negative if the HL7 laboratory test result was positive or negative, respectively. "RME" status was considered yes if the individual with the respective laboratory test was reported as a confirmed RME within 30 days before or after the collection date of the laboratory test. Likewise, "RME" status was considered no if the individual did not have an associated RME.

"Sensitivity" represents the percentage of true cases (i.e., all those with a positive laboratory test result) who were the subjects of confirmed RMEs. "Specificity" represents the percentage of individuals without infection (i.e., negative lab test) without a confirmed RME. PPV represents the proportion of all those individuals identified with a confirmed RME who also had a positive laboratory test.

TABLE 1. Two-by-two table to determine sensitivity, specificity, and positive predictive value (PPV) for confirmed reportable medical events (RMEs)

		Disease status: Pos	Disease status: Neg	
Confirmed RME	Yes	A	B	Total no. of lab tests with a confirmed RME
	No	C	D	Total no. of lab tests without a confirmed RME
		Total positive lab tests	Total negative lab tests	

Sensitivity	A/(A+C)
Specificity	D/(B+D)
PPV	A/(A+B)

A= Number of positive lab tests with confirmed RME
B= Number of negative lab tests with confirmed RME
C= Number of positive lab tests without a confirmed RME
D= Number of negative lab tests without a confirmed RME

TABLE 2. Sensitivity, specificity, and positive predictive value (PPV) for *Neisseria gonorrhoeae* reportable medical events (RMEs)

a. Total

		Lab test: Pos	Lab test: Neg	
Confirmed RME	Yes	4,135	750	4,885
	No	2,145	625,807	627,952
		6,280	626,557	

Sensitivity	65.84%
Specificity	99.88%
PPV	84.65%

b. Males

		Lab test: Pos	Lab test: Neg	
Confirmed RME	Yes	3,091	446	3,537
	No	1,583	233,061	234,644
		4,674	233,507	

Sensitivity	66.13%
Specificity	99.81%
PPV	87.39%

c. Females

		Lab test: Pos	Lab test: Neg	
Confirmed RME	Yes	1,044	304	1,348
	No	562	392,746	393,308
		1,606	393,050	

Sensitivity	65.01%
Specificity	99.92%
PPV	77.45%

TABLE 3. Sensitivity, specificity, and positive predictive value (PPV) for *Chlamydia trachomatis* reportable medical events (RMEs)

a. Total

Confirmed RME	Lab test: Pos	Lab test: Neg	
Yes	20,513	3,307	23,820
No	12,393	408,192	420,585
	32,906	411,499	

Sensitivity	62.34%
Specificity	99.20%
PPV	86.12%

b. Males

Confirmed RME	Lab test: Pos	Lab test: Neg	
Yes	12,243	1,541	13,784
No	7,726	153,166	160,892
	19,969	154,707	

Sensitivity	61.31%
Specificity	99.00%
PPV	88.82%

c. Females

Confirmed RME	Lab test: Pos	Lab test: Neg	
Yes	8,270	1,766	10,036
No	4,667	255,025	259,692
	12,937	256,791	

Sensitivity	63.93%
Specificity	99.31%
PPV	82.40%

RESULTS

Neisseria gonorrhoeae

During the surveillance period 632,837 nucleic acid tests satisfied the criteria for inclusion in this analysis for gonorrhea. Of these, 0.99 percent (n=6,280) were characterized as positive; 99.01 percent (n=626,557) were negative **(Table 2a)**. Of the 6,280 positive tests, 4,135 were associated with a confirmed reportable medical event; thus, the sensitivity of an RME for gonorrhea was 65.84 percent. The specificity was 99.88 percent and the PPV was 84.65 percent **(Table 2a)**.

A majority of the laboratory tests (62.36%) were performed in female service members (n=394,656); however, a greater proportion of the tests were positive among males (n=4,674, 1.96%) than females (n=1,606, 0.41%) **(Tables 2b-c)**. The sensitivity of an RME was slightly higher among males (66.13%) than females (65.01%), but the specificities were the same in both genders (>99.80%). The PPV was 10 percent higher in males (87.39%) than females (77.45%) **(Tables 2b-c)**.

Chlamydia trachomatis

For the surveillance period 444,405 nucleic acid tests were included in this analysis for chlamydia. Of these, 7.40 percent (n=32,906) were characterized as positive; 92.60 percent (n=411,499) were negative **(Table 3a)**. Of the 32,906 positive tests, 20,513 corresponded to a confirmed reportable medical event; thus, the sensitivity of an RME for chlamydia was 62.34 percent. The specificity was 99.20 percent and the PPV was 86.12 percent **(Table 3a)**.

A majority of the laboratory test results pertained to female service members (n=269,728; 60.69%); however, in males, a greater proportion of the tests were positive (n= 19,969; 11.43%) compared to females (n=12,937; 4.80%) **(Tables 3b-c)**. Among females, the sensitivity of an RME was slightly higher (63.93% females; 61.31% males). Specificity was similar in both genders (>99.00% in both). PPV was 6 percent higher in males (88.82%) than females (82.40%) **(Tables 3b-c)**.

EDITORIAL COMMENT

This report summarizes the use of a sample of gonorrhea and chlamydia nucleic acid test results from HL7 records to estimate the sensitivity, specificity, and positive predictive value (PPV) of confirmed RMEs for each STI. The greater proportion of tests performed in females, and the smaller proportion of positive cases, likely reflect the greater number of STI screening programs for female service members. STI screening is not routinely performed in male service members. Therefore, laboratory tests among males are more likely to reflect cases where an individual was symptomatic or was a sexual contact of a known case, thereby increasing the likelihood of a positive laboratory result. Because of the exclusions described in the methodology, the number of tests reported here does not reflect the total number of tests performed in active duty service members.

Despite the differences in the numbers of overall tests, the sensitivity – which reflects the proportion of "true cases" identified by confirmed RMEs – was similar for both gonorrhea and chlamydia. For both

infections, about 35 to 37 percent of positive laboratory tests did not have a confirmed RME. Previously, the Air Force reported approximately 26 percent and 43 percent of positive test results for chlamydia and gonorrhea, respectively, were not reported to the Air Force Reportable Events Surveillance System (AFRESS); reporting rates varied greatly by individual base.[14] Using RMEs alone to estimate the incidence and prevalence of gonorrhea and chlamydia, therefore, will likely underestimate the true burden of disease for these STIs.

The specificity – the percentage of individuals with negative laboratory tests who were not reported as confirmed RMEs – was high (>98%). This indicates that relatively few individuals who were laboratory test negative were reported as confirmed RMEs. The positive predictive value – the percentage of people with a confirmed RME who truly have the disease – was also relatively high (>80 percent, except for gonorrhea among females [77.45%]). This indicates that a large proportion of the confirmed RMEs are truly positive when compared to the disease status standard used in this study.

The results of this analysis must be considered in light of several limitations. In traditional sensitivity, specificity, and PPV analyses, candidate indicators of a disease are measured against a "gold standard" whose sensitivity and specificity for detection of the disease are postulated to be 100 percent.[12,13] For this analysis, results of nucleic acid tests were used as an "imperfect gold standard" for determining disease status. Although the sensitivity and specificity are high for these laboratory tests, a small proportion of test results may be presumed to be inaccurate (e.g., false positives, false negatives). The results of this analysis would differ if a "perfect gold standard" were used.

Changes to several methods used in this analysis might change the sensitivity, specificity, and PPV reported here. Sensitivity might be improved by using a longer window of time after the laboratory collection date to detect an RME. Most services require the RME to be reported within 30 days; therefore, this analysis was restricted to "timely" RMEs. This analysis used "collection date" as the start day of follow-up; sensitivity might be slightly improved by using the date the laboratory result was certified (i.e., "certified date"). Furthermore, modifying the 21-day laboratory test exclusion period could change the specificity and PPV; however, because these values were high, increasing or decreasing this value would change the results only slightly.

Despite these limitations, it is evident that using RMEs alone to estimate the disease burden of gonorrhea and chlamydia resulted in underestimates. A surveillance case definition that includes RMEs, laboratory data, and medical encounter data should be considered to improve estimates of the incidence and prevalence of gonorrhea and chlamydia.

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Brief Report

Chlamydia trachomatis Screening Initiative among U.S. Army Soldiers Assigned to Korea

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Chlamydia trachomatis (CT) infections are relatively common among members of the U.S. military. Historically, CT rates have been higher among U.S. military members than those reported nationally[1] and higher in the Army than the other military services.[2] Within the Army, an estimated 39,619 incident CT infections were detected during 2004 to 2009 among active duty soldiers (rate of 1,615 per 100,000 person-years).[3] In the U.S., groups at higher risk include females, ethnic minorities, and individuals younger than 25 years of age.[4] Prevalences of CT infections as high as 9 percent have been reported among active duty female soldiers under 25 years of age, and studies among Army female recruits have documented sustained high prevalences of approximately 10 percent.[2,5]

Because high proportions of CT infections among women (~80%) and men (~50%) are asymptomatic, screening is an important control measure.[6] Screening programs among sexually active women have demonstrated substantial cost savings in civilian and military populations.[7,8] CT screening among female recruits during basic military training (BMT) has been associated with decreased rates of pelvic inflammatory disease (PID), a complication of untreated CT infections.[9] Incidence rates of PID were 64 percent higher among females in the Army who were not provided screening during BMT than those in the Navy who were provided screening during BMT.[9] Also, the results of one study suggested that it may be cost effective to screen male accessions to military service for CT.[10]

This report summarizes the results of a universal screening program conducted among all U.S. soldiers who were in-processing to assignments in Korea during calendar year (CY) 2009.

