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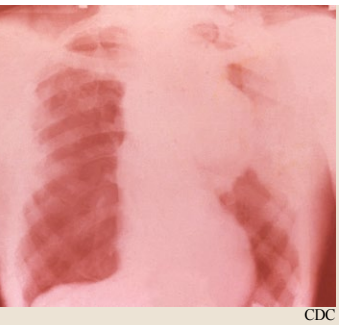
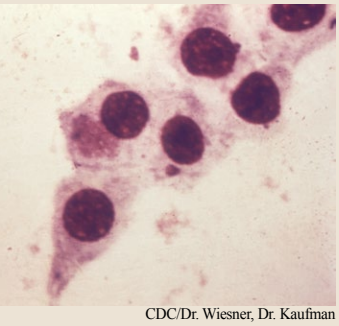


CDC



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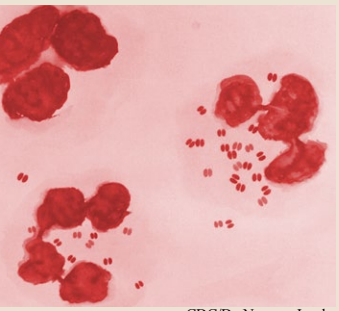

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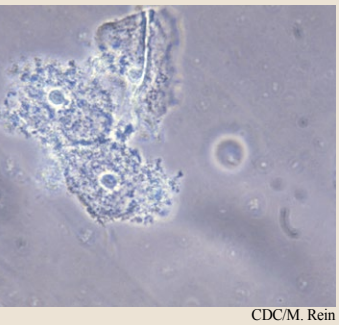


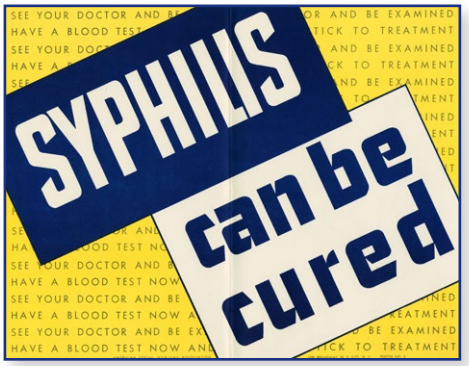
CDC/M. Rein

Sexually Transmitted Infections Issue

Editorial

What's Old Is New Again: Syphilis in the U.S. Army

Eric C. Garges, MD, MPH, MTM&H (LTC, MC, USA)



The history of syphilis in the Army is laced with nearly comedic World War II–era posters warning of venereal disease and marking infections such as syphilis and gonorrhea as the true enemies of Uncle Sam. Syphilis screening, treatment, and prevention campaigns were a focus of the post–World War II Army that achieved moderate success as rates in the Army dropped along with civilian rates across the second half of the 20th century. An increase in rates again in the late 1980s and 1990s in the civilian population would be mirrored in military populations, largely linked to the epidemic of cocaine use in the general population.[1] Not surprisingly, studies again indicated a high evidence of interplay between the military and surrounding civilian communities.[1] Syphilis rates decreased in both military and civilian populations to a nadir in 2000–2001.[2,3] What's old is new again and syphilis has reemerged as a public health threat in the U.S. Questions still remain about the threat of the current epidemic to force health protection and medical readiness within the Army and the Department of Defense (DoD). Issues of surveillance, screening, laboratory diagnostics, and targeting of prevention programs complicate the modern syphilis epidemic for the U.S. Army.

Current burden of disease

In 2014, the CDC reported the highest number of syphilis cases reported in the past 20 years.[3] The expansion of the current epidemic that began in the early 2000s was primarily attributable to increased cases among men who have sex with men (MSM). However, the most recent report from the CDC indicates that an epidemic largely limited to specific risk behaviors and demographic groups in men was making its way across the gender line. The most recent U.S. infection data demonstrated increases in rates among both men (14.4%) and among women (22.7%) nationally. Increases among civilian women are of national concern because of the potential risk of congenital syphilis. The recent increase in syphilis rates is seen in every region of the U.S. and in persons aged 15–44 years. Persons of black, non-Hispanic race/ethnicity have been the most greatly affected, but increased rates are evident among Hispanic, white, and Asian race/ethnicity groups as well.[3,4]

Data from the U.S. Army alone are limited. A 2015 analysis of reportable medical events (RMEs) from the Army Public Health Command showed rates of primary and secondary syphilis during 2011–2013 in the range of 1–2 cases per 10,000 soldiers per year.[5] A similar 2013 study of Army syphilis cases using administrative medical encounter (ICD-9) code data showed rates of 2–4 per 10,000 soldiers, but with rates distinctly increasing between 2010 and 2013 in black, non-Hispanic males.[6] This increase is consistent with the trends seen in the civilian populations. The overall rates of primary and secondary syphilis within the DoD reported by the Armed Forces Health Surveillance Center demonstrated a marked increase in rates across the DoD between 2011 and 2015.[2] In all published reports, the individual services found the highest rates occurred in black, non-Hispanic males **(Table)**. This observation is again consistent with the current civilian epidemic.

Direct comparisons between civilian and Army syphilis infection rates are difficult due to the different demographic proportions in these populations. As discussed earlier, age, race, and gender are significant risk factors. The differences between military and civilian populations with respect to these risk factors make direct comparison difficult. In addition, differences in data collection methodologies make even restricted comparisons tenuous at best.

HIV infection has long been reported as an important predictor for syphilis infection. AFHSC surveillance data, reported from across the DoD, noted that almost one-quarter of cases of syphilis were diagnosed in those co-infected with HIV.[2] Other studies of sexually transmitted infections in the military HIV population have also confirmed the association of syphilis and HIV across the military.[7–10] Although the Army has lower rates of HIV infection than the general U.S. population, the contribution of HIV to the current syphilis epidemic within the military should not be understated.

Screening

Screening for *Treponema pallidum* in the U.S. Army is one of the first examples of increasing medical readiness though infectious disease screening. In the early 20th century, it was estimated that 5% of Army enlistees had evidence of some type of venereal disease.[11] Wasserman developed the first non-treponemal test for syphilis in 1907, but because treatment options were limited, screening for this prevalent infection was not initiated.[12] The widespread use of the newly developed penicillin by the U.S. military,

TABLE. Comparative rates of primary and secondary syphilis reported for 2013 from various sources

Source	Population	Rate per 10,000 person-years			Data
		Total	Males	Black males	
Leamer, 2015[5]	U.S. Army	1.4	1.5	3.7	RMEs and laboratory data
Garges, 2014[6]	U.S. Army	1.9	4.0	5.0	RMEs and medical encounter (ICD-9) data
Armed Forces Health Surveillance Center, 2015[2]	Department of Defense	1.6	2.1[a]	3.3	RMEs; medical encounter; laboratory data
Navy Sexual Health and Responsibility Program, 2015[22]	U.S. Navy	Not available	2.7	5.7[b]	RMEs; medical encounter; laboratory data
Centers for Disease Control and Prevention (U.S. Population)[23,c]	U.S. civilian	1.6	2.8	9.4	RMEs

[a]Age strata 25–29, the age strata with the highest reported rate

[b]Data reported for 2013; however, rates in black, non-Hispanic males increased to 9.2 per 10,000 person-years in 2015.

[c]Age restricted to 20–29 years for general comparison to the Department of Defense population.

RME=reportable medical event

in conjunction with early screening during World War II, led to near eradication of syphilis among active duty Army soldiers.[11] Screening for syphilis in military recruits continued as part of routine medical accession processing across the remainder of the 20th century. Amid decreasing rates of infection across the U.S and a decrease in syphilis diagnoses on accession screening, a 1998 cost-effectiveness analysis demonstrated that syphilis had become both rare and treatable and as such, routine screening at accession should cease.[13] Since that time, the only systematic syphilis screening by Army policy is related to periodic screening of those soldiers known to be HIV positive (as outlined in Army Regulation 600-110, Identification, Surveillance, and Administration of Personnel Infected with Human Immunodeficiency Virus) and the screening for syphilis as part of prenatal screening in pregnancy.

Army medical providers are directed to follow the Centers for Disease Control and Prevention (CDC) treatment guidelines for sexually transmitted diseases (STDs) for routine screening, diagnosis, and treatment. The CDC guidelines include routinely asking about sexual partners and practices at medical encounters in order to make screening decisions for infections such as syphilis. Screening is central to the identification of syphilis. Although there can be well defined, easily identifiable signs of infection, syphilis is often asymptomatic or protean in its presentation. The two most useful tools for accurate diagnosis are the use of an appropriate sexual history coupled with an index of suspicion. Despite its resurgence, syphilis continues to be a relatively infrequent diagnosis in the primary care community.[2,3] This low prevalence in the general population drives the index of suspicion down among primary care providers in the absence of identifying those at high risk with an appropriate sexual history.

Although the current incidence of syphilis in the Army does not support screening at accession, the diagnosis of syphilis in any population requires cultural competence and knowledge of current screening and treatment guidelines. Because syphilis can be a challenging clinical diagnosis or go undetected for long periods of time, continued evaluation and improvement in screening practices should be the focus of any syphilis prevention program.

Surveillance

One difficulty in determining true infection rates for syphilis is surveillance methodology. There are difficulties in data collection, classification, and care-seeking behaviors that challenge the validity of syphilis estimates in the Army. Routine and systematic monitoring for syphilis is complicated by the classification of cases. In order to be classified as a case, the infection must be diagnosed in such a manner as to be reported within the military health system. This requires that a service member seek care for symptoms of disease or for STD screening. Mechanisms of passive surveillance utilizing ICD-9 and ICD-10 codes in administrative records of healthcare encounters tend to overestimate disease incidence because they depend on accurate coding by providers. Use of codes for syphilis during encounters for presumptive therapy for contacts, follow-up visits, or for STD screening may all be incorrectly captured as incident cases of syphilis infection. In addition, syphilis is a laboratory diagnosis and case confirmation requires analyses that are not routinely available at the time of the patient encounter. Any surveillance case definition requiring laboratory confirmation is further complicated by a sequential testing algorithm that is interpreted differently for

those with a first infection of syphilis than for those with a history of treated syphilis diagnosis and treatment, again potentially leading to misclassification of cases. Laboratory diagnostic challenges will be discussed below.

Surveillance efforts for STDs in the Army are also hindered by care-seeking behaviors in soldiers. It is well known to Army practitioners that soldiers may seek care outside of the Military Health System (MHS) for infections or injuries that they do not want to be documented in their military health records. In the case of STDs, public health officials presume that many soldiers routinely seek care at local private clinics or health departments for STD care. Cases of syphilis diagnosed in such settings will almost certainly not be captured in the passive military surveillance programs. The effect of such behavior would be an underestimate of the true magnitude of disease burden.

Laboratory diagnostics

According to the CDC's 2015 STD Treatment Guidelines, syphilis is a diagnosis that requires laboratory diagnosis. The dependence on serologic diagnosis that may not necessarily reflect current infection has generated significant challenges in the management of syphilis.[14] Historically, a sequential pathway of low specificity screening with nontreponemal antibody tests followed by high specificity confirmation with treponemal antibody tests has been the accepted standard of care. Screening and diagnosis of those with a history of prior infection can be more challenging to providers unfamiliar with syphilis management. Therefore, in addition to an often problematic clinical diagnosis, interpretation of lab results may not be intuitive. To complicate the matter, advanced molecular tests allow for alternate testing algorithms which are often misunderstood or misinterpreted by providers.[15] A recent survey of U.S. Army laboratories indicated that a variety of tests and testing pathways are used across the Army.[16] Although there is no evidence that such variation in testing methodologies hinders the treatment efforts for individual patients, the use of multiple diagnostic strategies further complicates an already cloudy diagnostic picture.

Syphilis in the post "Don't Ask, Don't Tell" era

Syphilis, like HIV, is a diagnosis that is often linked to high-risk behaviors of men who have sex with men. Although the "Don't Ask, Don't Tell" (DADT) policy was revoked in 2011, it is still evident that barriers exist to appropriate routine healthcare for gay and bisexual service members. Given that sexual behaviors of gay and bisexual men put them at higher risk for syphilis infection, it is critical both for the well being of the individual service member, as well as for force health protection, that culturally competent medical care be provided within the MHS. The barriers to care in the lesbian, gay, bisexual, and transgender (LGBT) population can be classified into two categories: issues of access to care, and issues of competence of care. There is evidence that the very population at highest risk of syphilis, the MSM community, lacks confidence in MHS providers when seeking assistance related to sexual health.[10,17] This finding permeates not just STD surveillance efforts, but extends to every aspect of sexual health to include wellness, screening, diagnosis, and therapy for sexual health issues. The post-DADT Army may be slow to change the culture of bias against LGBT sexual risk behaviors, which limits the effectiveness of screening and treatment guidelines that are targeted at these specific populations.

There is evidence to suggest that military healthcare providers do not routinely ask about sexual risk behavior, or lack knowledge of the treatment guidelines for the sexual health of MSM, which include screening for syphilis as well as other infections.[17–20] Therefore, the standard of care may not be met for routine care for MSM service members. Programs to educate providers in the MHS to increase culturally competent care are a critical component to reducing STDs in the community. In addition, care for LGBT service members goes beyond screening for STDs as this population has additional needs in the areas of mental and social health.[19]

Conclusion

The reemergence of syphilis in the civilian population, coupled with increases in cases in all services of the military suggests that the time has come to reevaluate the impact of syphilis on force health protection and readiness. The major risk factors for disease are all present within our ranks just as they are in civilian populations. The increase in syphilis burden should come as no surprise to military public health officials. The historical impact of syphilis and other STDs on the health of soldiers should not be underestimated, but is it not yet time to declare syphilis a paramount medical threat to Army readiness. The reemergence of syphilis should provide an opportunity to address concerns about STD screening surveillance, diagnostics, therapy, and prevention within the Army community. The pathogens are old, but public health research and bench science provide new methods and modalities to reduce the disease burdens in our populations.