METHODS

Due to a large number of clinically symptomatic CT infections in soldiers assigned to Korea, a command-directed initiative to provide universal screening for Eighth U.S. Army (EUSA) female soldiers during in-processing activities was successfully implemented in November 2007. Males were initially screened upon request; however, the program was expanded in November 2008 to include screening for male soldiers. The program was discontinued on 1 January 2010.

During CY 2009, all U.S. soldiers who were assigned to Korea were in-processed at the U.S. Army Garrison-Yongsan in Seoul. Each soldier participating in the CT screening program received an educational briefing on sexually transmitted diseases, completed a brief questionnaire, and submitted a urine specimen. The specimens were shipped to Tripler Army Medical Center, Hawaii, for testing using Aptima Genprobe® kits. Soldiers with positive results were contacted for further evaluation and treatment.

RESULTS

During November 2007 to January 2010, 17,735 soldiers were screened for CT infections; 17,546 had evaluable test results and 742 (4.2%) tested positive. The majority (71.0%) of testing was performed in 2009 when screening was conducted among both males and females. During 2009, 478 (3.8%) of 12,588 tests were positive.

Relative to their respective counterparts, CT infection prevalences were higher among women (5.8%), soldiers under 20 years of age (5.7%), black, non-Hispanic soldiers (7.0%), and enlisted members (4.2%) **(Table)**. Prevalences among women less than 20 years of age and women 20-24 years old were 12.6 percent and 7.2 percent, respectively; prevalences among men in the comparable age groups were 3.9 percent and 4.7 percent **(Table, footnote c)**.

EDITORIAL COMMENT

The screening program of interest for this report identified CT infections among soldiers who were in-processing to assignments in Korea. The program enabled the early detection and treatment of hundreds of CT infections; as such, the program diminished CT-related morbidity among those affected and prevented transmissions of CT infections to others.

A notable finding of this report was the lower age at which CT infections were diagnosed among female soldiers during, compared to prior to, the conduct of the screening program (mean age of diagnosis in relation to the screening program: during, 22 years; preceding, 26 years).[11] Earlier detection and treatment have the potential to reduce the subsequent incidence of PID and other complications. The program also demonstrated that screening and educating large numbers of soldiers during in-processing was practicable; this finding supports the feasibility of expanding the screening to other high risk military populations (e.g., Army recruits, deployers).

The Army currently does not screen for CT during BMT but does follow U.S. Preventive Services Task Force recommendations to annually screen women under 25 years of age as well as others at high risk for CT. Until June 2011 when guidance for screening among women in the Army was updated, initial CT screening was recommended within the first year of soldiers' first permanent duty assignments. The new recommendations now allow for earlier screening during advanced individual training (AIT), which occurs after BMT and prior to the first permanent duty assignment.[12]

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Acknowledgements: The Korea Chlamydia trachomatis *screening initiative was funded by the Department of Defense Global Emerging Infections Surveillance and Response System, Armed Forces Health Surveillance Center, Silver Spring, MD. The authors gratefully acknowledge the contributions of Ms. Jodie E. Fishman and Ms. Tanya P. Jacobsmuhlen in implementing and conducting the Chlamydia trachomatis screening initiative in Korea.*

TABLE. *Chlamydia trachomatis* prevalence and risk estimates among soldiers newly assigned to Korea, calendar year 2009[a]

Category	No. screened[b]	% positive	Odds ratio	95% confidence interval
Gender[c]				
Female	1,990	5.8	**1.3**	**1.1-1.6**
Male	10,241	3.5	1.0	
Age group[c]				
<20	1,883	5.7	**6.3**	**3.2-12.6**
20-24	4,330	5.1	**5.7**	**2.9-11.2**
25-29	2,460	3.1	**3.3**	**1.7-6.7**
30-34	1,473	2.8	**2.9**	**1.4-6.0**
35-39	1,175	1.9	2.0	0.9-4.4
40+	910	1.0	1.0	
Race/ethnicity				
Black, non-Hispanic	2,983	7.0	**3.2**	**2.5-3.9**
Hispanic	1,419	2.9	1.1	0.8-1.6
Asian/Pacific Islander	385	4.9	**2.1**	**1.2-3.4**
American Indian/Alaskan	301	5.0	**1.8**	**1.1-3.2**
Other	748	3.4	**1.5**	**1.0-2.4**
White, non-Hispanic	6,395	2.5	1.0	
Rank				
Enlisted	10,805	4.2	**2.1**	**1.3-3.3**
Officer	1,426	1.3	1.0	

[a]Summary based on logistic regression model; statistically significant results are in **bold**; odds ratios assigned 1.0 reflect the reference groups used in the model.

[b]A total of 12,588 tests were evaluated; demographics were missing for 357 records which resulted in their exclusion from the model.

[c]Unadjusted prevalence estimates by age and gender (F, M) were as follows: <20 years (12.6%F, 3.9%M), 20-24 years (7.2%F, 4.7%M), 25-29 years (2.4%F, 3.2%M), 30-34 years (1.3%F, 3.0%M), 35-39 years (2.5%F, 1.8%M), >40 years (1.4%F, 1.0%M).

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Incidence of Genital Warts Among U.S. Service Members Before and After the Introduction of the Quadrivalent Human Papillomavirus Vaccine

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Human papillomavirus (HPV) is the most common sexually transmitted infection among U.S. military members. The most frequent clinical manifestation of HPV is genital warts (GW). This investigation examined the annual incidence of diagnoses of GW among U.S. service members before and after the availability of the quadrivalent HPV (HPV4) vaccine in 2006. Incidence rates of GW diagnoses markedly declined among female service members in the HPV4 vaccine-eligible age range from 2007 (following introduction of the HPV4 vaccine) through 2010. In contrast, among women 25 years and older and men of all age groups, annual rates of GW diagnoses remained relatively low and stable from 2000 through 2010. The higher rates of diagnoses of GWs among female than male service members reflect the effects of routine periodic gynecologic screening. Slight increases in the incidence of GW diagnoses among men between 2010 and 2012 may in part reflect the repeal of the U.S. military's "Don't Ask Don't Tell" policy.

Genital warts (GW), also called anogenital warts or condyloma acuminata, are the most frequent clinical manifestation of human papillomavirus (HPV) infection.[1] Among U.S. military members, HPV is the most common sexually transmitted infection (STI).[2] While 20-30 percent of GWs spontaneously regress, they can cause significant psychosexual morbidity, typically necessitate multiple healthcare visits, and often recur.[3-5]

In 2006, the U.S. Food and Drug Administration licensed the 3-dose series, quadrivalent HPV (HPV4) vaccine, which confers protection against oncogenic HPV types 16 and 18 and non-oncogenic HPV types 6 and 11, with the latter two responsible for approximately 90 percent of GWs.[6,7] The vaccine was licensed for use in women aged 9-26 years in 2006 and for men 9-26 years in 2009.[8,9] Efficacy trials of the HPV4 vaccine have shown significant declines in incidence of GWs among fully vaccinated individuals naïve to the vaccine strains as early as three years following vaccination.[10-17] Ecological investigations of HPV4 vaccine effectiveness have also shown notable reductions in the incidence of GWs following the introduction of population-wide HPV4 immunization programs.[10,18,19]

Service members who are vaccinated against HPV4 should be relatively protected from HPV infection and the development of GWs.[9,10] Since its licensure, HPV4 vaccine has been added to U.S. civilian and Department of Defense (DoD) immunization programs. This investigation examined the annual incidence of GWs among U.S. service members before and after the availability of the HPV4 vaccine in 2006.

METHODS

The Defense Medical Surveillance System (DMSS) maintains records that document demographic, military, and medical information related to U.S. service members throughout their military service careers.[21] All individuals who served in the active component of the U.S. Armed Forces at any time between 1 January 2000 and 31 December 2012 were included in the study. The study population ranged from 1,544,029 in 2000 to 1,440,362 in 2012. Data on age, sex and healthcare encounters were obtained from DMSS.

An incident case of GW was defined by a DMSS record of a healthcare encounter with a "genital warts" diagnosis (ICD-9-CM code 078.1) in any diagnostic position. Service members with GW diagnoses prior to the start of the surveillance period were excluded. For service members with more than one encounter with a GW diagnosis, only the first encounter was included in the analysis.

Poisson regression was used to estimate annual age-specific incidence rates of GWs among male and female service members aged 17 years and older from 2000 through 2012. Service members were followed from the study start date or the date they joined the active military component if later. Follow-up was censored at the earliest date that a service member left the active component, died, had a GW diagnosis, or the study ended. Incidence risk ratios and corresponding 95 percent confidence intervals were calculated to assess whether there was a significant difference in the incidence of genital warts before and after the introduction of HPV4 vaccine in 2006. All analyses were performed using SAS® 9.2.

RESULTS

During each year of the study period except 2012, crude incidence rates of GWs were higher among females than males **(Table)**. Among females, incidence rates were markedly higher among those younger than 30 years versus older; and

among those younger than 30 years, rates were highest among the youngest (<21 years), intermediate among the 21-24-year-olds, and relatively low among the oldest (25-29 years) **(Figure 1)**.

Among women younger than 25 years, annual incidence rates of GWs sharply declined from 2007 through 2010. In contrast, among women 25 years and older and men of all age groups, annual rates of GW diagnoses remained relatively low and stable from 2000 through 2010 **(Figures 1,2)**. During the last two years of the period, incidence rates of GWs increased among women older than 24 years and men of all age groups **(Figure 2)**.

EDITORIAL COMMENT

This report documents the incidence of recorded diagnoses of GWs among U.S. service members before and after the 2006 licensure of the HPV4 vaccine. Because of the short latency between HPV infection and detection of GWs, monitoring trends in GW incidence should provide an early assessment of population-level HPV4 vaccine effectiveness.[22]

Of note, incidence rates of GW diagnoses markedly declined among female service members in the HPV4 vaccine-eligible age range from 2007 (following the introduction of the HPV4 vaccine) through 2010. The sharp decline in GW incidence rates among women occurred despite low initiation and completion rates for the HPV4 vaccine series in eligible civilian and military women.[20,23] Declines in GW rates among younger women (such as those reported here) have been documented in insured populations in the U.S. and in Swedish and Australian populations in which the HPV4 vaccine was introduced.[10,18,19]

In this report, GW incidence rates were higher among U.S. military women than men. The U.S. military services require periodic gynecologic and STI screening of their female members; there is much less emphasis on STI screening of men.[1] In the context of the U.S. military's free access to health care, the higher rate of diagnoses of GWs among female than male service members reflects at least in part the effects of routine periodic screening; such screening facilitates the diagnosis and recording of GWs that may otherwise resolve without documentation.

Incidence rates of GW diagnoses increased slightly among older women and among all age groups of men between 2010 and 2012. The reason(s) for these increases are unclear. The increase in GW incidence rates starting in 2011 may reflect at least in part the repeal of the U.S. military's "Don't Ask Don't Tell" policy. (The repeal of "Don't Ask, Don't Tell," Public Law 103–160 [10 U.S.C. § 654] was signed by the President on 22 December 2010 and was fully implemented on 20 September 2011.) The change in policy may have encouraged some service members at risk of GWs through homosexual contacts to seek medical care through the U.S. military health system. Monitoring incidence trends of GWs and other STIs among service members is warranted to better understand the impacts of the repeal of this legislation.

The findings of this report should be considered in light of several limitations. For example, since data were obtained from administrative databases, misclassifications of some of the diagnoses of interest are inevitable. In particular, the increases in diagnoses of GWs observed in 2011-2012 may reflect improper uses of the diagnosis code for "genital warts" to report vaccinations to prevent genital warts. Of

TABLE. Incident diagnoses and incidence rates (per 100,000 person-years) of genital warts, by gender and age group, active component, U.S. Armed Forces, 2000-2012

	2000		2001		2002		2003		2004		2005	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Females												
All ages	4,825	2,558.1	3,905	2,203.5	4,453	2,256.1	4,422	2,210.6	4,425	2,239.0	4,348	2,309.8
<21	1,594	4,186.9	1,354	3,619.4	1,450	3,727.4	1,351	3,618.0	1,166	3,418.5	1,123	3,853.8
21-24	1,561	3,131.0	1,298	2,669.3	1,502	2,667.6	1,525	2,567.6	1,561	2,607.0	1,659	2,913.2
25-29	740	1,932.7	556	1,609.9	686	1,745.0	783	1,918.9	858	2,048.5	827	1,970.8
30-34	407	1,619.0	279	1,212.5	358	1,413.0	312	1,234.5	355	1,419.8	286	1,171.8
35-39	290	1,340.1	229	1,197.1	253	1,219.8	215	1,071.4	225	1,166.6	226	1,215.0
40+	233	1,491.6	189	1,303.0	204	1,215.5	236	1,375.4	260	1,488.1	227	1,321.2
Male												
All ages	19,868	1,740.4	16,147	1,504.7	17,451	1,510.5	17,277	1,478.7	18,291	1,572.7	17,966	1,585.1
<21	3,541	1,908.5	2,979	1,628.0	3,175	1,707.3	2,971	1,632.9	2,890	1,655.7	2,686	1,671.5
21-24	5,594	2,082.2	4,887	1,834.8	5,274	1,782.4	5,450	1,740.2	5,908	1,852.2	5,774	1,852.7
25-29	3,982	1,779.7	3,120	1,538.8	3,302	1,514.7	3,375	1,494.8	3,921	1,687.3	4,024	1,698.8
30-34	2,573	1,462.5	1,859	1,160.7	2,014	1,185.9	2,015	1,196.8	2,016	1,214.0	2,030	1,254.7
35-39	2,437	1,400.9	1,868	1,212.3	2,044	1,258.6	1,741	1,128.1	1,773	1,214.3	1,665	1,194.0
40+	1,741	1,531.2	1,434	1,343.5	1,642	1,332.5	1,725	1,382.6	1,783	1,425.9	1,787	1,452.7

note in this regard, rates of other sexually transmitted infections also increased during 2011-2012 among U.S. service members. It is unlikely that inaccurate reporting accounted for simultaneous increases in diagnoses of all STIs throughout the military services.

Although a causal relationship between the HPV4 vaccine and the decline in incidence of genital warts among younger female service members cannot be documented, the results of this longitudinal study provide encouraging evidence that the HPV4 vaccine may be preventing GWs among service women in the vaccine-eligible age range. Further, because the highest GW incidence rates are among the youngest service women, providing the HPV4 vaccine at the earliest opportunity after accession would offer the greatest protection against HPV infections and GWs. Continued surveillance of GW rates is warranted. Additionally, since military health care records document only HPV vaccinations received during – not prior to – military service, a serum-based vaccine effectiveness study is needed to estimate vaccine effectiveness in military members. Such a study would permit consideration of protective antibodies secondary

FIGURE 1. Incidence rates of genital warts among females, active component, U.S. Armed Forces, 2000-2012

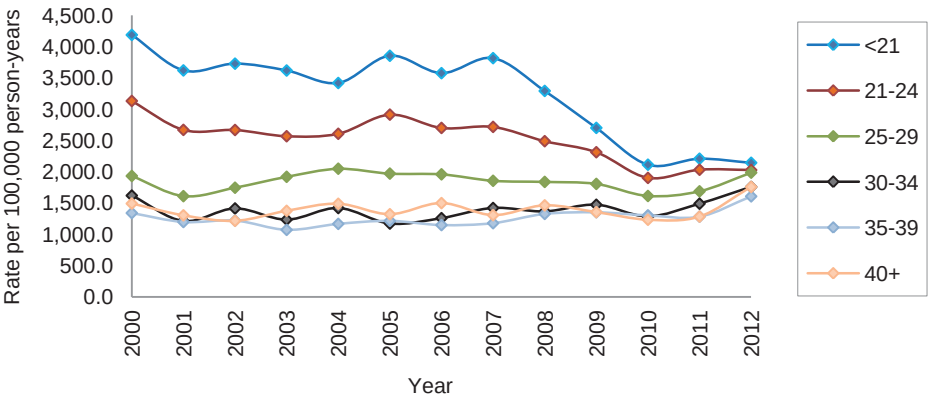

FIGURE 2. Incidence rates of genital warts among males, active component, U.S. Armed Forces, 2000-2012

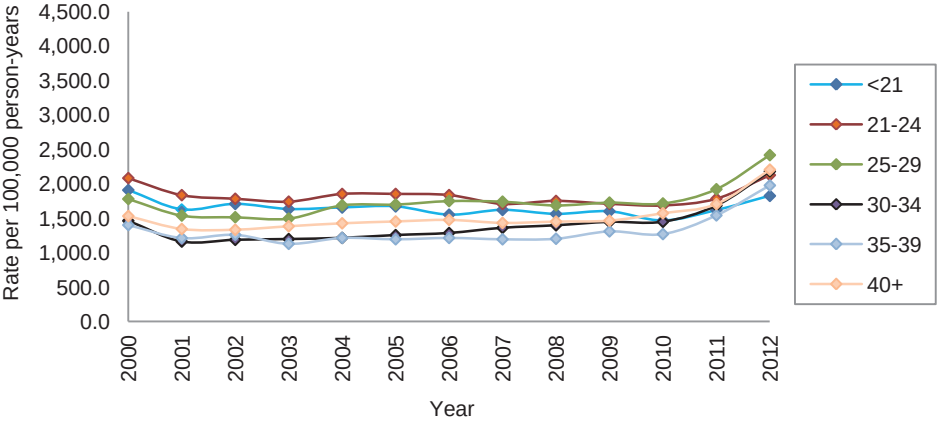

TABLE. (continued). Incident diagnoses and incidence rates (per 100,000 person-years) of genital warts, by gender and age group, active component, U.S. Armed Forces, 2000-2012

2006		2007		2008		2009		2010		2011		2012	
No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
4,103	2,215.9	4,062	2,231.0	3,813	2,095.5	3,614	1,948.5	3,126	1655.7	3,331	1751.5	2,718	1927.5
1,022	3,575.6	1,065	3,815.7	909	3,291.6	726	2,701.3	564	2112.6	558	2208.4	389	2143.2
1,485	2,700.2	1,430	2,716.8	1,281	2,488.4	1,211	2,312.0	1,009	1901.6	1,095	2031.9	808	2027.3
834	1,958.8	802	1,855.7	816	1,837.7	837	1,805.8	772	1612.5	823	1687.3	718	1985.7
299	1,258.1	336	1,420.5	327	1,365.5	369	1,472.6	337	1286.6	408	1489.4	368	1756.6
213	1,147.5	217	1,177.9	242	1,326.2	247	1,351.7	237	1302.8	229	1281.7	214	1606.8
250	1,498.9	212	1,306.2	238	1,462.6	224	1,354.5	207	1233.1	218	1283.2	221	1757.0
17,793	1,586.1	17,435	1,563.3	17,627	1,565.7	18,190	1,590.9	18,062	1572.7	19,929	1748.7	18,054	2163.9
2,428	1,551.1	2,478	1,620.4	2,416	1,562.4	2,393	1,599.4	2,095	1466.5	2,158	1617.5	1,770	1824.5
5,703	1,835.9	5,304	1,707.5	5,486	1,751.0	5,454	1,708.8	5,356	1684.8	5,576	1782.3	4,790	2125.4
4,219	1,749.2	4,264	1,740.3	4,284	1,686.5	4,598	1,726.7	4,736	1714.0	5,439	1920.9	5,047	2416.4
2,006	1,284.8	2,092	1,360.1	2,150	1,397.0	2,287	1,446.8	2,362	1448.2	2,818	1683.2	2,748	2180.4
1,665	1,213.7	1,623	1,193.8	1,614	1,201.6	1,738	1,308.7	1,640	1269.6	1,909	1541.0	1,770	1975.9
1,772	1,475.4	1,674	1,431.3	1,677	1,450.6	1,720	1,464.9	1,873	1572.4	2,029	1705.7	1,929	2205.1

to natural infections as well as vaccinations with HPV4 prior to entry into military service.