Army senior leadership should continue to support studies of sexual networks and other applied research to better understand behavioral risks that are influenced by military service. The behaviors and social context of soldiers, sailors, airmen, and Marines are unique. Transmission of syphilis, as with other STDs, depends not only on the behaviors and risks of the individual, but also on the attributes, risks, and behaviors of their sexual partners.[21] Application of new methodologies, interventions, and prevention strategies requires a detailed knowledge of the context of the sexual interactions within military populations.

Because there is no single paradigm that can be applied to reduce STD risk in an ever-changing society, Army public health officers should increase evidence-based prevention efforts with targeting that specifically addresses identified risk factors in communities.[20] Generic messaging is not likely to be effective in reducing the burden of STDs within the ranks. In addition, Army public health coordination with local and regional civilian public health institutions will increase the efficiency of prevention programs as well as deliver military healthcare messaging to beneficiaries, even if care is sought outside of the MHS.

Surveillance institutions should evaluate the current status of case definitions. Incorporating the complexities of laboratory diagnosis may improve the accuracy of case

classification and the validity of our syphilis estimates in the MHS. Improvement in the accuracy of coding of syphilis medical encounters would increase the validity of administratively collected surveillance data. Programs to improve provider knowledge of syphilis diagnostics and staging would support this effort as well, although use of administrative data for syphilis surveillance will likely continue to suffer this limitation.

Finally, military health providers must have the necessary skills and confidence to take a complete sexual history from a diverse group of patients and act in accordance with the accepted clinical practice guidelines. A cultural change is under way within the Army toward a reduction in biases against LGBT service members. However, as with most culture change, progress is slow. Army healthcare providers can foster the change and improve the health of soldiers by actively working to improve their cultural competence in initiating conversations about sexual health across the force.

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the official policy of the Army Public Health Center (Provisional), Department of the Army, Department of Defense, or the U.S. Government.

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REFERENCES

1. McKee KT, Jr., Burns WE, Russell LK, et al. Early syphilis in an active duty military population and the surrounding civilian community, 1985–1993. *Mil Med.* 1998;163(6):368–376.
2. Clark LL, Hunt DJ. Incidence of syphilis, active component, U.S. Armed Forces, 1 January 2010 through 31 August 2015. *MSMR.* 2015;22(9):8–16.
3. Centers for Disease Control and Prevention. 2014 Sexually Tranmitted Disease Surveillance. 2015; Syphilis Statistical Report for 2014. Available at: www.cdc.gov/std/stats14/syphilis.htm. Accessed on 2 February 2016.
4. Patton ME, Su JR, Nelson R, Weinstock H, Centers for Disease Control and Prevention. Primary and secondary syphilis—United States, 2005–2013. *MMWR Morb Mortal Wkly Rep.* 2014;63(18):402–406.
5. Leamer NK CN, Jordan NN, Pacha LA. Syphilis among U.S. Army active duty personnel identified at Army medical treatment facilities, 2011–2013. Paper presented at: International Union Against Sexually Transmistted Diseases Conference 2015; Barcelona, Spain.
6. Garges E, Jordan N, Leamer N, Clark L, Gaydos, JC. Syphilis and the U.S. Army, new concerns for an old disease. STD Prevention Science; 2014; Atlanta, GA.
7. Tzeng JS, Clark LL, Garges EC, Otto JL. Epidemiology of sexually transmitted infections among human immunodeficiency virus positive United States military personnel. *J Sex Transm Dis.* 2013;2013:610258.
8. Ganesan A, Fieberg A, Agan BK, et al. Results of a 25-year longitudinal analysis of the serologic incidence of syphilis in a cohort of HIV-infected patients with unrestricted access to care. *Sex Transm Dis.* 2012;39(6):440–448.
9. Ganesan A, Mesner O, Okulicz JF, et al. A single dose of benzathine penicillin G is as effective as multiple doses of benzathine penicillin G for the treatment of HIV-infected persons with early syphilis. *Clin Infect Dis.* 2015;60(4):653–660.
10. Hakre S, Armstrong AW, O'Connell RJ, Michael NL, Scott PT, Brett-Major DM. A pilot online survey assessing risk factors for HIV acquisition in the Navy and Marine Corps, 2005–2010. *J Acquir Immune Defic Syndr.* 2012;61(2):125–130.
11. Brown WJ. *Syphilis and Other Venereal Diseases.* Cambridge, MA: Harvard University Press; 1970.
12. Morabia A, Zhang FF. History of medical screening: from concepts to action. *Postgrad Med J.* 2004;80(946):463–469.
13. Clark KL, Kelley PW, Mahmoud RA, et al. Cost-effective syphilis screening in military recruit applicants. *Mil Med.* 1999;164(8):580–584.
14. Tuddenham S, Ghanem KG. Emerging trends and persistent challenges in the management of adult syphilis. *BMC Infect Dis.* 2015;15:351.
15. Centers for Disease Control and Prevention. Discordant results from reverse sequence syphilis screening—five laboratories, United States, 2006–2010. *MMWR Morb Mortal Wkly Rep.* 2011;60(5):133–137.
16. Leamer NK, Jordan NN, Nauschuetz WF, Garges EC, Gaydos JC. Survey of sexually transmitted disease laboratory methods in U.S. Army laboratories, 2012 (publication pending). U.S. Army Public Health Command; 2016.
17. Ramirez MH, Rogers SJ, Johnson HL, et al. If we ask, what they might tell: clinical assessment lessons from LGBT military personnel post-DADT. *J Homosex.* 2013;60(2-3):401–418.
18. Tong RL, Lane J, McCleskey P, Montenegro B, Mansalis K. A pilot study describing knowledge and practices in the health care of men who have sex with men by U.S. Air Force primary care providers. *Mil Med.* 2013;178(2):e248–e254.
19. Pacha LA, Hakre S, Myles O, et al. Centralized HIV program oversight. *Medicine (Baltimore).* 2015;94(46):e2093.
20. Gaydos JC, McKee KT Jr, Faix DJ. Sexually transmitted infections in the military: new challenges for an old problem. *Sex Transm Infect.* 2015;91(8):536–537.
21. Aral SO. Sexual network patterns as determinants of STD rates: paradigm shift in the behavioral epidemiology of STDs made visible. *Sex Transm Dis.* 1999;26(5):262–264.
22. Riegodedios A, MacDonald MR, Beckett CG, Rompalo A. Syphilis in the Navy 2010–2015. 2016; www.med.navy.mil/sites/nmcphc/health-promotion/Pages/webinars.aspx
23. Prevention USCfDCa. CDC Wonder Database–Sexually Transmitted Disease Morbidity. 2016; http://wonder.cdc.gov/std.html. Accessed on 19 February 2016.

Use of Quadrivalent Human Papillomavirus Vaccine and the Prevalence of Antibodies to Vaccine-targeted Strains Among Female Service Members Before and After Vaccination

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The quadrivalent human papillomavirus vaccine (HPV4) has been shown to generate a robust immune response among fully vaccinated individuals; however, among U.S. service members, HPV vaccine completion rates are low. This study compared the immunogenicity of HPV4 vaccine among partially and fully vaccinated service members at 4–6 years post-vaccination. A random sample was obtained of 2,091 female service members, aged 17–26 years, who received 1–3 HPV4 doses during 2006–2012, stratified by number of doses (one, two, or three). Pre- and post-immunization sera from these service members were tested for antibodies to the HPV strains covered by the vaccine. Prior to immunization 42% were seropositive for HPV strain 6; 34% for strain 11; 29% for strain 16; and 16% for strain 18. Among those naive to all four strains prior to immunization, there was 100% seroconversion after one, two, or three doses. The results indicate that many service members had already been exposed to strains of HPV prior to receiving the vaccine; however, seropositivity prevalence was lower for the oncogenic HPV strains 16 and 18. The data demonstrate sustained immunogenicity after a single dose of vaccine, with modest improvement with successive doses for all strains except 18.

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) diagnosed in U.S. military service members. An estimated 304,021 incident cases of HPV were diagnosed during 2000–2012 among active component U.S. service members at a rate of 175.5 per 10,000 person-years.[1] Although the majority of HPV cases are asymptomatic and may clear within 1–2 years, persistent HPV infection has been established as a necessary cause of all cervical cancers.[2] HPV strains 16 and 18 are considered high-risk HPVs and are collectively responsible for more than 68% of cervical cancer cases worldwide.[2] HPV infection is also implicated in a sizeable proportion of anogenital and oral cancers, although these cancers are less prevalent than cervical cancer.[3] Infection with low-risk non-oncogenic HPV strains (primarily strains 6 and 11) is associated with genital warts.[2]

Currently, three vaccines are approved by the Food and Drug Administration to prevent HPV infection: a bivalent vaccine providing protection against the two oncogenic strains 16 and 18; a quadrivalent HPV vaccine (HPV4) providing protection from strains 16 and 18 as well as the two non-oncogenic HPV subtypes 6 and 11; and a newly licensed nonavalent vaccine, which adds protection for five additional oncogenic strains. All three vaccines are administered in a three-dose series. Even though the three-dose regimen provides nearly complete protection against HPV16 and HPV18, in the U.S., only 12% and 19% of female adolescents among commercial and Medicaid plans, respectively, complete the series.[4] Limited rationale supports the recommended three-dose schedule. A limited number of studies compared three-dose schedules of HPV4 to one- or two-dose schedules and showed that immune responses were comparable, even though results varied by age groups and follow-up time.[5–7] Dobson et al. compared antibody levels for HPV16 and HPV18 after a two-dose schedule (0 and 6 months) and a three-dose schedule (0, 2, and 6 months) and found that the two doses among girls (aged 9–13 years) were non-inferior to those among young women (aged 16–26 years) who received three doses.[6] Safaeian et al. found that HPV16 and HPV18 antibody titers remained stable and higher when compared to naturally infected women from 6–48 months after receiving only one dose.[8] More research is needed to evaluate the effectiveness of alternatives to the three-dose schedule.

Of the three HPV vaccines, the quadrivalent HPV vaccine is currently the most widely used by the U.S. military. Consistent with the Advisory Committee on Immunization Practices (ACIP) recommendations, the Department of Defense (DoD) recommends routine vaccination of eligible service members aged 17–26 years with the three-dose series at 0, 2, and 6 months.[2,9–11] As in the civilian population, across DoD, only 22.5% of eligible service members initiated the series, and of those, only 39.1% completed the full three-dose series as of June 2011.[12] Because the immunogenicity of fewer doses of the HPV4 vaccine has not been studied extensively, the state of protection of the largely undervaccinated U.S. service members is unknown. Consequently, the effectiveness of the DoD's HPV vaccine program is also unknown.

This study was designed to investigate whether there is a difference in the immune response to each of the four HPV4 vaccine strains (6, 11, 16, 18) among female service members who received one dose, two doses, or the full three-dose series 4–6 years following the last dose received. The findings of this study will inform DoD policy aimed at optimizing the HPV4 vaccine schedule to reduce the burden of HPV-related infections.

METHODS

A retrospective cohort analysis was performed using data from the Defense Medical Surveillance System (DMSS), a database of medical encounters, immunization, demographic, and service records for U.S. military service members. Immunization records were obtained of all female active component service members, aged 17–26 years, who had received one to three doses of HPV4 during 2006–2012. Any service members with documented immunization with the bivalent HPV vaccine or with more than three doses of HPV4 were excluded. This group of potential study subjects was further restricted to those having pre- and post-immunization serum specimens in the Department of Defense Serum Repository (DoDSR). To meet the inclusion criteria, the pre-immunization serum specimen had to have been drawn within 1 year prior to the first HPV4 dose and the post-immunization specimen drawn 4–6 years after the last HPV4 dose. Potential study subjects meeting these criteria were then stratified by the total number of HPV4 doses received, and a random sample was obtained of 411 subjects who received one dose, 420 subjects who received two doses, and 1,260 subjects who completed the three-dose series. Total sample size was 2,091 subjects.

Demographic and military service data, including age, race/ethnicity, and education level were obtained from DMSS for each subject. Additional data on the timing of HPV4 dose receipt, and any medical encounters prior to HPV4 immunization through the end of the study period containing a diagnosis of a sexually transmitted infection (STI) were obtained from DMSS. The list of ICD-9 codes used to identify STI diagnoses is shown in **Table 1**.

The pre- and post-immunization serum specimens (0.5 ml aliquots) for each subject were retrieved from the DoDSR, labeled with randomly generated unique identifiers, and shipped to The Johns Hopkins University for HPV serological testing. Enzyme-linked immunosorbent assays (ELISA) to detect antibodies to virus-like particles (VLPs) of HPV were used to test for seropositivity to each of the four HPV strains (6, 11, 16, 18) for which the HPV4 vaccine was designed to provide protection. For each specimen, the dichotomous results for each strain, seropositive or seronegative, were provided back to AFHSB, using the unique specimen identifier, for linkage with each subject's demographic, immunization, and medical encounter data.

The percentage of subjects who tested positive by each HPV strain prior to receiving their first HPV4 immunization was calculated and stratified by age group in 2-year increments, education (high school, some college, college, unknown), service, race/ethnicity (non-Hispanic white, non-Hispanic black, non-Hispanic other race, Hispanic), time to second and third doses, and history of an STI diagnosis (none, diagnosis before first HPV4 dose, diagnosis after first HPV4 dose). The percentage of subjects who tested negative for all four strains of HPV in their pre-immunization serum and were seropositive for all four strains in their post-immunization serum were calculated by the number of doses received. The binomial proportion of those who were positive for seroconversion were calculated for those receiving one, two, and three doses in each stratified demographic category. The 95% CIs of the binomial proportions were calculated using the Agresti-Coull method, and Fisher's exact test was used to test for statistically significant differences between the proportions for the number of doses. Similar analyses were performed for each HPV strain independently. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC), and a P value less than 0.05 was considered statistically significant.