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Acknowledgements: The authors would like to thank CAPT (Dr.) Eileen Dunne of the Division of Sexually Transmitted Diseases at the Centers for Disease Control for reviewing aspects of this work and for her helpful comments.

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Human Papillomavirus Seroprevalence Among Men Entering Military Service and Seroincidence After Ten Years of Service

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Vaccination against human papillomavirus (HPV) is recommended to prevent cervical cancer among women. Vaccinating men against human papillomavirus (HPV) can prevent penile, anal, and oral cancers, anogenital warts, and the transmission of HPV to their sexual partners. This study characterized HPV acquisition among male military members by evaluating both seroprevalence at entry into service and seroincidence of HPV infection after ten years of service. At entry, 29 of 200 (14.5%) male service members were positive for HPV serotypes 6, 11, 16, or 18. Of 199 initially seronegative for at least one of the four HPV serotypes, 68 (34.2%) seroconverted to one or more serotypes at ten years; more than one-third of these were seropostive for oncogenic HPV serotypes. This estimate of HPV seroprevalence among male military accessions is higher than that reported among U.S. civilian males. Vaccination to prevent genital warts and cancers resulting from HPV infection may decrease health care system burdens. Further analyses are warranted to understand the potential costs and benefits of a policy to vaccinate male service members.

Human papillomavirus (HPV) is responsible for more health care visits among active duty service members than gonorrhea (GC) and chlamydia (CT) combined.[1] An effective vaccine to prevent infection with serotypes 6, 11, 16 and 18 is available, although administration of the three-dose series is expensive.[2] Infection with the oncogenic HPV serotypes 16 and 18 can cause long-term morbidity or mortality due to cervical and vulvo-vaginal cancer among women, penile cancer among men, and anal and oropharyngeal cancers in both genders. HPV may also play a role in esophageal and lung cancer.[3] Annual numbers of HPV-associated cancers are estimated at 25,000 and 550,000 cases in the U.S. and worldwide, respectively.[3] Based on demonstrated efficacy and evidence of cost effectiveness, HPV vaccine is currently approved for the prevention of cervical cancer.[2] Recently the U.S. Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) recognized the potential benefits of immunizing young men and recommended vaccination for both males and females.[2] The U.S. military's implementation of this recommendation has been slow, as evidenced by low initiation and completion rates among service women.[4,5] Assessment of HPV infection rates among male service members is important to evaluate the potential benefits of vaccination.

As obtaining genital HPV DNA samples from large populations is difficult, HPV serology is increasingly used to characterize the epidemiology of HPV infection,[6-8] despite evidence of incomplete seroconversion and possible antibody decline.[9,10] In one study, seropositivity was observed in approximately 60 percent of women with newly detected cervical HPV DNA.[11] The correlation between HPV seroprevalence and cervical DNA positivity is reportedly high (r=0.81).[12] Several assays are available including a multiplex Luminex® assay that quantitates neutralizing antibodies to HPV serotypes 6, 11, 16 and 18. This assay was used in the recent U.S. National Health and Nutrition Examination Survey (NHANES) serosurvey[8] and has been well validated.[13-16]

Population-based studies have demonstrated that HPV seroprevalence is low in late adolescence (1-8%), increases over the first decade of adulthood, and among those at risk, is high (15-35%) by age 40.[6-8,12,13,17,18] The timeline of HPV acquisition may be accelerated in a highly sexually active population such as military personnel.[19-21] Among female service members attending a sexually transmitted infections clinic, HPV seroprevalence was reported at 45 to 51 percent.[19] The present report describes an effort to characterize HPV acquisition among U.S. military males by evaluating both seroprevalence at entry into service and seroincidence of HPV infection after ten years of service.

METHODS

The study population consisted of males who entered the active component of the U.S. military in 2000, were between 17 and 26 years of age at entry, and had serum samples available in the DoD Serum Repository[22] within one year of entry into service and at 10 years (+/-1 year) after entry into service. Qualifying individuals were stratified into the eight U.S. census regions based on the state of their home of record. A random sample of 25 individuals per region was selected for the study for a total sample size of 200 individuals. By chance alone, due to multiple selection criteria, no Air Force members were included in the study population. Serum samples from both time points were assayed for HPV serotypes 6, 11, 16, and 18 using a validated, commercially available, Luminex®

assay (PPD Vaccines & Biologics, Wayne, PA).[14-16,23] Individuals were classified as positive or negative by serotype according to published assay cutoffs.[24] Demographic and military characteristics were derived from the Defense Medical Surveillance System.[22] The study protocol was approved by scientific and institutional review boards of the Uniformed Services University of the Health Sciences.

Prevalent HPV cases were defined as individuals who were seropositive for one or more HPV serotypes at accession. Incident cases were individuals who were negative for one or more HPV serotypes at the first time point and subsequently positive for a prior negative serotype approximately 10 years later. Thus, incident infection could be observed among those with a baseline (prevalent) infection at accession due to seroconversion to different serotypes.

RESULTS

The demographic and military characteristics of the population at accession were typical of active component military members **(Table 1)**. Overall seroprevalence for any of the four studied HPV serotypes at accession was 14.5 percent **(Table 1)**. At entry, 20 (10.1%) service members were seropositive to serotypes 6 or 11 (genital wart group) and 9 (4.5%) were seropositive to serotypes 16 or 18 (oncogenic group; **data not shown**). The highest proportions of HPV seropositivity at accession were among males older than 23 years and ever-married. By race, a higher proportion of white (16.1%) than black, non-Hispanic (8.8%) service members were seropositive for any serotype.

Of the 199 males initially seronegative for at least one of the four HPV serotypes (one individual was excluded due to assay failure on his 2010 specimen), 68 (34.2%) seroconverted to one or more serotypes at ten years **(Table 2)**. Sixty-six subjects were newly positive for one or two serotypes, two for three serotypes, and none for all four. Incident infection was most commonly seen for the genital wart group (28.6%) as compared to the oncogenic group (12.6%) **data not shown**). Seroincidence was higher among service members of black, non-Hispanic than white, non-Hispanic or "other" race, (50.0%, 33.1% and 20.7%, respectively), and among those in the Army and Navy (34.1% and 36.1%, respectively) compared to the Marine Corps (25.8%). There were no statistically significant differences in seroincidence by educational level, marital status, or rank.

TABLE 1. Demographic characteristics and HPV seropositivity at accession among a sample of 200 active component service members who began service in 2000 and served at least 10 years, U.S. Armed Forces

Demographic/ military characteristics	No. (%)	HPV seropositive[a] No. (%[b])
All individuals	200	29 (14.5)
Age group		
17-19	107 (53.5)	14 (13.1)
20-21	39 (19.5)	2 (5.1)
22-23	35 (17.5)	6 (17.1)
24-26	19 (9.5)	7 (36.8)[c]
Race/ethnicity		
White, non-Hispanic	137 (68.5)	22 (16.1)
Black, non-Hispanic	34 (17.0)	3 (8.8)
Other	29 (14.5)	4 (13.8)
Education		
High school or less	168 (84.0)	24 (14.3)
Some college	4 (2.0)	0 (0.0)
College or more	7 (3.5)	1 (14.3)
Unknown	21 (10.5)	4 (19.1)
Marital status		
Married	14 (7.0)	5 (35.7)
Single	183 (91.5)	22 (12.0)[c]
Divorced/widowed	3 (1.5)	2 (66.7)
Rank		
Enlisted	192 (96.0)	28 (14.6)
Officer/Warrant	8 (4.0)	1 (12.5)
Service		
Army	90 (45.0)	16 (17.8)
Marine Corps	34 (17.0)	4 (11.8)
Navy	76 (38.0)	9 (11.8)

[a]For HPV serotypes 6, 11, 16 or 18
[b]Percent of individuals at risk
[c]Statistically significant ($p<0.05$) in univariate analysis

DISCUSSION

This study found that 14.5 percent of males entering military service were seropositive for one or more of the four vaccine preventable HPV serotypes. This estimate of seroprevalence is higher than those previously reported among U.S. civilians; the NHANES HPV serosurvey found prevalences of 4.2 and 7.2 percent among males aged 20 to 24 and 25 to 29 years, respectively.[8] The finding of higher seroprevalence among military accessions is consistent with reports of sexually transmitted disease rates among U.S. military members,[25-28] who may be more prone to risk-taking than their civilian counterparts.

This study also found that incident infections with these four serotypes were common; more than one-third (34.2%) of male service members seroconverted to one or more vaccine serotypes. This finding offers data-based evidence of the potential

TABLE 2. Incident HPV infection among U.S. service members (n=199) after 10 years[a] of military service, U.S. Armed Forces, 2010

Demographic/ military characteristics	HPV seroincidence (%)[b]
All individuals	68 (34.2)
Age group	
27-29	41 (38.7)
30-31	8 (20.5)
32-33	10 (28.6)
34-37	9 (47.4)
Race/ethnicity	
White, non-Hispanic	45 (33.1)
Black, non-Hispanic	17 (50.0)
Other	6 (20.7)
Education	
High school or less	49 (32.9)
Some college	5 (27.8)
College or more	9 (42.9)
Unknown	5 (45.5)
Marital status	
Married	51 (32.7)
Single	8 (36.4)
Other	9 (42.9)
Rank	
Enlisted	56 (33.1)
Officer/Warrant	8 (38.1)
Other	4 (44.4)
Service	
Army	30 (34.1)
Marine Corps	8 (25.8)
Navy	26 (36.1)
Unknown	4 (50.0)

[a]+/-1 year
[b]Percent of individuals at risk

benefit of a military HPV vaccination program for males. While the majority of new infections were due to genital wart group types, about one-third were due to oncogenic types. Prevention of genital warts and cancers resulting from HPV infection seems likely to decrease health care system burdens and associated long-term costs.[29] Individual consequences are also notable, especially for individuals who suffer HPV-related malignancies. While cervical cancer risk among women has been significantly mitigated through the use of routine Papanicolaou smears, screening for anal and oropharyngeal cancers associated with HPV infection remains difficult and rates of these cancers continue to rise.[30] Given the associated mortality and potentially debilitating morbidities of these malignancies and their treatments, prevention of infection with oncogenic HPV types offers a relevant benefit.

Black, non-Hispanic service members were approximately 50 percent more likely than their white, non-Hispanic counterparts to acquire a new infection with one or more of the four studied serotypes. This is in contrast to the prevalence at the time of accession which was nearly 50 percent lower among black, non-Hispanic than white, non-Hispanic service members. Sexual risk behavior differences between these groups including number and type of partners, use of protective measures such as condoms, and sexual partner networks may account for this finding and merit further study.

This investigation was limited by the small size of the sample in general, which included only 34 service members of black, non-Hispanic race/ethnicity. Another limitation was that the study population included only those individuals with at least 10 years of service, who may not be representative of all military accessions. Of note in this regard, the high prevalence of HPV at entrance to military service indicates that men entering active duty service are at a relatively high risk for sexually transmitted infections and would likely benefit from preventive interventions, including HPV vaccination at accession.

Although the assay for serotype 11 was challenged by high variability in positive controls, results were qualitatively consistent with the other serotypes (comparable rates of positivity with similar titers) suggesting this variability did not affect our findings. Finally, HPV vaccination status was not available for analysis. However, since HPV vaccination was not recommended for routine use among males until 2011 (after the 2010 cutoff for this study), HPV vaccination was probably not a confounding factor in this analysis.

Although the serologic method used in this study may have underestimated the true infection rate by up to 40 percent, more than one-third of service members demonstrated evidence of a new HPV infection and more than one-third of these were seropositive for oncogenic HPV serotypes. These findings provide strong evidence of the potential benefit of male HPV vaccination upon entry into military service. Further analyses are warranted to understand the potential costs and benefits of such a policy.

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Acknowledgements: The authors would like to express appreciation to Dr. Angelia Eick-Cost for her support of this investigation and in obtaining data and specimens. We also thank J. Connor Eggleston for managing the specimens and Alice Y. Tsai for her tireless support of AFHSC-GEIS directed STI initiatives.

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The U.S. Military's *Neisseria gonorrhoeae* Resistance Surveillance Initiatives in Selected Populations of Five Countries

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Multi-drug resistant *Neisseria gonorrhoeae* (GC) threatens the successful treatment of gonorrhea. This report presents preliminary findings with regard to the prevalence of laboratory-confirmed GC and the extent of drug-resistance among sample populations in five countries. Between October 2010 and January 2013, 1,694 subjects (54% male; 45% female; 1% unknown) were enrolled and screened for the presence of laboratory-confirmed GC in the United States, Djibouti, Ghana, Kenya, and Peru. Overall, 108 (6%) of enrolled subjects tested positive for GC. Antimicrobial susceptibility testing results were available for 66 GC isolates. Resistance to at least three antibiotics was observed at each overseas site. All isolates tested in Ghana (n=6) were resistant to ciprofloxacin, penicillin, and tetracycline. In Djibouti, preliminary results suggested resistance to penicillin, tetracycline, ciprofloxacin, cefepime, and ceftriaxone. The small sample size and missing data prevent comparative analysis and limit the generalizability of these preliminary findings.

Gonorrhea is a sexually transmitted infection (STI) caused by the Gram-negative bacterium *Neisseria gonorrhoeae* (GC). Globally, gonorrhea is responsible for about 88 million new infections each year.[1] In the United States, it constitutes the second most commonly reported notifiable disease; in 2011, more than 320,000 gonorrhea cases were reported; the incidence rate was estimated at 104 cases per 100,000 persons.[2] By comparison, incidence rates in the U.S. military ranged from 180 to 200 cases per 100,000 person-years during 2004-2009.[3]

Like many multidrug-resistant organisms, genetic mutability enables the emergence of resistant strains. Specifically, the ability of gonococci to acquire resistance traits via acquisition of chromosomally-mediated or plasmid-mediated genetic determinants from other bacteria[4] facilitates rapid dissemination of resistant GC strains and threatens the successful treatment of gonorrhea.[5] The continued spread of antibiotic-resistant GC has limited treatment options. Decreased susceptibility of GC to oral cephalosporins led to a change in U.S. treatment guidelines in 2010[6] and studies indicate a persistent resistance to penicillins, sulphonamides, tetracyclines, fluoroquinolones and macrolides. The World Health Organization has recognized the multi-drug resistance of GC[1] and a recent editorial in the *New England Journal of Medicine* highlights the risk of "untreatable gonorrhea".[7]

Military-related GC drug resistance dates back to the 1960s when soldiers deployed in Southeast Asia returned to the United States with penicillin-resistant GC.[8,9] Today, the threat of multi-drug resistance calls for an integrated public health response to monitor and control drug-resistant GC. In collaboration with U.S. and international military and civilian partners, the Armed Forces Health Surveillance Center's Division of Global Emerging Infectious Disease Surveillance (AFHSC-GEIS) has launched a global GC resistance surveillance network in seven countries: United States, Cameroon, Djibouti, Georgia, Ghana, Kenya and Peru. This report presents preliminary findings of the prevalence of laboratory-confirmed *N. gonorrhoeae* and the extent of drug-resistance among sample populations in five of these seven countries.

METHODS

Participants enrolled since October 2010 include U.S. and foreign military personnel and other military health care beneficiaries, local civilians, and risk groups such as men who have sex with men (MSM) and female commercial sex workers (FCSW). As of January 2013, participants had been recruited at one military treatment facility in the U.S. (Fort Bragg, NC), four military clinics in Ghana, two civilian district hospitals in Kenya, one civilian hospital-based referral clinic in Djibouti, and two civilian clinics in Peru. All subjects presenting with urethritis, cervicitis or vaginal discharge were enrolled with consent at participating clinics, except in Kenya and Peru, where asymptomatic FCSW and MSM subjects were screened for GC.

Urethral or vaginal swabs and urine specimens were collected from all participants, with pharyngeal and rectal swabs collected from some MSMs. Diagnoses were made by culture identification, nucleic acid amplification testing (NAAT), and real-time polymerase chain reaction (PCR) with testing performed on-site and at regional laboratories. Antimicrobial susceptibility testing was conducted on all identified GC cases using real-time PCR,[10] disc diffusion, and E-test strip methods.[11] Participants were treated according CDC[6] and WHO[1] guidelines. All study protocols were approved by scientific and institutional review boards in the host countries and in the United States.

RESULTS

Between October 2010 and January 2013, a total of 1,694 subjects (54% male, 45% female, 1% unknown) were enrolled and screened for the presence of laboratory-confirmed *N. gonorrhoeae* in the U.S., Djibouti, Ghana, Kenya, and Peru. About one-third of enrolled subjects were 20 to 29 years of age. Military-affiliated participants were enrolled in the U.S., Ghana, and Peru (15% of all enrolled); civilians were enrolled at all non-U.S. sites. In Peru, most participants were FCSWs (37%) or MSMs (33%) and MSMs comprised one-third of those enrolled in Kenya.

Overall, 108 (6%) of enrolled subjects tested positive for GC **(Table 1)**. The prevalence was highest in Kenya, with 33 (38%) GC positive participants, of whom 25 (76%) of were FCSWs.

Antimicrobial susceptibility testing results were available for 66 GC isolates **(Table 2)**. Resistance to at least three antibiotics was observed at each overseas surveillance site. Of note, all isolates tested in Ghana were resistant to ciprofloxacin, penicillin, and tetracycline. A greater variability in the antibiotic resistance profile was noted in Djibouti; isolates were resistant to penicillin (100%), tetracycline (88%), ciprofloxacin (38%), levofloxacin (17%), cefepime (13%), and ceftriaxone (13%).