RESULTS

Table 2 shows the number and percentage of study subjects by various demographic factors. Except for those aged 17–18 years, who represented only 6.6% of the study population, the older age groups consisted of roughly equivalent proportions of the subjects, ranging from 21.2% to 25.3%. Most subjects' highest level of education at the time of first dose was high school (79.2%). Viewed by race/ethnicity, the greatest percentage of study subjects were non-Hispanic whites (49.1%). Air Force service members represented 51.7% of the subjects.

Among the 1,680 subjects receiving at least two doses of the HPV4 vaccine, 94.0% received their second dose within 6 months of the first dose. Among the 1,260 subjects who received all three doses, 86.7% received their last dose within 6 months of the second dose **(Table 2)**.

A large percentage of subjects were diagnosed with an STI **(Table 1)** prior to receiving their first HPV4 dose (32.9%) or after their first HPV4 dose (24.5%) **(Table 2)**.

The number and percentage of subjects who were seropositive for at least

TABLE 1. ICD-9 codes used to identify sexually transmitted infections (STIs)

STI	ICD-9 codes
Human papillomavirus	078.1,[a] 079.4, 795.05, 795.09, 795.15, 795.19, 796.75, 796.79
Chlamydia	099.41, 099.5
Genital herpes simplex virus	054.1
Gonorrhea	098.x
Syphilis (excludes congenital)	091.x–097.x

[a]Code for viral warts, included to increase sensitivity of case definition, because the majority of genital warts have been found to be due to human papillomavirus.

TABLE 2. Demographic and vaccine dose characteristics, seropositivity for the four human papillomavirus (HPV) strains prior to first vaccine dose, and sexually transmitted disease diagnoses, among the cohort of vaccine recipients

			Positive for HPV strain prior to first HPV4 immunization										
	Cohort		Strain 6		Strain 11		Strain 16		Strain 18		Positive for one or more strains		
	N	Col %	N	%	N	%	N	%	N	%	N	%	p-value[a]
All	2,091	100.0	878	42.0	713	34.1	596	28.5	331	15.8	1,299	62.1	
No. of doses													0.4777
1	411	19.7	198	48.2	165	40.1	147	35.8	59	14.4	265	64.5	
2	420	20.1	167	39.8	133	31.7	117	27.9	66	15.7	254	60.5	
3	1,260	60.3	513	40.7	415	32.9	332	26.3	206	16.3	780	61.9	
Age (years)													0.0003
17–18	138	6.6	39	28.3	38	27.5	26	18.8	19	13.8	68	49.3	
19–20	443	21.2	148	33.4	122	27.5	78	17.6	84	19.0	250	56.4	
21–22	527	25.2	249	47.3	218	41.4	179	34.0	78	14.8	347	65.8	
23–24	528	25.3	242	45.8	183	34.7	163	30.9	80	15.2	339	64.2	
25–26	455	21.8	200	44.0	152	33.4	150	33.0	70	15.4	295	64.8	
Service													
Army	438	21.0	207	47.3	191	43.6	152	34.7	67	15.3	289	66.0	<0.0001
Navy	475	22.7	207	43.6	149	31.4	134	28.2	65	13.7	280	59.0	
Air Force	1,080	51.7	433	40.1	341	31.6	286	26.5	180	16.7	673	62.3	
Marine Corps	44	2.1	16	36.4	14	31.8	10	22.7	10	22.7	26	59.1	
Coast Guard	54	2.6	15	27.8	18	33.3	14	25.9	9	16.7	31	57.4	
Education													0.1556
High school	1,655	79.2	703	42.5	569	34.4	464	28.0	261	15.8	1,045	63.1	
Some college	100	4.8	37	37.0	31	31.0	26	26.0	13	13.0	61	61.0	
College graduate	288	13.8	125	43.4	103	35.8	99	34.4	47	16.3	169	58.7	
Unknown	48	2.3	13	27.1	10	20.8	7	14.6	10	20.8	24	50.0	
Race/ethnicity													0.0056
Non-Hispanic White	1,026	49.1	418	40.7	328	32.0	292	28.5	175	17.1	643	62.7	
Non-Hispanic Black	465	22.2	224	48.2	180	38.7	146	31.4	69	14.8	314	67.5	
Non-Hispanic Other	313	15.0	123	39.3	97	31.0	83	26.5	51	16.3	179	57.2	
Hispanic	287	13.7	113	39.4	108	37.6	75	26.1	36	12.5	163	56.8	
Time to second dose													0.6756
Within 2 months	184	11.0	74	40.2	66	35.9	49	26.6	38	20.7	115	62.5	
Within 6 months	1,394	83.0	563	40.4	446	32.0	368	26.4	213	15.3	854	61.3	
More than 6 months	102	6.1	43	42.2	36	35.3	32	31.4	21	20.6	65	63.7	
Time to third dose													0.5224
Within 2 months	8	0.6	1	12.5	1	12.5	1	12.5	2	25.0	3	37.5	
Within 6 months	1,085	86.1	445	41.0	367	33.8	293	27.0	173	15.9	676	62.3	
More than 6 months	167	13.3	67	40.1	47	28.1	38	22.8	31	18.6	101	60.5	
STI diagnosis													<0.0001
No STI diagnosis	892	42.7	315	35.3	270	30.3	206	23.1	146	16.4	492	55.2	
STI diagnosis prior to first dose	687	32.9	349	50.8	281	40.9	259	37.7	96	14.0	487	70.9	
STI diagnosis after first dose	512	24.5	214	41.8	162	31.6	131	25.6	89	17.4	320	62.5	

[a]Calculated using chi-square or Fisher's exact test

TABLE 3. Seroconversion among vaccine recipients who tested negative for all four human papillomavirus (HPV) strains prior to immunization

	No. of doses received	No. negative prior to HPV4 immunization		No. who seroconverted to all four strains			
		N	Col %	N	%	95% CI[a]	p-value[b]
All							
	1	146	18.4	146	100.0	96.9, 100.0	1.0
	2	166	21.0	166	100.0	97.3, 100.0	
	3	480	60.6	479	99.8	98.7, 100.0	
Age (years)							
17–18	1	24	34.3	24	100.0	83.7, 100.0	1.0
	2	16	22.9	16	100.0	77.3, 100.0	
	3	30	42.9	30	100.0	86.5, 100.0	
19–20	1	40	20.7	40	100.0	89.6, 100.0	1.0
	2	54	28.0	54	100.0	92.1, 100.0	
	3	99	51.3	98	99.0	94.0, 100.0	
21–22	1	29	16.1	29	100.0	86.1, 100.0	1.0
	2	37	20.6	37	100.0	88.8, 100.0	
	3	114	63.3	114	100.0	96.1, 100.0	
23–24	1	28	14.8	28	100.0	85.7, 100.0	1.0
	2	34	18.0	34	100.0	87.9, 100.0	
	3	127	67.2	127	100.0	96.5, 100.0	
25–26	1	25	15.6	25	100.0	84.2, 100.0	1.0
	2	25	15.6	25	100.0	84.2, 100.0	
	3	110	68.8	110	100.0	96.0, 100.0	
Service							
Army	1	41	27.5	41	100.0	89.8, 100.0	1.0
	2	45	30.2	45	100.0	90.6, 100.0	
	3	63	42.3	63	100.0	93.1, 100.0	
Navy	1	65	33.3	65	100.0	93.3, 100.0	1.0
	2	73	37.4	73	100.0	94.0, 100.0	
	3	57	29.2	57	100.0	92.5, 100.0	
Air Force	1	31	7.6	31	100.0	86.9, 100.0	1.0
	2	34	8.4	34	100.0	87.9, 100.0	
	3	342	84.0	341	99.7	98.2, 100.0	
Marine Corps	1	5	27.8	5	100.0	51.1, 100.0	1.0
	2	4	22.2	4	100.0	45.4, 100.0	
	3	9	50.0	9	100.0	65.5, 100.0	
Coast Guard	1	4	17.4	4	100.0	45.4, 100.0	1.0
	2	10	43.5	10	100.0	67.9, 100.0	
	3	9	39.1	9	100.0	65.5, 100.0	
Education							
High school	1	119	19.5	119	100.0	96.2, 100.0	1.0
	2	131	21.5	131	100.0	96.6, 100.0	
	3	360	59.0	359	99.7	98.3, 100.0	
Some college	1	6	15.4	6	100.0	55.7, 100.0	1.0
	2	6	15.4	6	100.0	55.7, 100.0	
	3	27	69.2	27	100.0	85.2, 100.0	
College graduate	1	15	12.6	15	100.0	76.1, 100.0	1.0
	2	20	16.8	20	100.0	81.0, 100.0	
	3	84	70.6	84	100.0	94.8, 100.0	
Unknown	1	6	25.0	6	100.0	55.7, 100.0	1.0
	2	9	37.5	9	100.0	65.5, 100.0	
	3	9	37.5	9	100.0	65.5, 100.0	
Race/ethnicity							
Non-Hispanic White	1	65	17.0	65	100.0	93.3, 100.0	1.0
	2	66	17.2	66	100.0	93.4, 100.0	
	3	252	65.8	251	99.6	97.6, 100.0	
Non-Hispanic Black	1	28	18.5	28	100.0	85.7, 100.0	1.0
	2	36	23.8	36	100.0	88.5, 100.0	
	3	87	57.6	87	100.0	94.9, 100.0	
Non-Hispanic Other	1	25	18.7	25	100.0	84.2, 100.0	1.0
	2	29	21.6	29	100.0	86.1, 100.0	
	3	80	59.7	80	100.0	94.5, 100.0	
Hispanic	1	28	22.6	28	100.0	85.7, 100.0	1.0
	2	35	28.2	35	100.0	88.2, 100.0	
	3	61	49.2	61	100.0	92.9, 100.0	

[a]Calculated using Agresti-Coull method
[b]Calculated using Fisher's exact test

one of the HPV strains prior to receiving the first dose of the HPV4 vaccine are also shown in **Table 2**. The highest pre-vaccination seroprevalence occurred with strain 6 (42.0%). Seroprevalence declined monotonically to a low of 15.8% with strain 18. Overall, 62.1% of the subjects were seropositive for at least one strain of HPV prior to immunization. Seroprevalence for at least one strain of HPV increased across the age groups from 49.3% of those aged 17–18 years to 64.8% of those aged 25–26 years. Army service members had a significantly higher seroprevalence (66.0%) for at least one strain of HPV prior to immunization compared with Coast Guard members (57.4%). The percentage of subjects who were seropositive for an HPV strain prior to immunization was higher among those with a diagnosis of an STI prior to receiving the initial HPV4 dose (70.9%), compared with those never diagnosed with an STI (55.2%) or those diagnosed with an STI after the first dose (62.5%).

Among those who were seronegative to all four covered strains of HPV prior to receiving the HPV4 vaccine, seroconversion was virtually complete for all four strains, regardless of the number of doses received **(Table 3)**. All 146 subjects who received only one dose seroconverted for all four strains following immunization. All 166 subjects receiving two doses seroconverted following immunization, and 479 of 480 subjects who received all three doses seroconverted following immunization. There were no statistically significant differences between seroconversion ratios by number of doses when the data were stratified by age, education, or race/ethnicity.

Focusing on those subjects who were seronegative to strain 6 prior to HPV4 immunization, seroconversion increased with increasing numbers of doses **(Table 4)**. For subjects receiving only one dose, 92.0% seroconverted, while seroconversion increased to 96.8% of those receiving two doses, and to 98.1% of those receiving three doses. Results stratified by demographic groups are shown in **Table 4**.

Seroconversion among those subjects naive to strain 11 prior to HPV4 immunization is shown in **Table 5**. For those receiving one dose, 97.6% seroconverted. This increased slightly to 99.7% and 99.4%

TABLE 4. Seroconversion among vaccine recipients who tested negative for human papillomavirus (HPV) strain 6 prior to immunization

	No. of doses received	No. negative prior to HPV4 immunization		No. who seroconverted to HPV strain 6			
		N	Col %	N	%	95% CI[a]	p-value[b]
All							
	1	213	17.6	196	92.0	87.5, 95.0	<0.0001
	2	253	20.9	245	96.8	93.8, 98.5	
	3	747	61.6	733	98.1	96.9, 98.9	
Age (years)							
17–18	1	30	30.3	28	93.3	77.6, 99.2	0.2597
	2	27	27.3	26	96.3	80.2, 100.0	
	3	42	42.4	42	100.0	90.0, 100.0	
19–20	1	57	19.3	50	87.7	76.5, 94.2	0.0240
	2	80	27.1	78	97.5	90.8, 99.7	
	3	158	53.6	153	96.8	92.6, 98.8	
21–22	1	45	16.2	41	91.1	78.7, 97.0	0.0111
	2	53	19.1	50	94.3	84.0, 98.7	
	3	180	64.8	178	98.9	95.8, 100.0	
23–24	1	38	13.3	35	92.1	78.5, 98.0	0.0521
	2	45	15.7	44	97.8	87.4, 100.0	
	3	203	71.0	200	98.5	95.5, 99.7	
25–26	1	43	16.9	42	97.7	86.8, 100.0	1.0
	2	48	18.8	47	97.9	88.1, 100.0	
	3	164	64.3	160	97.6	93.7, 99.3	
Service							
Army	1	62	26.8	60	96.8	88.3, 99.8	0.2996
	2	74	32.0	70	94.6	86.5, 98.3	
	3	95	41.1	94	99.0	93.7, 100.0	
Navy	1	90	33.6	82	91.1	83.2, 95.7	0.3568
	2	100	37.3	96	96.0	89.8, 98.8	
	3	78	29.1	74	94.9	87.2, 98.4	
Air Force	1	48	7.4	41	85.4	75.5, 93.1	0.0001
	2	56	8.7	56	100.0	92.3, 100.0	
	3	543	83.9	534	98.3	96.8, 99.2	
Marine Corps	1	7	25.0	7	100.0	59.6, 100.0	1.0
	2	8	28.6	8	100.0	62.8, 100.0	
	3	13	46.4	13	100.0	73.4, 100.0	
Coast Guard	1	6	15.4	6	100.0	55.7, 100.0	1.0
	2	15	38.5	15	100.0	76.1, 100.0	
	3	18	46.2	18	100.0	79.3, 100.0	
Education							
High school	1	175	18.4	160	91.4	86.3, 94.8	<0.0001
	2	199	20.9	192	96.5	92.8, 98.4	
	3	578	60.7	566	97.9	96.4, 98.9	
Some college	1	11	17.5	11	100.0	70.0, 100.0	1.0
	2	12	19.1	12	100.0	71.8, 100.0	
	3	40	63.5	38	95.0	82.6, 99.5	
College graduate	1	19	11.7	17	89.5	67.4, 98.3	0.0135
	2	29	17.8	28	96.6	81.4, 100.0	
	3	115	70.6	115	100.0	96.1, 100.0	
Unknown	1	8	22.9	8	100.0	62.8, 100.0	1.0
	2	13	37.1	13	100.0	73.4, 100.0	
	3	14	40.0	14	100.0	74.9, 100.0	
Race/ethnicity							
Non-Hispanic White	1	95	15.6	87	91.6	84.0, 95.9	0.0006
	2	114	18.8	109	95.6	89.9, 98.4	
	3	399	65.6	394	98.8	97.0, 99.6	
Non-Hispanic Black	1	43	17.8	42	97.7	86.8, 100.0	0.0545
	2	49	20.3	47	95.9	85.5, 99.7	
	3	149	61.8	149	100.0	97.0, 100.0	
Non-Hispanic Other	1	33	17.4	29	87.9	72.1, 95.8	0.0656
	2	40	21.1	40	100.0	89.6, 100.0	
	3	117	61.6	111	94.9	89.0, 97.9	
Hispanic	1	42	24.1	38	90.5	77.4, 96.8	0.2576
	2	50	28.7	49	98.0	88.5, 100.0	
	3	82	47.1	79	96.3	89.4, 99.2	

[a]Calculated using Agresti-Coull method
[b]Calculated using Fisher's exact test

among those receiving two and three doses, respectively. Results stratified by demographic groups are also shown.

Table 6 shows the seroconversion prevalence among subjects who were negative to strain 16 prior to receiving the first HPV4 dose. Those who received just one dose had an 89.8% seroconversion ratio. Seroconversion increased to 97.0% among those who received two doses, and 98.8% among those receiving three doses. This increase in seroconversion with increasing doses was statistically significant.

The greatest numbers of subjects were seronegative to strain 18 prior to HPV4 immunization. Among this group, there were no statistically significant differences in seroconversion ratios by number of doses **(Table 7)**. The proportion of subjects naive to strain 18 who seroconverted following HPV4 immunization was substantially lower (80.5%) than the proportion of subjects who seroconverted to the other strains (96.8% for strain 6, 99.1% for strain 11, 96.9% for strain 16).

EDITORIAL COMMENT

These data provide useful and important information regarding both the epidemiology of HPV in active component female service members and seroprotection by HPV strain after fewer than three doses of the quadrivalent vaccine.

It is clear from these data that a large proportion of female service members (62.1%) are positive for one or more HPV strains prior to initiation of vaccination. A much smaller proportion of female service members are positive for the oncogenic strains of HPV covered by the quadrivalent vaccine (HPV16: 28.5%; HPV18: 15.8%). Multiple published studies have illustrated the challenges of delivering all three doses of the quadrivalent vaccine. Given the relatively low percentage of service members who complete the three-dose series, it is somewhat reassuring to note that this analysis echoes similar findings in dose comparative studies of immunogenicity for HPV vaccination; namely, that two doses are immunologically non-inferior to three doses. Similar findings have been reported

TABLE 5. Seroconversion among vaccine recipients who tested negative for human papillomavirus (HPV) strain 11 prior to immunization

	No. of doses received	No. negative prior to HPV4 immunization		No. who seroconverted to HPV strain 11			
		N	Col %	N	%	95% CI[a]	p-value[b]
All							
	1	246	17.9	240	97.6	94.7, 99.0	0.0258
	2	287	20.8	286	99.7	97.9, 100.0	
	3	845	61.3	840	99.4	98.6, 99.8	
Age (years)							
17–18	1	32	32.0	29	90.6	75.0, 97.5	0.0509
	2	28	28.0	28	100.0	85.7, 100.0	
	3	40	40.0	40	100.0	89.6, 100.0	
19–20	1	66	20.6	64	97.0	89.0, 99.8	0.1698
	2	85	26.5	85	100.0	94.8, 100.0	
	3	170	53.0	169	99.4	96.4, 100.0	
21–22	1	45	14.6	44	97.8	87.4, 100.0	0.2672
	2	60	19.4	59	98.3	90.3, 100.0	
	3	204	66.0	203	99.5	97.0, 100.0	
23–24	1	50	14.5	50	100.0	91.5, 100.0	1.0
	2	54	15.7	54	100.0	92.1, 100.0	
	3	241	69.9	240	99.6	97.5, 100.0	
25–26	1	53	17.5	53	100.0	91.9, 100.0	1.0
	2	60	19.8	60	100.0	92.8, 100.0	
	3	190	62.7	188	99.0	96.0, 100.0	
Service							
Army	1	70	28.3	69	98.6	91.6, 100.0	0.2834
	2	86	34.8	86	100.0	94.9, 100.0	
	3	91	36.8	91	100.0	95.1, 100.0	
Navy	1	109	33.4	106	97.3	91.9, 99.4	0.5314
	2	119	36.5	118	99.2	94.9, 100.0	
	3	98	30.1	97	99.0	93.9, 100.0	
Air Force	1	53	7.2	51	96.2	86.5, 99.7	0.0867
	2	58	7.9	58	100.0	92.6, 100.0	
	3	628	85.0	624	99.4	98.3, 99.8	
Marine Corps	1	8	26.7	8	100.0	62.8, 100.0	1.0
	2	7	23.3	7	100.0	59.6, 100.0	
	3	15	50.0	15	100.0	76.1, 100.0	
Coast Guard	1	6	16.7	6	100.0	55.7, 100.0	1.0
	2	17	47.2	17	100.0	78.4, 100.0	
	3	13	36.1	13	100.0	73.4, 100.0	
Education							
High school	1	207	19.1	201	97.1	93.7, 98.8	0.0360
	2	231	21.3	230	99.6	97.3, 100.0	
	3	648	59.7	643	99.2	98.2, 99.7	
Some college	1	10	14.5	10	100.0	67.9, 100.0	1.0
	2	13	18.8	13	100.0	73.4, 100.0	
	3	46	66.7	46	100.0	90.8, 100.0	
College graduate	1	22	11.9	22	100.0	82.5, 100.0	1.0
	2	31	16.8	31	100.0	86.9, 100.0	
	3	132	71.4	132	100.0	96.6, 100.0	
Unknown	1	7	18.4	7	100.0	59.6, 100.0	1.0
	2	12	31.6	12	100.0	71.8, 100.0	
	3	19	50.0	19	100.0	80.2, 100.0	
Race/ethnicity							
Non-Hispanic White	1	111	15.9	108	97.3	92.0, 99.4	0.0720
	2	127	18.2	127	100.0	96.5, 100.0	
	3	460	65.9	457	99.4	98.0, 99.9	
Non-Hispanic Black	1	51	17.9	51	100.0	91.6, 100.0	0.6534
	2	66	23.2	65	98.5	91.1, 100.0	
	3	168	59.0	167	99.4	96.4, 100.0	
Non-Hispanic Other	1	41	19.0	40	97.6	86.3, 100.0	0.3832
	2	43	19.9	43	100.0	90.2, 100.0	
	3	132	61.1	131	99.2	95.4, 100.0	
Hispanic	1	43	24.0	41	95.4	83.7, 99.6	0.0567
	2	51	28.5	51	100.0	91.6, 100.0	
	3	85	47.5	85	100.0	94.8, 100.0	

[a]Calculated using Agresti-Coull method
[b]Calculated using Fisher's exact test

for the bivalent vaccine as well.[8,13] However, until recently there were no published data evaluating the efficacy of a single dose of the quadrivalent vaccine. A recently published report by Sankaranarayanan and colleagues was the first to report on vaccine-targeted HPV infection and HPV strain–specific antibody concentrations after one, two, and three doses of the quadrivalent vaccine.[14] The novel findings in their study were that one dose of the quadrivalent vaccine provided similar short-term protection as two or three doses. In addition, detectable antibody titers were induced by one dose and remained stable, although at lower concentrations than the other dosing groups.

The data in this analysis also indicate that a single dose of vaccine results in seroconversion in 82%–100% of servicewomen, depending on strain type. However, as noted by Sankaranarayanan et al., "…seroconversion is an arbitrary cutoff and does not represent the minimum threshold for protection."[14] Their study also reported that women receiving single-dose vaccination had significantly lower antibody titers than those receiving two or three doses. Further assessment is needed to understand to what degree, and how long, a single dose might confer protection and whether that protection differs by strain type. The results of this analysis indicated that protection from a single dose may last at least 4–6 years.

Air Force service members represented 51.7% of the study subjects. It is notable that seroconversion among Air Force service members who received just one dose was lower than for the other services for strains 6, 11, and 16 (but not for strain 18). It is unclear why this group would have had lower seroconversion than subjects in the other services. The relative overrepresentation of Air Force in this sample, along with strain-specific differences in seroconversion by service, should be considered when interpreting these findings and may limit their generalizability.

Of note, a comparison between seroconversion proportions reported in this analysis compared to that reported in the vaccine registration trial data for Gardasil® after three doses indicates that for all but HPV18, seroconversion proportions were similar to the results reported in this analysis after three doses.

TABLE 6. Seroconversion among vaccine recipients who tested negative for human papillomavirus (HPV) strain 16 prior to immunization

	No. of doses received	No. negative prior to HPV4 immunization		No. who seroconverted to HPV strain 16			
		N	Col %	N	%	95% CI[a]	P value[b]
All							
	1	264	17.7	237	89.8	85.5, 92.9	<0.0001
	2	303	20.3	294	97.0	94.4, 98.5	
	3	928	62.1	917	98.8	97.9, 99.4	
Age (years)							
17–18	1	40	35.7	36	90.0	76.4, 96.6	0.2826
	2	29	25.9	28	96.6	81.4, 100.0	
	3	43	38.4	42	97.7	86.8, 100.0	
19–20	1	71	19.5	64	90.1	80.7, 95.4	0.0023
	2	94	25.8	91	96.8	90.6, 99.3	
	3	200	54.8	198	99.0	96.2, 100.0	
21–22	1	56	16.1	49	87.5	76.1, 94.1	0.0010
	2	63	18.1	61	96.8	88.5, 99.8	
	3	229	65.8	226	98.7	96.0, 99.7	
23–24	1	52	14.3	49	94.2	83.8, 98.6	0.0615
	2	54	14.8	54	100.0	92.1, 100.0	
	3	259	71.0	256	98.8	96.5, 99.8	
25–26	1	45	14.8	39	86.7	73.5, 94.1	0.0007
	2	63	20.7	60	95.2	86.4, 98.9	
	3	197	64.6	195	99.0	96.1, 100.0	
Service							
Army	1	75	26.2	70	93.3	85.0, 97.5	0.0808
	2	92	32.2	89	96.7	90.5, 99.3	
	3	119	41.6	118	99.2	94.9, 100.0	
Navy	1	118	34.6	106	89.8	82.9, 94.2	0.0397
	2	119	34.9	115	96.6	91.4, 99.0	
	3	104	30.5	101	97.1	91.5, 99.4	
Air Force	1	57	7.2	47	82.5	70.4, 90.4	<0.0001
	2	68	8.6	67	98.5	91.4, 100.0	
	3	669	84.3	662	99.0	97.8, 99.5	
Marine Corps	1	9	26.5	9	100.0	65.5, 100.0	1.0
	2	10	29.4	10	100.0	67.9, 100.0	
	3	15	44.1	15	100.0	76.1, 100.0	
Coast Guard	1	5	12.5	5	100.0	51.1, 100.0	0.4750
	2	14	35.0	13	92.9	66.5, 100.0	
	3	21	52.5	21	100.0	81.8, 100.0	
Education							
High school	1	226	19.0	205	90.7	86.2, 93.9	<0.0001
	2	243	20.4	238	97.9	95.1, 99.3	
	3	722	60.6	713	98.8	97.6, 99.4	
Some college	1	11	14.9	9	81.8	51.2, 96.0	0.0599
	2	13	17.6	12	92.3	64.6, 100.0	
	3	50	67.6	49	98.0	88.5, 100.0	
College graduate	1	20	10.6	16	80.0	57.8, 92.5	0.0005
	2	32	16.9	30	93.8	78.8, 99.3	
	3	137	72.5	136	99.3	95.6, 100.0	
Unknown	1	7	17.1	7	100.0	59.6, 100.0	0.5366
	2	15	36.6	14	93.3	68.2, 100.0	
	3	19	46.3	19	100.0	80.2, 100.0	
Race/ethnicity							
Non-Hispanic White	1	113	15.4	98	86.7	79.1, 91.9	<0.0001
	2	129	17.6	124	96.1	91.0, 98.6	
	3	492	67.0	486	98.8	97.3, 99.5	
Non-Hispanic Black	1	57	17.9	56	98.3	89.8, 100.0	0.3398
	2	68	21.3	67	98.5	91.4, 100.0	
	3	194	60.8	193	99.5	96.8, 100.0	
Non-Hispanic Other	1	44	19.1	37	84.1	70.3, 92.4	0.0009
	2	44	19.1	42	95.5	84.0, 99.6	
	3	142	61.7	140	98.6	94.7, 99.9	
Hispanic	1	50	23.6	46	92.0	80.7, 97.4	0.1237
	2	62	29.3	61	98.4	90.6, 100.0	
	3	100	47.2	98	98.0	92.6, 99.9	

[a]Calculated using Agresti-Coull method
[b]Calculated using Fisher's exact test

However, the seroconversion proportion for HPV18 in this analysis (79.6%) is lower than that reported in the original trial data (99.1%).*[15] It is unclear why the HPV18 seroconversion proportions observed in this analysis are lower than those reported in the trial data. One possible explanation could be that loss of a detectable antibody response over time is greater for HPV18 than for the other vaccine-specific strains. In 2007, in an evaluation of post-vaccination type-specific immune memory, Olsson et al. reported that, 5 years after receipt of the quadrivalent HPV vaccine, 35% of vaccinated women had lost detectable antibodies to HPV 18 VLPs but only 1% of vaccinated women had undetectable antibody to HPV 16 VLPs.[16] Evaluating other possible explanations for this observation, as well as correlating antibody levels with clinical outcomes, would be informative future analyses.[17]

**Data reported in the HPV Registration Study for Gardasil (ClinicalTrials.gov Identifier: NCT00157950) reported the proportion of study participants who seroconverted to each type covered by the vaccine after three doses; reported seroconversion proportions were 98.2% (93.6, 99.8) for HPV6, 100% (96.8, 100) for HPV11, 99.1% (95.2, 100) for HPV16, and 99.1% (95.0, 100) for HPV18.*

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REFERENCES

1. Armed Forces Health Surveillance Center. Sexually transmitted infections, active component, U.S. Armed Forces, 2000–2012. *MSMR*. 2013;20(2):5–10.