TABLE 1. Prevalence of *Neisseria gonorrhoeae* among participants in a GC resistance surveillance network, October 2010-January 2013

Surveillance sites	United States[a]		Djibouti		Ghana		Kenya		Peru	
No. of participants (n=1,694)	26		168		118		86		1,296	
	No.	%	No.	%	No.	%	No.	%	No.	%
GC positive (n=108)	1	4	38	23	6	5	33	38	30	2
Risk groups										
Heterosexual	Data not available				6	100	6	18	1	3
MSM[b]					0	0	0	0	27	90
FCSW[c]					0	0	25	76	2	7
Unknown					0	0	2	6	0	0

[a]U.S military installation at Fort Bragg, NC
[b]Men who have sex with men
[c]Female commercial sex worker

TABLE 2. Antimicrobial susceptibility testing of *Neisseria gonorrhoeae* (GC) isolates collected from participants in a GC resistance surveillance network, October 2010-January 2013

Surveillance sites[a]	Djibouti		Ghana		Kenya		Peru	
No. of GC isolates tested[b] (n=66)	24		6		6		30	
Antimicrobial susceptibility testing (AST) (resistant-equivalent level only)[c,d]								
Drug name	No.	%	No.	%	No.	%	No.	%
Azithromycin	0	0	1[e]	50	0	0	-	-
Cefepime	3	13	-	-	0	0	-	-
Ceftriaxone	3	13	0	0	0	0	-	-
Ciprofloxacin	9	38	6	100	2	33	7	23
Doxycycline	-	-	-	-	1	17	-	-
Levofloxacin	1[e]	17	-	-	0	0	7	23
Norfloxacin	-	-	-	-	0	0	7	23
Penicillin	6[e]	100	6	100	0	0	-	-
Tetracycline	21	88	6	100	6	100	-	-

[a]The United States was omitted; the AST result of the 1 isolate obtained was unavailable at the time of this report.
[b]AST results for female commercial sex workers in Kenya (n=25) were unavailable at the time of this report.
[c]A dash (-) denotes "not tested". In Peru, testing was limited to detection of quinolone-resistant genes.
[d]Results for the following drugs not shown because no resistance was found or testing was not performed: cefixime, ceftazidime, gentamycin and spectinomycin.
[e]In Djibouti, resistance to levofloxacin and penicillin conducted on 6 of 24 isolates. In Ghana, azithromycin resistance tested in 2 of 6 isolates.

EDITORIAL COMMENT

Our preliminary findings indicate the presence of drug-resistant GC in various regions of the world. The initial suggestion of third-generation cephalosporin resistance in Djibouti requires confirmation through more definitive sensitivity testing and additional sprecimens; these are underway. The findings highlight the importance of vigilant monitoring and active surveillance of GC resistance.

Some limitations should be considered when interpreting these data. Diagnostic and antimicrobial susceptibility testing methods vary across the network, thus limiting the validity of laboratory-confirmed positive results and comparability of resistance levels in different settings. The small sample size and missing data prevent comparative analysis and limit the generalizability of these findings. Self-reported risk group characterization may be biased or inaccurately captured due to social stigma. For example, military members seek STI treatment in civilian clinics to protect confidentiality and avoid retribution by military authorities.

Currently, the network continues to focus on the standardization of GC identification and resistance testing methods across the network. More data is needed to assess the threat of GC drug resistance to U.S. military members and at-risk populations in regions of military importance.

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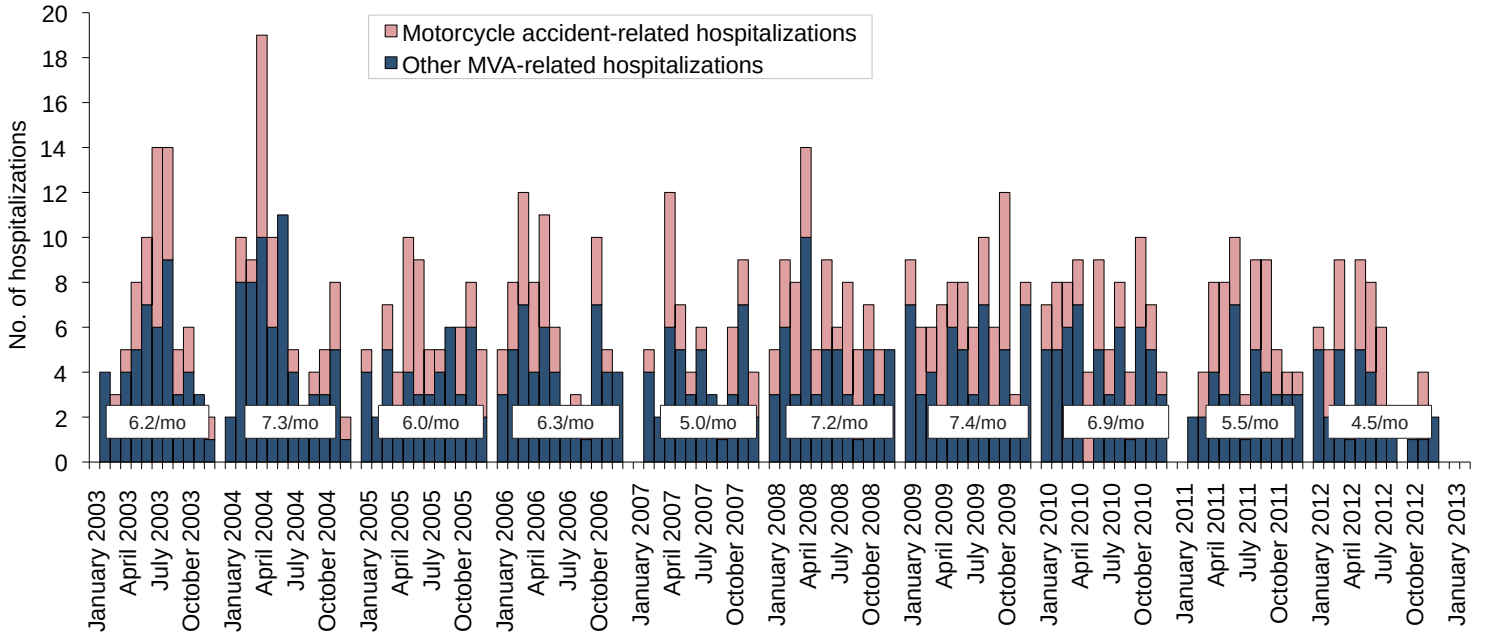
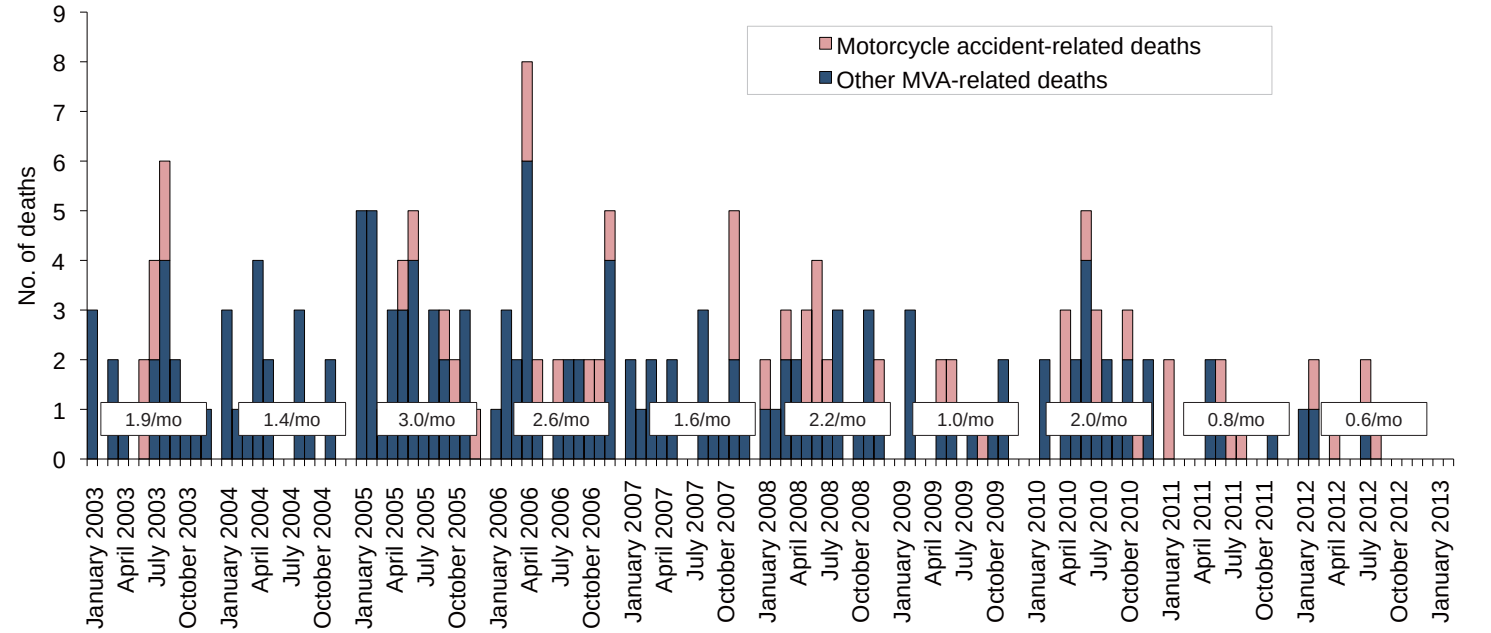
Deployment-Related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003-January 2013 (data as of 18 January 2013)

Hospitalizations outside of the operational theater for motor vehicle accidents occurring in non-military vehicles (ICD-9-CM: E810-E825; NATO Standard Agreement 2050 (STANAG): 100-106, 107-109, 120-126, 127-129)



Note: Hospitalization (one per individual) while deployed to/within 90 days of returning from OEF/OIF/OND. Excludes accidents involving military-owned/special use motor vehicles. Excludes individuals medically evacuated from CENTCOM and/or hospitalized in Landstuhl, Germany within 10 days of another motor vehicle accident-related hospitalization.