TABLE 7. Seroconversion among vaccine recipients who tested negative for human papillomavirus (HPV) strain 18 prior to HPV4 immunization

	No. of doses received	No. negative prior to HPV4 immunization		No. who seroconverted to HPV strain 18			
		N	Col %	N	%	95% CI[a]	p-value[b]
All							
	1	352	20.0	291	82.7	78.4, 86.3	0.4473
	2	354	20.1	287	81.1	76.7, 84.8	
	3	1054	59.9	839	79.6	77.1, 81.9	
Age (years)							
17–18	1	44	37.0	38	86.4	72.9, 94.0	0.5202
	2	28	23.5	23	82.1	63.9, 92.6	
	3	47	39.5	36	76.6	62.6, 86.6	
19–20	1	74	20.6	62	83.8	73.6, 90.6	0.4512
	2	93	25.9	79	85.0	76.2, 90.9	
	3	192	53.5	152	79.2	72.9, 84.3	
21–22	1	104	23.2	89	85.6	77.5, 91.2	0.4762
	2	75	16.7	59	78.7	68.0, 86.5	
	3	270	60.1	221	81.9	76.8, 86.0	
23–24	1	62	13.8	49	79.0	67.2, 87.5	0.6900
	2	75	16.7	57	76.0	65.1, 84.3	
	3	311	69.4	249	80.1	75.3, 84.1	
25–26	1	68	17.7	53	77.9	66.6, 86.3	0.5604
	2	83	21.6	69	83.1	73.5, 89.8	
	3	234	60.8	181	77.4	71.6, 82.3	
Service							
Army	1	123	33.2	99	80.5	72.6, 86.6	0.3198
	2	105	28.3	82	78.1	69.2, 85.0	
	3	143	38.5	122	85.3	78.5, 90.3	
Navy	1	146	35.6	121	82.9	75.9, 88.2	0.2013
	2	142	34.6	116	81.7	74.5, 87.2	
	3	122	29.8	91	74.6	66.2, 81.5	
Air Force	1	65	7.2	56	86.2	75.5, 92.8	0.3467
	2	78	8.7	66	84.6	74.9, 91.1	
	3	757	84.1	604	79.8	76.8, 82.5	
Marine Corps	1	10	29.4	8	80.0	47.9, 95.4	0.5912
	2	12	35.3	8	66.7	38.8, 86.5	
	3	12	35.3	7	58.3	31.9, 80.7	
Coast Guard	1	8	17.8	7	87.5	50.8, 99.9	0.5907
	2	17	37.8	15	88.2	64.4, 98.0	
	3	20	44.4	15	75.0	52.8, 89.2	
Education							
High school	1	271	19.4	226	83.4	78.5, 87.4	0.4814
	2	287	20.6	229	79.8	74.8, 84.1	
	3	836	60.0	672	80.4	77.6, 82.9	
Some college	1	12	13.8	8	66.7	38.8, 86.5	0.3884
	2	16	18.4	14	87.5	62.7, 97.8	
	3	59	67.8	48	81.4	69.5, 89.4	
College graduate	1	62	25.7	50	80.7	69.0, 88.7	0.2537
	2	39	16.2	34	87.2	72.8, 94.9	
	3	140	58.1	105	75.0	67.2, 81.5	
Unknown	1	7	18.4	7	100.0	59.6, 100.0	0.3485
	2	12	31.6	10	83.3	54.0, 96.5	
	3	19	50.0	14	73.7	50.9, 88.6	
Race/ethnicity							
Non-Hispanic White	1	158	18.6	133	84.2	77.6, 89.1	0.7885
	2	151	17.7	123	81.5	74.5, 86.9	
	3	542	63.7	444	81.9	78.5, 84.9	
Non-Hispanic Black	1	83	21.0	67	80.7	70.9, 87.9	0.6879
	2	83	21.0	69	83.1	73.5, 89.8	
	3	230	58.1	181	78.7	72.9, 83.5	
Non-Hispanic Other	1	56	21.4	44	78.6	66.0, 87.4	0.7825
	2	45	17.2	36	80.0	66.0, 89.3	
	3	161	61.5	121	75.2	67.9, 81.2	
Hispanic	1	55	21.9	47	85.5	73.6, 92.7	0.4418
	2	75	29.9	59	78.7	68.0, 86.5	
	3	121	48.2	93	76.9	68.5, 83.5	

[a]Calculated using Agresti-Coull method
[b]Calculated using Fisher's exact test

2. Markowitz LL, Dunne EF, Saraiya M, et al. Quadrivalent human papillomavirus vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2007;56(RR-2):1–24.
3. Parkin DM, Bray F. Chapter 2: The burden of HPV-related cancers. *Vaccine*. 2006;24 Suppl 3:S3/11–25.
4. Ng J, Ye F, Roth L, et al. Human papillomavirus vaccination coverage among female adolescents in managed care plans—United States, 2013. *MMWR* 2013;64:1185–1189.
5. Donken RR, Knol MJ, Bogaards JA, *et al.* Inconclusive evidence for non-inferior immunogenicity of two- compared with three-dose HPV immunization schedules in preadolescent girls: A systematic review and meta-analysis. *J Infect.* 2015;71(1):61–73.
6. Dobson SR, McNeil S, Dionne M, *et al.* Immunogenicity of 2 doses of HPV vaccine in younger adolescents vs 3 doses in young women. *JAMA*. 2013;309(17):1793–1802.
7. Kreimer AR, Rodriguez AC, Hildesheim A, et al. Proof-of-principle evaluation of the efficacy of fewer than three doses of a bivalent HPV16/18 vaccine. *J Natl Cancer Inst.* 2011;103(19):1444–1451.
8. Safaeian M, Porras C, Pan y, et al. Durable antibody response following one dose of the bivalent human papillomavirus L1 virus-like particle vaccine in the Costa Rica Vaccine Trial. *Cancer Prev Res*. 2013;6(11):1242–1250.
9. Human Papilloma Virus (HPV) Vaccine in Navy and Marine Beneficiaries. 2007; http://www.vaccines.mil/documents/1067NAVMED_Policy_07_017.pdf. Accessed on 16 February 2016.
10. U.S. Army Medical Command. Provisional Recommendations on Use of Quadrivalent Human Papillomavirus (HPV) Vaccine. 2007.
11. U.S. Department of the Air Force. Human Papillomavirus Vaccination Policy. 2007; www.vaccines.mil/documents/1062AFHumanPapillomavirusPolicy.pdf. Accessed on 16 February 2016.
12. Maktabi H, Ludwig SL, Eick-Cost AA, Yerubandi UD, Gaydos JC. Quadrivalent human papillomavirus vaccine initiation, coverage, and compliance among U.S. active component service women, 2006–2011. *MSMR*. 2012;19(5):16.
13. Kreimer AR, Struyf F, Del Rosario-Raymundo MR, et al. for the Costa Rica Vaccine Trial and the PATRICIA study groups. Efficacy of fewer than three doses of an HPV-16/18 ASO4-adjuvanted vaccine: combined analysis of data from the Costa Rica Vaccine and PATRICIA trials. *Lancet Oncol.* 2015;16(7):775–786.
14. Sankaranarayanan R, Ramesh Prabhu P, Pawlita M, et al. for the Indian HPV vaccine study group. Immunogenicity and HPV infection after one, two, and three doses of quadrivalent HPV vaccine in girls in India: early results from a multicenter cohort study. *Lancet Oncol.* 2016;17(1):67–77.
15. Merck Sharp & Dohme Corp. Human Papillomavirus (HPV) Registration Study (Gardasil) (V501-023). https://clinicaltrials.gov/ct2/show/NCT00157950?term=nct00157950&rank=1. Accessed on 11 February 2016.
16. Olsson SE, Villa LL, Cost RL, et al. Induction of immune memory following administration of a prophylactic quadrivalent human papillomavirus (HPV) types 6/11/16/18 L1 virus-like particle (VLP) vaccine. *Vaccine.* 2007;25(26):4931–4939.
17. Schiller JT, Lowy DR. Immunogenicity testing in human papillomavirus virus-like particle vaccine trials. *J Infect Dis.* 2009; 200(2):166–171.

Brief Report

Human Papillomavirus (HPV) 6, 11, 16, and 18 Seroprevalence Among Males and Females Entering Military Service During 2011–2012

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Human papillomavirus (HPV) seroprevalence is a useful way to estimate cumulative HPV exposure in a population. Since the introduction of vaccines targeting specific HPV strains, recent estimates of HPV seroprevalence in the U.S. civilian population have increased over estimates prior to the introduction of these vaccines. Increased HPV seroprevalence has been most pronounced in those aged 14–17 and 18–24 years[1]; the latter group reflects the age range of the majority of new accessions to the military. Currently, the Department of Defense (DoD) recommends routine vaccination of all service members aged 17–26 years without consideration of HPV serostatus.

Agan et al. have previously reported on HPV seroprevalence in males entering military service in 2000 and serving at least 10 years; in a randomly selected sample of 200 males, 14.5% were seropositive for at least one of the four vaccine-preventable (VP) HPV strains (e.g., HPV6, 11, 16, or 18) at entry into service. This estimate is two to three times higher than seroprevalence estimates in U.S. civilian men of similar age.[2] Recent estimates of HPV seroprevalence in military women indicate that 62.1% were seropositive for at least one VP HPV strain prior to HPV vacccination.[3]

This analysis reports the seroprevalence of the four HPV types targeted by the current quadrivalent vaccine in new accessions to the U.S. military during 2011–2012.

METHODS

The study population consisted of a stratified (by age and gender) random sample of 1,000 new accessions who entered the active component of the U.S. military between 1 January 2011 and 31 December 2012 and who had an accession serum specimen available for testing. In addition, to be eligible for inclusion, an individual had to be between 17 and 42 years of age.

Detailed methods for serum testing and linkage to demographic data have been described elsewhere.[2] In brief, serum samples from a sex and age stratified random sample of 1,000 recruits were obtained from the DoD serum repository. Specimens were provided to The Johns Hopkins University, Baltimore, MD, for testing for each of the four VP HPV strains using virus-like particle (VLP)-based enzyme-linked immunosorbent assay (ELISA). Dichotomized results (e.g., negative or positive) for each strain were provided back to the Armed Forces Health Surveillance Branch for linkage with demographic data.

RESULTS

The overall demographic characteristics of the sample are presented in **Table 1.** The proportion of females (15.1%) in this sample approximates the proportion of females in the active component. The majority (87.6%) of the sample was under 25 years of age. More than 90% had a high school education or less and more than half entered service into the U.S. Army (58.3%) and were of white, non-Hispanic race/ethnicity (59.7%). **(Table 1)**

Of the 151 females tested, 49.7% and 49.0% were seropositive for strains 6 and 11, respectively **(Table 2)**. For the oncogenic strains, 47.0% of females were seropositive for HPV 16 and 38.4% were seropositive to serotype 18. Of the 849 males tested, 14.6% and 10.5% were seropositive for strains 6 and 11, respectively. The lowest seroprevalence overall by strain for males was 2.1% for HPV18, while 2.7% were seropositive for strain 16. The proportion of females seropositive for at least one of the VP strains (59.6%) was more than three times the proportion of males (18.9%) seropositive for any VP serotype. Almost half (48.0%) of females under 20 years of age were seropositive for all four strains, while only 2.4% of males of this age group were seropositive for all four strains. **(Table 2)**.

TABLE 1. Demographic and military characteristics of the sample of 1,000 new military accessions, 2011–2012

	N	% of total
All	1,000	100.0
Gender		
Male	849	84.9
Female	151	15.1
Age (years)		
17–19	488	48.8
20–24	388	38.8
25–29	98	9.8
30–35	20	2.0
36+	6	0.6
Race/ethnicity		
White, non-Hispanic	597	59.7
Black, non-Hispanic	165	16.5
Other	238	23.8
Service		
Air Force	75	7.5
Army	583	58.3
Marine Corps	124	12.4
Navy	218	21.8
Education		
High school or less	904	90.4
Some college or above	95	9.5
Unknown	1	0.1

TABLE 2. Percentage of new military accessions seropositive for antibody to specific HPV strain by gender, age and race/ethnicity, 2011–2012

	% HPV6+	% HPV11+	% HPV16+	% HPV18+	% positive for any strain	% positive for all four strains
All	19.9	16.3	9.4	7.6	25.0	6.1
Female	49.7	49.0	47.0	38.4	59.6	33.8
Age (years)						
17–19	54.7	54.7	54.7	49.3	58.7	48.0
20–24	50.9	50.9	43.4	32.1	60.4	26.4
25–29	23.5	23.5	29.4	11.8	58.8	5.9
30–35	33.3	33.3	0.0	0.0	33.3	0.0
36+	66.7	33.3	66.7	66.7	100.0	0.0
Race/ethnicity						
White, non-Hispanic	51.4	51.4	48.6	40.0	58.6	34.3
Black, non-Hispanic	48.7	48.7	48.7	35.9	66.7	30.8
Other	47.6	45.2	42.9	38.1	54.8	35.7
Male	14.6	10.5	2.7	2.1	18.9	1.2
Age (years)						
17–19	18.7	12.8	3.3	3.1	22.5	2.4
20–24	9.5	8.3	1.5	1.2	14.4	0.0
25–29	11.1	7.4	3.7	1.2	16.1	0.0
30–35	25.0	12.5	6.3	0.0	25.0	0.0
36+	33.3	0.0	0.0	0.0	33.3	0.0
Race/ethnicity						
White, non-Hispanic	16.7	10.4	2.5	2.3	20.3	1.3
Black, non-Hispanic	8.1	8.9	4.0	2.4	15.3	0.8
Other	13.3	11.3	2.6	1.5	16.8	1.0

EDITORIAL COMMENT

This study found that 18.9% of males and 59.6% of females entering military service were seropositive for one or more of the four VP HPV serotypes. This estimate of HPV seroprevalence in male recruits is slightly higher than was previously reported, and higher than the seroprevalence estimates reported in similarly aged men in the NHANES HPV serosurvey.[2]

As has been demonstrated in numerous previous studies of HPV seroprevalence, HPV seroprevalence was much higher in females than in males. In these data, a large proportion (59.6%) of females entering military service were seropositive for at least one VP HPV type. A much higher proportion of females under 25 years of age were seropositive for all four VP HPV strains than those females over 25 years of age. These data are highly suggestive that a much greater proportion of these younger females may have received the quadrivalent HPV vaccination prior to entry into the military.

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REFERENCES

1. Brouwer AF, Eisenberg MC, Carey TE, Meza R. Trends in HPV cervical and seroprevalence and associations between oral and genital infection and serum antibodies in NHANES 2003–2012. *BMC Infect Dis.* 2015;15(1):575.
2. Agan BK, Macalino GE, Nsouli-Maktabi H, et al.. Human papillomavirus seroprevalence among men entering military service and seroincidence after ten years of service. *MSMR.* 2013;20(2):21–24.
3. Hurt L, Nsouli-Maktabi H, Rohrbeck P, Clark L. Use of quadrivalent human papillomavirus vaccine and the prevalence of antibodies to vaccine-targeted strains among female service members before and after vaccination. *MSMR.* 2016;23(2):6–13.

Sexually Transmitted Infections in U.S. Air Force Recruits in Basic Military Training

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This study reports the counts, prevalence, and trends of five common sexually transmitted infections (STIs) among U.S. Air Force recruits during 2012–2014 (N=101,426). Chlamydia and genital herpes simplex virus (HSV) were the most commonly identified STIs in females, with a prevalence of 4,841.2 and 432.3 per 100,000, respectively. Genital HSV was the most commonly identified STI in males at 133.4 per 100,000. There were 13 cases of chlamydia and gonorrhea co-infection among females and none among males. STI prevalence was lower than in a similarly aged U.S. civilian population.

As previously described,[1] if the 63 communicable diseases in the *U.S. Armed Forces Reportable Medical Events Guidelines and Case Definitions*[2] were ranked by incidence rate, three sexually transmitted infections (STIs) would top the list: chlamydia, gonorrhea, and syphilis. Their rates are matched or exceeded by those for two non-reportable STIs: human papillomavirus (HPV) and genital herpes simplex virus (HSV).[1] Although these observations suggest high incidence rates of STIs during military service, some of these infections are clearly present at the time of service entry. For example, Gaydos and colleagues found that nearly 10% of female U.S. Army recruits in the late 1990s tested positive for *Chlamydia trachomatis*.[3,4] In a sample of males joining the military in 2000, 14.5% were seropositive for one or more HPV serotypes.[5]

This report describes the prevalence of five common STIs[1] in recruits in U.S. Air Force basic military training (BMT). Conducted exclusively at Joint Base San Antonio–Lackland, TX, BMT is an 8-week program required for all persons entering the enlisted corps of the U.S. Air Force. Near the start of BMT, usually within 3 days of arrival, all females provide a first-catch urine specimen for chlamydia and gonorrhea screening via the Aptima Combo 2 (Hologic/Gen-Probe Inc., San Diego, CA) nucleic acid amplification test (NAAT) assay. Those who test positive are evaluated by a medical provider and screened for syphilis and viral hepatitis by rapid plasma reagin and an acute hepatitis viral panel, respectively, as outlined in local policy.[6] No additional universal STI screening, including cervical cancer screening, is conducted during BMT. All other STIs detected during training depend on a recruit self-reporting to sick call.

Because sexual contact is prohibited during BMT, recruits' exposures to the infectious causes of STIs can be presumed to have occurred prior to arrival, thus enabling estimates of baseline STI prevalence at the time of military accession. Such estimates may clarify the relative burden of prevalent and incident STIs in the U.S. Armed Forces. Moreover, comparing the prevalence of STIs in this cohort and in a similarly aged U.S. civilian population may illustrate the relative entry-level sexual health of military recruits.

METHODS

Cases of STI diagnosed between 1 January 2012 and 31 December 2014 were ascertained from the local disease and non-battle injury database, which includes demographic, all diagnostic, and select laboratory data for all U.S. Air Force recruits. The population included everyone who entered U.S. Air Force BMT during this surveillance period.

The database was queried for previously published ICD-9 diagnostic codes consistent with the five most commonly diagnosed STIs in the U.S. military: chlamydia, gonorrhea, genital HSV, HPV, and syphilis (all types included).[1] A case was defined as receiving an applicable ICD-9 code in any diagnostic position during an outpatient medical encounter, restricted to one case per infectious agent per person during the surveillance period. The chlamydia and gonorrhea case definition for both females and males also required a positive NAAT.

Co-infection rates for chlamydia and gonorrhea were calculated as the percentage of recruits with laboratory-confirmed diagnoses of both infections during training. Counts, prevalence, and trends for all STIs were obtained for the entire recruit population and stratified by sex.

RESULTS

A total of 101,426 persons (79,448 males and 21,978 females) entered U.S. Air Force BMT during the surveillance period. The median age for both sexes was 20 years.

Chlamydia was the most common STI identified in the entire cohort (1,067.8

TABLE. Numbers and prevalence of sexually transmitted infections, recruits, U.S. Air Force basic military training, 2012–2014

	Females		Males		Total	
	No.	Prevalence[a]	No.	Prevalence[a]	No.	Prevalence[a]
Chlamydia	1,064	4,841.2	19	23.9	1,083	1,067.8
Gonorrhea	35	159.3	5	6.3	40	39.4
Genital herpes simplex virus	95	432.3	106	133.4	201	198.2
Human papillomavirus	13	59.2	11	13.8	24	23.7
Syphilis (all types)	1	4.6	3	3.8	4	3.9

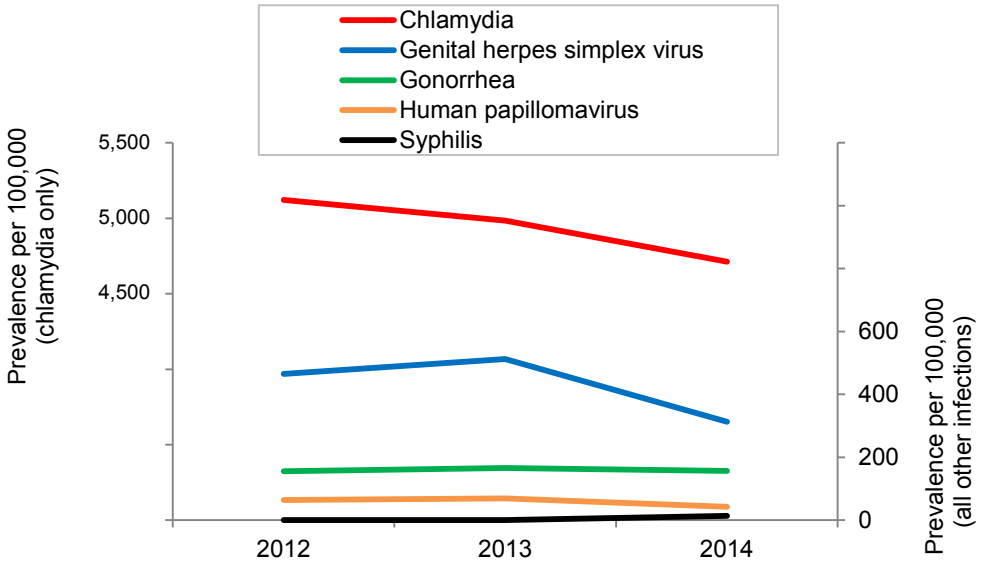
[a]Cases per 100,000 recruits

per 100,000 recruits) and among females (4,841.2 per 100,000 recruits). Genital HSV was the most commonly diagnosed STI among males (133.4 per 100,000 recruits) and second most commonly diagnosed among females (432.3 per 100,000) **(Table)**. Among female recruits, all cases of chlamydia (n=1,064; 4.8% of recruits) and gonorrhea (n=35; 0.2% of recruits) infections were detected by screening NAAT.

Prevalence of most STIs among females decreased or remained stable over the course of the surveillance period. Most notably, genital HSV prevalence decreased by 33% and chlamydia by 8% **(Figure 1)**. Chlamydia prevalence also decreased among males, by 53%, whereas genital HSV prevalence increased by 13% **(Figure 2)**.

Of all females diagnosed with chlamydia, 1.2% (n=13) were also diagnosed with gonorrhea. However, among all diagnosed with gonorrhea, 37.1% were also diagnosed with chlamydia. All chlamydia and gonorrhea co-infections were identified concurrently during baseline screening. The annual numbers of cases of co-infections with both chlamydia and gonorrhea among females declined throughout the surveillance period, from seven in 2012 to one in 2014. No co-infections were diagnosed among males.

FIGURE 1. Trends of annual prevalence of sexually transmitted infections, female recruits, U.S. Air Force basic military training, 2012–2014

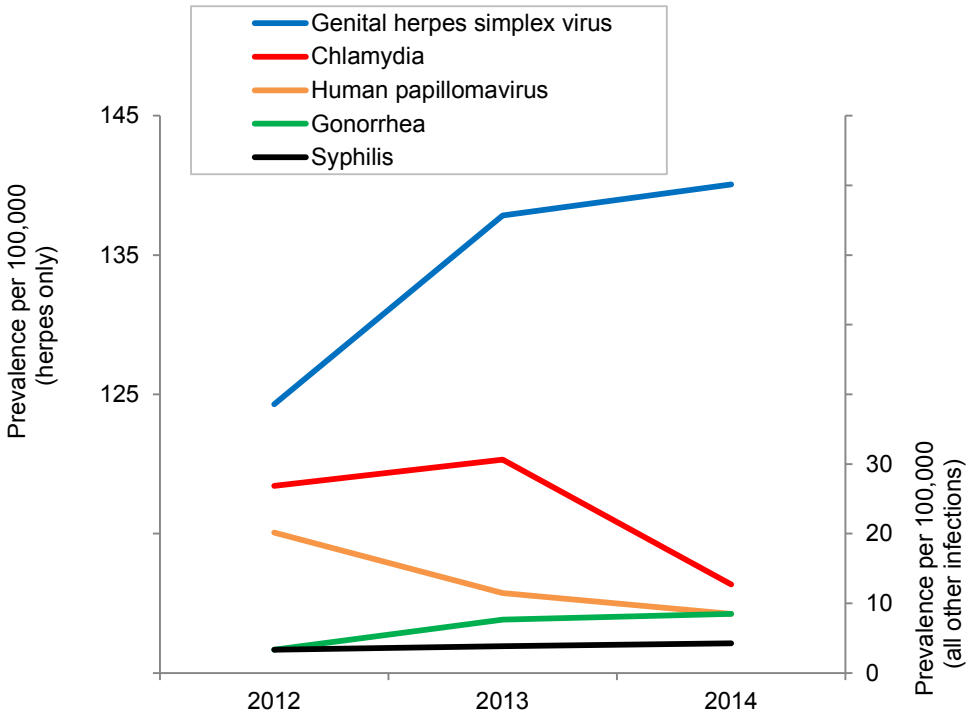


EDITORIAL COMMENT

This study reports the prevalence of five common STIs among U.S. Air Force recruits who entered BMT during 2012–2014. These estimates—particularly those for chlamydia and gonorrhea infections among females, which were identified within the context of universal screening—may be interpreted as the baseline prevalence of STIs among individuals entering the enlisted corps of the U.S. Air Force. Although disease prevalence connotes current infections, whereas disease incidence implies new infections, STI prevalence in this population may be compared to STI incidence in the active component U.S. military to help guide screening policies and implement effective preventive and treatment measures. For chlamydia and genital HSV, the prevalence among U.S. Air Force recruits (1,068 and 198 per 100,000 recruits, respectively) mirrored the incidence rates among active component service members (1,073 and 224 per 100,000 person-years),[1] suggesting that many "incident" infections may be present at the time of entry into the military. However, for the other three STIs, the prevalence among recruits was much lower than the incidence among active component service members: for gonorrhea, 39.4 per 100,000 recruits vs. 226 per 100,000 service member person-years; for syphilis, 3.9 vs. 31; and for HPV, 23.7 vs. 1,755. These discrepancies may be related to STI acquisition after BMT and, for females, cervical cancer screening with HPV testing after BMT.

Compared to non-institutionalized U.S. civilians aged 20–24 years during the same 3-year surveillance period,[7] much lower proportions of U.S. Air Force recruits were diagnosed with chlamydia (1.1% of recruits vs. 2.5% of civilians), gonorrhea (0.04% vs. 0.51%), and syphilis (0.004% vs. 0.016%). Although age-stratified civilian data are not readily available for the other two STIs, the seroprevalence of HSV type 2 in the general population between 2005 and 2008 was reported to be 16.2%,[8] and the cervicovaginal prevalence

FIGURE 2. Trends of annual prevalence of sexually transmitted infections, male recruits, U.S. Air Force basic military training, 2012–2014



of four common HPV serotypes among females aged 20–24 years was roughly 20% between 2007 and 2010.[9] Taken together, these figures suggest that incoming U.S. Air Force recruits have a lower STI burden than their civilian counterparts.