Deaths following motor vehicle accidents occurring in non-military vehicles and outside of the operational theater (per the DoD Medical Mortality Registry)[a]



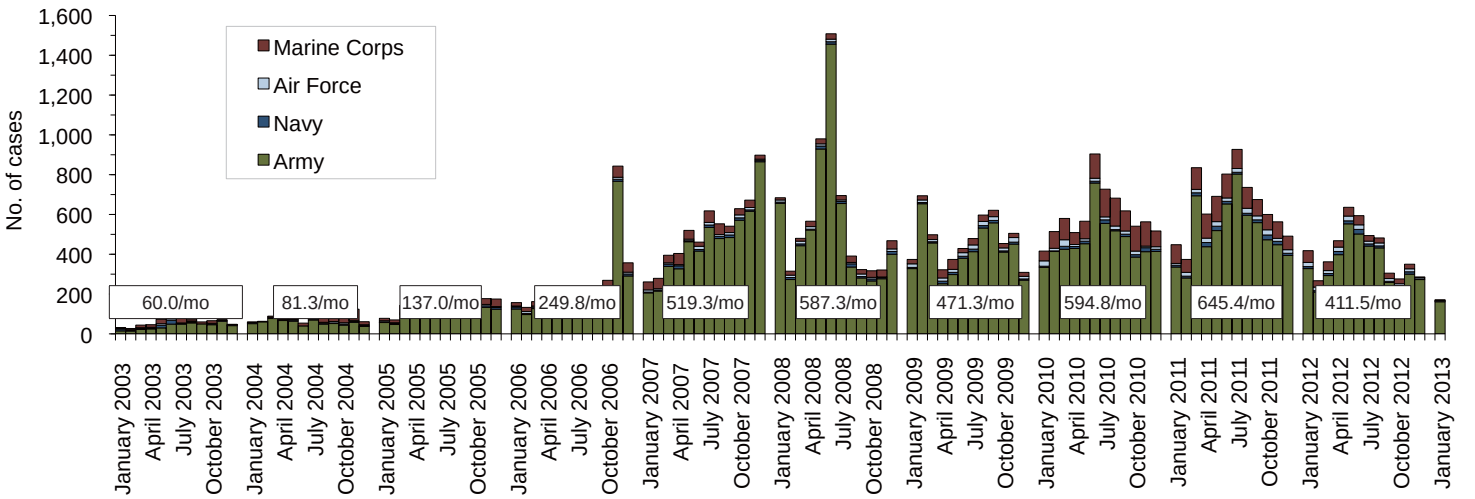
[a]Data pertaining to deaths that occurred since the fall of 2012 is incomplete.

Reference: Armed Forces Health Surveillance Center. Motor vehicle-related deaths, U.S. Armed Forces, 2010. Medical Surveillance Monthly Report (*MSMR*). Mar 11;17(3):2-6.

Note: Death while deployed to/within 90 days of returning from OEF/OIF/OND. Excludes accidents involving military-owned/special use motor vehicles. Excludes individuals medically evacuated from CENTCOM and/or hospitalized in Landstuhl, Germany within 10 days prior to death.

Deployment-Related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003-January 2013 (data as of 18 January 2013)

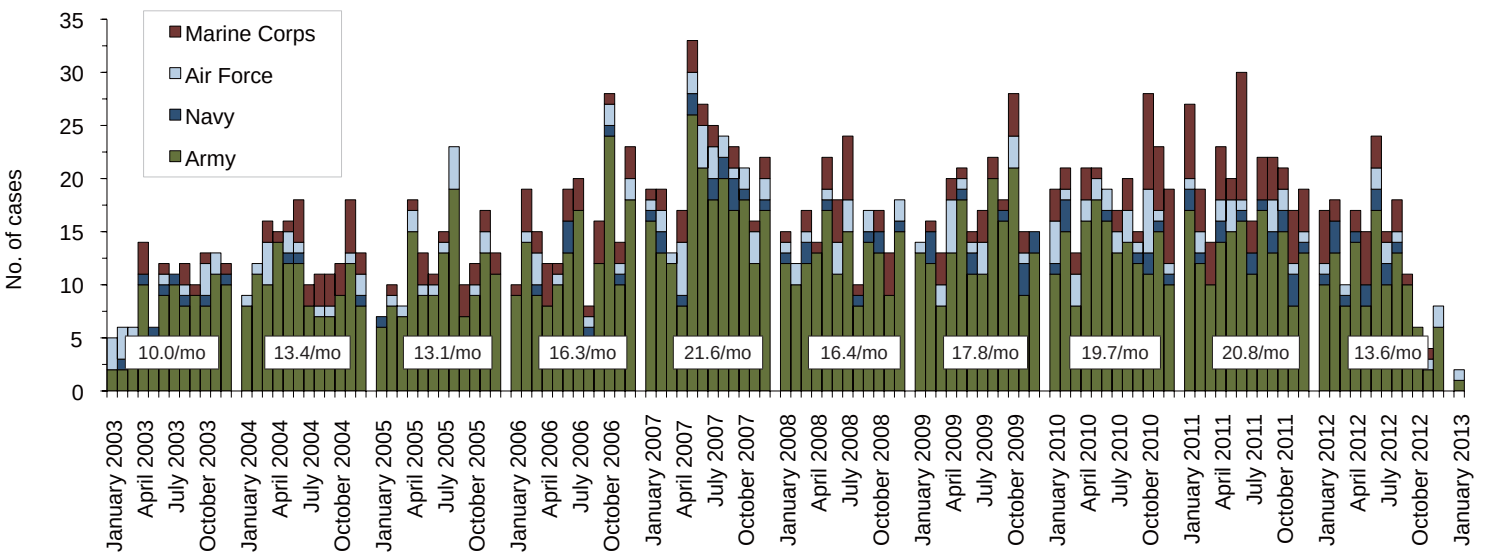
Traumatic brain injury (ICD-9: 310.2, 800-801, 803-804, 850-854, 907.0, 950.1-950.3, 959.01, V15.5_1-9, V15.5_A-F, V15.52_0-9, V15.52_A-F, V15.59_1-9, V15.59_A-F)[a]



Reference: Armed Forces Health Surveillance Center. Deriving case counts from medical encounter data: considerations when interpreting health surveillance reports. *MSMR*. Dec 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 OEF/OIF. (Includes in-theater medical encounters from the Theater Medical Data Store [TMDS] and excludes 4,137 deployers who had at least one TBI-related medical encounter any time prior to OEF/OIF).

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]

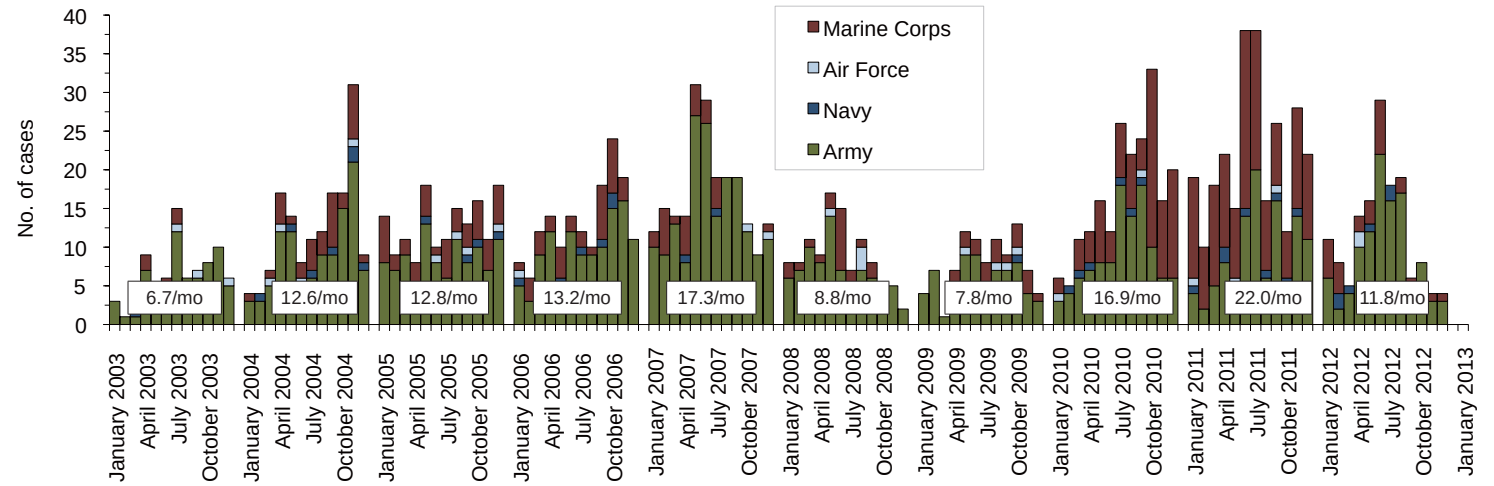


Reference: Isenbarger DW, Atwood JE, Scott PT, et al. Venous thromboembolism among United States soldiers deployed to Southwest Asia. *Thromb Res*. 2006;117(4):379-83.