The U.S. Preventive Services Task Force (USPSTF) and the Centers for Disease Control and Prevention recommend chlamydia and gonorrhea screening for all sexually active women under 25 years of age and for older women at increased risk for infection.[10,11] Because the median age of the U.S. Air Force recruit population is 20 years—and because individualized assessment of sexual activity and associated risk factors is unfeasible in the time-constrained environment of BMT—all females are screened upon entry. Screening allows for treatment of asymptomatic infections and has been shown to decrease the risk of complications, including pelvic inflammatory disease, infertility, and ectopic pregnancy.[10,11] In U.S. Air Force BMT, those who screen positive are referred to the trainee health clinic for treatment and to Public Health for counseling, contact tracing, and state health department notification. The preferred treatment for chlamydia is azithromycin (1 gram orally in a single dose), whereas for gonorrhea a dual regimen with azithromycin and ceftriaxone (250 milligrams intramuscularly in a single dose) is recommended to treat co-infections and to prevent the development of antibiotic resistance.[11] Early screening and treatment of STIs that can cause profound long-term sequelae—including chlamydia, gonorrhea, and syphilis—is an important component of women's health in the U.S. military and increasingly among veterans; females are anticipated to comprise 15% of the veteran population by 2036, nearly double the percentage in 2012.[12]

In addition to screening for particular STIs, the USPSTF recommends high-intensity behavioral counseling as a primary preventive tool for all sexually active adolescents and for adults at high risk.[13] The U.S. Air Force implements this recommendation via a basic sexual health briefing during BMT and a focus on positive sexual health behavior and contraception during the First Term Airmen Center course, a required brief for all U.S. Air Force enlisted members at their first permanent-duty assignment. In light of the time interval between BMT and a member's first assignment, which may range from a few weeks to several months, behavioral counseling during technical training (the phase of U.S. Air Force enlisted training after BMT) deserves consideration.

This study should be interpreted in light of its limitations. First, case ascertainment for genital HSV, HPV, and syphilis relied on ICD-9 codes entered by a variety of providers and coders; only chlamydia and gonorrhea cases were laboratory confirmed. Second, although urine NAAT assays are the preferred testing method for chlamydia and gonorrhea[10,11] and have specificities exceeding 99% (i.e., few false positives), their sensitivities are frequently in the 90%–95% range, and may be even lower when urine specimens, rather than self- or clinician-collected vaginal and endocervical swabs, are used to test females.[14] Therefore, the prevalence reported here may slightly underestimate true disease burden. Third, given potential differences in demographics and sexual risk factor profiles, generalization of these findings to the other U.S. armed services should be made cautiously.

Disclaimer: The opinions expressed in this report are solely those of the authors and do not represent an endorsement by or the views of the U.S. Air Force, the Department of Defense, or the U.S. Government.

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REFERENCES

1. Armed Forces Health Surveillance Center. Sexually transmitted infections, active component, U.S. Armed Forces, 2000–2012. *MSMR.* 2013;20(2):5–10.
2. Armed Forces Health Surveillance Center. Armed Forces Reportable Medical Events Guidelines and Case Definitions. March 2012. www.afhsc.mil/documents/pubs/documents/TriService_CaseDefDocs/ArmedForcesGuidlinesFinal14Mar12.pdf. Accessed on 9 December 2015.
3. Gaydos CA, Howell MR, Pare B, et al. *Chlamydia trachomatis* infections in female military recruits. *N Engl J Med.* 1998;339(11):739–744.
4. Gaydos CA, Howell MR, Quinn TC, McKee KT Jr., Gaydos JC. Sustained high prevalence of *Chlamydia trachomatis* infections in female army recruits. *Sex Transm Dis.* 2003;30(7):539–544.
5. Agan BK, Macalino GE, Nsouli-Maktabi H, et al. Human papillomavirus seroprevalence among men entering military service and seroincidence after ten years of service. *MSMR.* 2013;20(5):21–24.
6. 559 Medical Operations Squadron. Operating Instruction 44-6: Gonorrhea and Chlamydia Screening and Evaluation. 5 Aug 14.
7. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2014. Atlanta: U.S. Department of Health and Human Services; 2015. www.cdc.gov/std/stats14/surv-2014-print.pdf. Accessed on 23 December 2015.
8. Centers for Disease Control and Prevention. Seroprevalence of herpes simplex virus type 2 among persons aged 14–49 years—United States, 2005–2008. *MMWR Morb Mortal Wkly Rep.* 2010;59(15):456–459.
9. Markowitz LE, Hariri S, Lin C, et al. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003–2010. *J Infect Dis.* 2013;208(3):385–393.
10. LeFevre ML, U.S. Preventive Services Task Force. Screening for chlamydia and gonorrhea: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2014;161(12):902–910.
11. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep.* 2015;64(3):1–140.
12. Goyal V, Mattocks KM, Sadler AG. High-risk behavior and sexually transmitted infections among U.S. active duty service women and veterans. *J Womens Health.* 2012;21(11):1155–1169.
13. LeFevre ML, U.S. Preventive Services Task Force. Behavioral counseling interventions to prevent sexually transmitted infections: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2014;161(12):894–901.
14. Centers for Disease Control and Prevention. Recommendations for the laboratory-based detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014. *MMWR Recomm Rep.* 2014;63(RR-02):1–19.

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Incident and Recurrent *Chlamydia trachomatis* and *Neisseria gonorrhoeae* Infections, Active Component, U.S. Armed Forces, 2010–2014

Alfred J. Owings, MD (LCDR, USN); Leslie L. Clark, PhD, MS; Patricia Rohrbeck, DrPH, MPH (Lt Col(S), USAF)

Chlamydia trachomatis and *Neisseria gonorrhoeae* infections impose a significant clinical and public health burden on the Military Health System. Repeat infections contribute significantly to that burden. This report summarizes rates and relative risks of true incident (i.e., initial or "first time ever") and recurrent (i.e., repeat) chlamydia and gonorrhea infections among active component members between 1 January 2010 and 31 December 2014. During the surveillance period, a total of 66,396 initial chlamydia and 9,138 initial gonorrhea cases were diagnosed. Annual crude rates of initial chlamydia infections increased by 23%. Crude rates of initial gonorrhea infections remained stable overall, but female rates decreased by 28.3% over the period. Among the incident cohorts, 11,699 cases of repeat chlamydia, and 1,138 cases of repeat gonorrhea were diagnosed over the period, accounting for 15.0% and 11.1% of overall cohort chlamydia and gonorrhea infections, respectively. The Army branch, those aged 17–19 years, females, non-Hispanic black service members, junior enlisted ranks, and single/never-married service members had the highest crude rates of initial chlamydia and gonorrhea infection, and (single/never-married service members excepted) highest adjusted relative risk of repeat chlamydia infection.

The public health and clinical burdens imposed by *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections are significant. According to the Centers for Disease Control and Prevention (CDC), *C. trachomatis* and *N. gonorrhoeae* infections are the first and second most commonly reported notifiable diseases, respectively, in the U.S. In 2013, there were 1,401,906 chlamydia infections and 333,004 gonorrhea infections reported to the CDC.[1] Because most infections with these organisms are asymptomatic in women (as are most chlamydia infections in men),[2] these figures likely underestimate the true number of infections by a large margin. Additionally, there is some evidence suggesting that both of these infections increase the transmission of HIV, and *N. gonorrhoeae* has developed resistance to each of the antibiotics historically used to treat it—now necessitating dual therapy for treatment.[3,4] Clinically, if untreated in women, both chlamydia and gonorrhea can result in ascending infection and lead to pelvic inflammatory disease (PID). PID, in turn, is a significant cause of infertility, ectopic pregnancy, and chronic pelvic pain.[4]

Risk factors for acquiring chlamydia and gonorrhea have been well characterized among both civilian and Department of Defense active component populations. Nationally, women in general, men and women aged 20–24 years, non-Hispanic blacks, and those from the South region have consistently had the highest reported rates of chlamydia.[1] The same groups have had the highest reported rates of gonorrhea, with the notable exception that, for the first time since 2000, male gonorrhea rates overtook female rates in 2013.[1] Among active component service members, risk for both infections has mirrored that in the civilian population, with two important exceptions: First, reported chlamydia and gonorrhea rates "almost always exceed those in the civilian setting, even after adjusting for age, race/ethnicity, and U.S. geographic region of origin."[5] Second, during 2000–2012, gonorrhea infection rates among active component women remained two to three times higher than among active component men.[6]

Frequent recurrent (or repeat) infections add significantly to the clinical and epidemiologic burdens imposed by *C. trachomatis* and *N. gonorrhoeae*. The frequency of repeat infections (as opposed to treatment failures) has led both the CDC and the American College of Obstetricians and Gynecologists to recommend re-testing all women 3–6 months after a confirmed infection.[7,8] Epidemiologically, in a 2009 systematic review, researchers estimated that, in the U.S. and other industrialized nations, chlamydia reinfection rates are as high as 20% at 8–10 months. The median proportion of recurrent gonorrhea was estimated to be 11.7%.[9] A 2010 *MSMR* report estimated that, among active component service members between 2000 and 2009, 7.2%–12.2% of chlamydia diagnoses in a given year were recurrent infections.[10]

Importantly, chlamydia and gonorrhea case definitions and incidence (or recurrence) rules used in those and other reports have varied, affecting the interpretability and comparability of estimates.

In light of that, and of the impact that these infections and their sequelae have on active component readiness, this report seeks to further characterize the burden and risk of *C. trachomatis* and *N. gonorrhoeae* infections among active component members of the U.S. Armed Forces. Specifically, rates of true incident (i.e., initial) infections among active component service members during 2010–2014 are summarized. Additionally, counts, frequencies, and relative risks of true recurrent (i.e., repeat) infections are summarized for the incident cohorts.

METHODS

The surveillance period was 1 January 2010 through 31 December 2014. The surveillance population consisted of all active component service members who served at any time during the surveillance period. Those members with a diagnosis of chlamydia or gonorrhea during their service at any time prior to the start of the surveillance period were excluded. For purposes of this analysis, an incident case of *C. trachomatis* or *N. gonorrhoeae* infection was defined as a service member's first such infection during their military service (i.e., their initial chlamydia or gonorrhea infection). A recurrent infection was considered to be any chlamydia or gonorrhea infection that occurred 30 days or more after the service member's incident (initial) infection.

Diagnoses of *C. trachomatis* and *N. gonorrhoeae* infections were derived from medical administrative data and reports of notifiable medical events routinely provided to the Armed Forces Health Surveillance Branch and maintained in the Defense Medical Surveillance System (DMSS). Data from the Theater Medical Data Store (TMDS) are included in DMSS. Health Level 7 laboratory data were not utilized for this analysis. ICD-9 codes utilized in case ascertainment for this report can be found in **Table 1**. An incident or recurrent case of chlamydia or gonorrhea was defined by the presence of one of the ICD-9 codes listed in Table 1 in either the first or second diagnostic position of an outpatient medical encounter, or through a confirmed reportable medical event. An individual was counted as having a recurrent (or repeat) case only if at least 30 days had passed since the last medical encounter or reportable medical event with a case-defining diagnosis of the same infection.

For each included at-risk service member, the amount of time spent in active military service any time after the start of the surveillance period was calculated and aggregated into a total for each calendar year, and for the overall period. This total was expressed as person-years (p-yrs) of service, and was used as the denominator for incident and recurrent rate calculations. Counts and rates of incident *C. trachomatis* and *N. gonorrhoeae* infections were calculated. Counts and rates of recurrent chlamydia and gonorrhea infection among the cohorts with an incident infection were also calculated, and relative risk of recurrence was assessed via Poisson univariate and multivariate regression for the following covariates: gender, age, ethnicity, marital status, education level, branch of service, rank, and proximity to re-deployment. Proximity to re-deployment was categorized as either 180 days or less from return, or "other" (i.e., more than 180 days from return or never deployed).

TABLE 1. ICD-9 codes for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections

Infection	ICD-9 codes
C. trachomatis	099.41, 099.5x
N. gonorrhoeae	098.x

RESULTS

Between 1 January 2010 and 31 December 2014, there were 66,396 incident (i.e., new or initial) cases of chlamydia among active component members. Overall, annual crude incidence rates increased from 83.2 to 102.3 cases per 10,000 p-yrs **(Table 2)**. The Army had the highest rates among service branches, but their rates remained stable over the surveillance period. Navy and Marine Corps rates more than doubled over the surveillance period, increasing from 48.8 and 43.2 to 108.1 and 91.9 cases per 10,000 p-yrs respectively **(Figure 1)**. Rates for females remained stable over the surveillance period, while rates for males increased steadily **(Figure 2)**. The following groups had the highest crude incidence rates among covariate categories: Army branch, age 17–19 years, junior enlisted ranks, females, non-Hispanic blacks, single/never-married service members, high school or less education, and those greater than 180 days from re-deployment (or never deployed). However, the 20- to 24-year-old age group and non-Hispanic whites accounted for the greatest proportion of cases within their respective demographic categories **(Table 2)**.

There were 9,138 initial cases of gonorrhea over the 5-year period. Overall, annual crude incidence rates remained stable, ranging from 12.4 to 13.9 cases per 10,000 p-yrs, and increasing only from 13.3 to 13.4 per 10,000 p-yrs from 2010 to 2014 **(Table 3)**. The Army had the highest rates among service branches, but all service branch rates remained relatively stable, with Army rates increasing slightly, and Air Force and Marine Corps rates decreasing slightly **(Figure 3)**. Notably, female rates of initial gonorrhea infection decreased steadily over the period, from 21.2 to 15.2 cases per 10,000 p-yrs, while male rates increased slightly **(Figure 4)**. By 2014, the gonorrhea incidence rate ratio (IRR) for active component females compared to males was only 1.16 (contrasted with the female-to-male IRR for initial chlamydia infection of 2.90 in 2014). Among covariate categories, highest-rate groups were the same for initial gonorrhea cases as for initial chlamydia cases. However, in contrast to chlamydia counts, non-Hispanic blacks accounted for 1,898 more initial gonorrhea cases than did non-Hispanic whites.