[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 OEF/OIF.

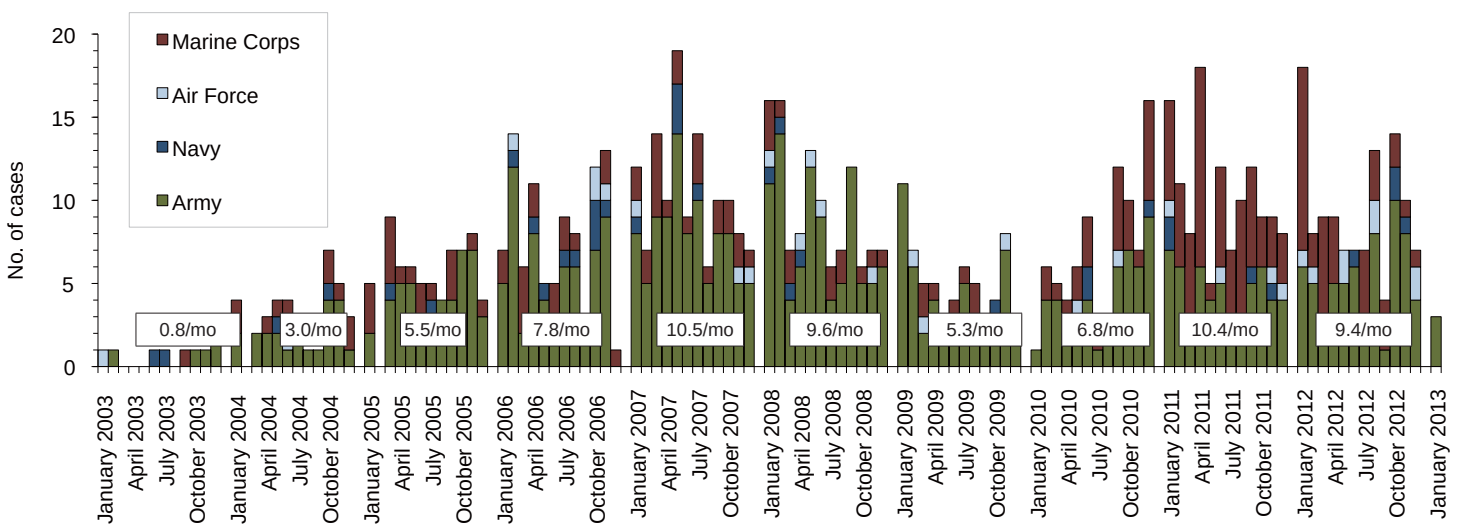
Deployment-Related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003-January 2013 (data as of 18 January 2013)

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*. Jan 2005;11(1):2-6.
[a]Indicator diagnosis (one per individual) during a hospitalization while deployed to/within 365 days of returning from OEF/OIF/OND.

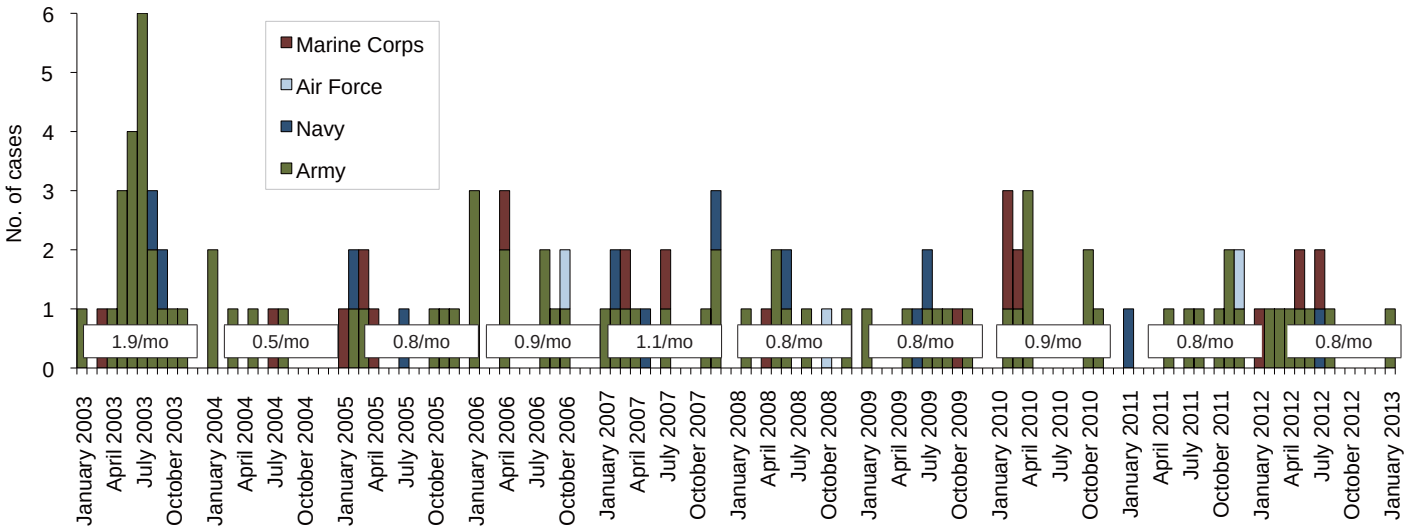
Heterotopic ossification (ICD-9: 728.12, 728.13, 728.19)[b]



Reference: Army Medical Surveillance Activity. Heterotopic ossification, active components, U.S. Armed Forces, 2002-2007. *MSMR*. Aug 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 OEF/OIF/OND.

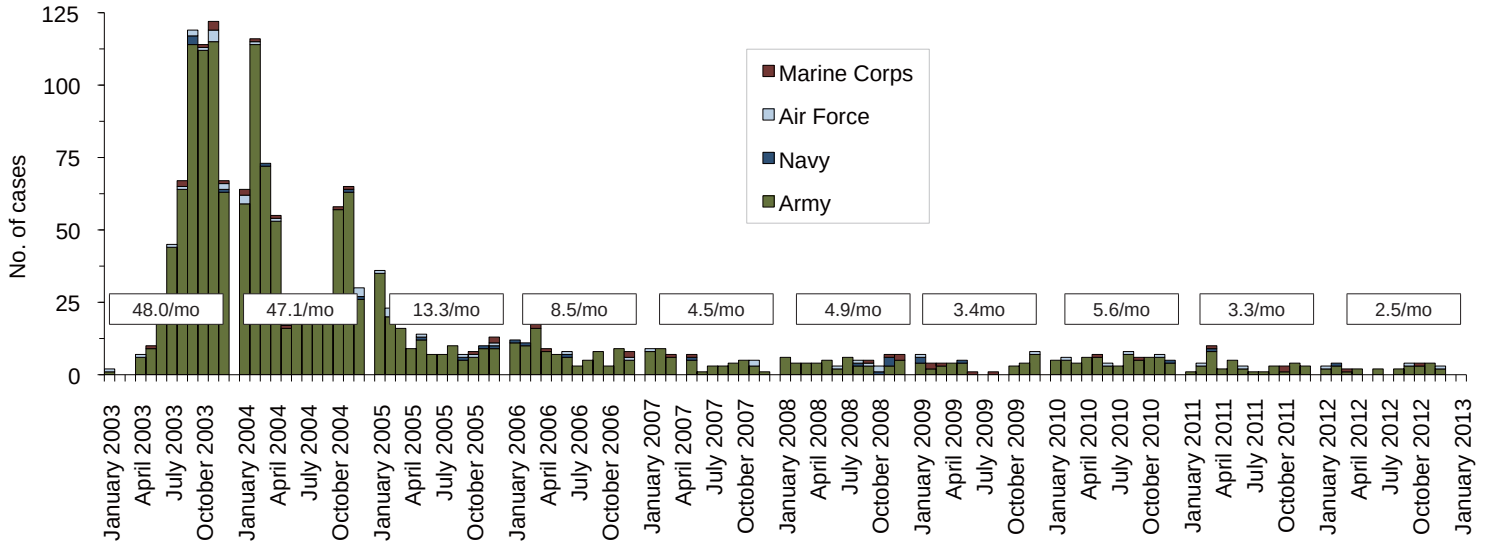
Deployment-Related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003-January 2013 (data as of 18 January 2013)

Severe acute pneumonia (ICD-9: 518.81, 518.82, 480-487, 786.09)[a]



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: severe acute pneumonia. Hospitalizations for acute respiratory failure (ARF)/acute respiratory distress syndrome (ARDS) among participants in Operation Enduring Freedom/Operation Iraqi Freedom, active components, U.S. Armed Forces, January 2003-November 2004. MSMR. Nov/Dec 2004;10(6):6-7.
[a]Indicator diagnosis (one per individual) during a hospitalization while deployed to/within 30 days of returning from OEF/OIF/OND.

Leishmaniasis (ICD-9: 085.0 to 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. Nov/Dec 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.

Medical Surveillance Monthly Report (MSMR)
Armed Forces Health Surveillance Center
11800 Tech Road, Suite 220 (MCAF-CS)
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ISSN 2158-0111 (print)
ISSN 2152-8217 (online)