TABLE 2. Numbers and incidence rates of incident (initial) *Chlamydia trachomatis* infections, active component, U.S. Armed Forces, 2010–2014

	Total			2010		2011		2012		2013		2014	
	No.	Rate[a]	Incidence rate ratio (crude)	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
Total	66,396	95.8		11,786	83.2	13,759	97.2	13,578	97.7	13,577	99.1	13,696	102.3
Service													
Army	30,287	111.7	1.41	6,331	113.0	6,394	113.4	5,889	107.3	5,822	109.8	5,851	115.0
Navy	13,853	86.7	1.09	1,582	48.8	2,799	87.1	2,883	91.3	3,125	98.6	3,464	108.1
Air Force	14,456	88.3	1.11	2,998	90.6	2,963	90.0	3,016	91.7	2,840	86.4	2,639	82.4
Marine Corps	7,800	79.2	Ref	875	43.2	1,603	79.7	1,790	90.7	1,790	91.9	1,742	91.9
Age (years)													
17–19	9,534	231.6	25.45	1,818	219.0	1,943	248.4	1,853	234.2	1,959	225.2	1,961	232.6
20–24	38,521	174.8	19.20	6,607	141.8	8,010	175.9	7,904	181.4	7,933	186.0	8,067	191.9
25–29	12,732	74.9	7.64	2,323	67.5	2,694	76.4	2,637	76.0	2,586	77.4	2,492	77.7
30–39	4,932	26.3	2.89	915	24.4	941	24.9	1,031	27.3	991	26.5	1,054	28.6
40+	677	9.1	Ref	123	8.2	171	11.3	153	10.2	108	7.3	122	8.5
Rank													
Jr. enlisted	52,042	171.5	9.02	9,167	146.2	10,908	173.6	10,715	175.8	10,578	177.8	10,674	185.4
Sr. enlisted	12,098	44.6	2.35	2,240	40.2	2,428	44.1	2,408	44.4	2,508	46.7	2,514	47.8
Officer	2,256	19.0	Ref	379	16.2	423	17.8	455	19.1	491	20.6	508	21.4
Gender													
Female	23,482	231.0	3.19	4,603	226.1	5,082	247.9	4,509	222.2	4,635	228.2	4,653	230.5
Male	42,914	72.5	Ref	7,183	59.2	8,677	71.7	9,069	76.4	8,942	76.6	9,043	79.5
Race/ethnicity													
White, non-Hispanic	30,800	71.9	Ref	5,431	61.2	6,304	71.5	6,424	74.6	6,343	75.5	6,298	77.7
Black, non-Hispanic	20,315	181.5	2.52	3,919	171.3	4,244	186.5	3,974	178.5	4,043	183.0	4,135	188.8
Hispanic	8,405	106.4	1.48	1,361	87.2	1,772	111.7	1,745	110.7	1,755	110.7	1,772	111.4
Asian/Pacific Islander	2,145	74.6	1.04	402	69.6	447	77.4	396	69.2	424	73.9	476	82.6
American Indian/ Alaskan Native	718	92.4	1.29	105	64.7	144	90.0	165	106.8	144	94.6	160	108.2
Other/unknown	4,013	106.5	1.48	568	80.2	848	114.4	874	115.0	868	111.0	855	110.0
Marital status													
Single, never married	43,533	159.3	3.18	7,341	131.8	8,766	159.4	8,861	163.6	9,142	167.2	9,423	175.1
Married	19,455	50.1	Ref	3,751	47.1	4,293	53.7	3,994	51.0	3,761	49.4	3,656	49.2
Other/unknown	3,408	107.7	2.15	694	108.0	700	106.5	723	110.5	674	107.5	617	105.8
Education													
High school or less	58,630	124.8	3.78	10,477	104.5	12,312	124.4	12,028	128.2	11,920	132.3	11,893	137.0
Some college or more	6,806	33.0	Ref	1,136	30.0	1,233	31.7	1,356	32.4	1,472	33.7	1,609	36.6
Unknown	960	55.3	1.68	173	46.6	214	58.3	194	56.1	185	56.1	194	60.4
Re-deployment													
180 days or less	5,820	37.6	Ref	1,188	33.9	1,602	38.1	1,396	41.2	914	37.3	720	37.2
More than 180 days	60,576	112.5	2.99	10,598	99.3	12,157	122.1	12,182	115.9	12,663	112.5	12,976	113.3

[a]Rate per 10,000 person-years

FIGURE 1. Annual incidence rates of initial *Chlamydia trachomatis* infections, by service, active component, U.S. Armed Forces, 2010–2014

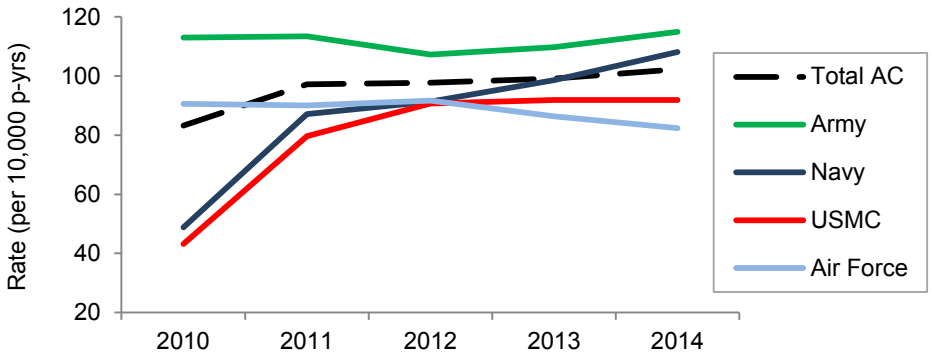
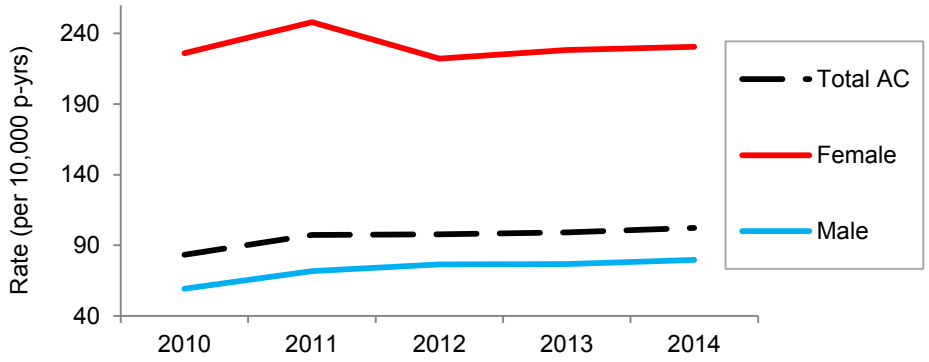


FIGURE 2. Annual incidence rates of initial *Chlamydia trachomatis* infections, by gender, active component, U.S. Armed Forces, 2010–2014



Among the 66,396 service members who had initial chlamydia infections between 2010 and 2014 (i.e., the incident cohort), there were 11,699 recurrent, or repeat, infections over the same period **(Table 4)**. Among those in the incident cohort, 9,658 (14.5%) had one or more repeat infections, with the majority of those (83.1%) having a single repeat infection. Among the 9,138 service members who had initial gonorrhea infections over the 5-year period, there were 1,138 repeat infections **(Table 5)**. Recurrences were diagnosed in 952 members (10.4%) of the cohort. As was true for chlamydia, the majority (85.0%) of those had a single repeat infection. Overall, repeat infections accounted for 15.0% of all chlamydia infections, and 11.1% of all gonorrhea infections, for the incident cohorts.

Results of multivariate regression analysis of repeat infection risk for the incident cohorts are shown in **Table 6** and **Table 7**. When all covariates were controlled for, five of the eight groups previously identified as having highest rates of initial chlamydia infection remained at highest statistically significant risk of repeat infection **(Table 6)**. These groups included the Army branch, age 17–19 years, junior enlisted ranks, females, and non-Hispanic blacks. Those with high school or less education and those greater than 180 days from re-deployment (or never deployed) were no longer at statistically significant elevated risk. Additionally, although single/never-married service members had a slightly higher relative risk of repeat infection than married members, those in the "other/unknown" category had the highest adjusted relative risk. Regarding risk of repeat gonorrhea infection, when all factors were controlled for, those in the Army, the junior enlisted ranks, and non-Hispanic black and Hispanic groups were found to have statistically significant elevated risks of recurrence **(Table 7)**. Finally, adjusted IRRs for all high-risk groups were markedly lower for recurrent infection than were crude IRRs for incident infection.

EDITORIAL COMMENT

This report documents a marked increase (16.8%) in true incident, or initial, crude chlamydia infection rates among active component service members between 2010 and 2011, with a less dramatic but continued increase (5.2%) during 2011–2014. Rates of initial gonorrhea infections, by contrast, remained level over the 5-year period. The Army consistently had the highest rates of both initial chlamydia and gonorrhea infections among service branches. However, initial chlamydia rates more than doubled among Navy and Marine Corps branches over the period, and appeared to drive the overall active component rate increase between 2010 and 2011. The crude rates of incident infection calculated in this report include only true incident infections, and thus are not directly comparable to reported rates for the overall U.S. population, which include incident and recurrent infections. However, extrapolated overall chlamydia incident rates calculated here are still more than twice the reported CDC rates for 2013, and extrapolated gonorrhea rates are approximately 25% higher than 2013 CDC rates.

This report also documents a marked decrease (28.3%) in female initial gonorrhea infection rates over the surveillance period, continuing the downward trend that began in 2008 as reported previously in the *MSMR*.[6] By 2014, the most recent year of the surveillance period, female incident gonorrhea rates were only 2.1 per 10,000 p-yrs higher than male active component rates—mirroring the trend

TABLE 3. Numbers and incidence rates of incident (initial) *Neisseria gonorrhoeae* infections, active component, U.S. Armed Forces, 2010–2014

	Total			2010		2011		2012		2013		2014	
	No.	Rate[a]	Incidence rate ratio (crude)	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
Total	9,138	13.2		1,880	13.3	1,762	12.4	1,801	13.0	1,903	13.9	1,792	13.4
Service													
Army	5,272	19.4	2.69	1,030	18.4	1,052	18.7	1,079	19.7	1,092	20.6	1,019	20.0
Navy	1,648	10.3	1.43	369	11.4	274	8.5	285	9.0	354	11.2	366	11.4
Air Force	1,172	7.2	Ref	265	8.0	225	6.8	237	7.2	229	7.0	216	6.7
Marine Corps	1,046	10.6	1.47	216	10.7	211	10.5	200	10.1	228	11.7	191	10.1
Age (years)													
17–19	1,096	26.6	12.09	243	29.3	234	29.9	174	22.0	212	24.4	233	27.6
20–24	5,027	22.8	10.36	1,011	21.7	951	20.9	1,016	23.3	1,054	24.7	995	23.7
25–29	1,888	11.1	5.05	409	11.9	351	9.9	385	11.1	395	11.8	348	10.8
30–39	961	5.1	2.32	181	4.8	183	4.8	197	5.2	216	5.8	184	5.0
40+	166	2.2	Ref	36	2.4	43	2.8	29	1.9	26	1.8	32	2.2
Rank													
Jr. enlisted	7,018	23.1	9.24	1,448	23.1	1,349	21.5	1,383	22.7	1,459	24.5	1,379	24.0
Sr. enlisted	1,828	6.7	2.68	377	6.8	361	6.6	350	6.4	389	7.2	351	6.7
Officer	292	2.5	Ref	55	2.4	52	2.2	68	2.9	55	2.3	62	2.6
Gender													
Female	1,814	17.8	1.44	432	21.2	392	19.1	324	16.0	360	17.7	306	15.2
Male	7,324	12.4	Ref	1,448	11.9	1,370	11.3	1,477	12.4	1,543	13.2	1,486	13.1
Race/ethnicity													
White, non-Hispanic	2,788	6.5	Ref	548	6.2	533	6.0	554	6.4	593	7.1	560	6.9
Black, non-Hispanic	4,686	41.9	6.45	1,008	44.0	921	40.5	912	41.0	938	42.5	907	41.4
Hispanic	951	12	1.85	192	12.3	176	11.1	193	12.2	210	13.2	180	11.3
Asian/Pacific Islander	228	7.9	1.22	44	7.6	48	8.3	45	7.9	49	8.5	42	7.3
American Indian/ Alaskan Native	76	9.8	1.51	16	9.9	13	8.1	8	5.2	14	9.2	25	16.9
Other/unknown	409	10.9	1.68	72	10.2	71	9.6	89	11.7	99	12.7	78	10.0
Marital status													
Single, never married	5,928	21.7	3.01	1,191	21.4	1,122	20.4	1,141	21.1	1,263	23.1	1,211	22.5
Married	2,782	7.2	Ref	606	7.6	552	6.9	561	7.2	566	7.4	497	6.7
Other/unknown	428	13.5	1.88	83	12.9	88	13.4	99	15.1	74	11.8	84	14.4
Education													
High school or less	8,050	17.1	3.64	1,670	16.7	1,601	16.2	1,576	16.8	1,666	18.5	1,537	17.7
Some college or more	966	4.7	Ref	176	4.7	141	3.6	201	4.8	209	4.8	239	5.4
Unknown	122	7	1.49	34	9.2	20	5.4	24	6.9	28	8.5	16	5.0
Re-deployment													
Less than 180 days	937	6.1	Ref	189	5.4	235	5.6	248	7.3	160	6.5	105	5.4
More than 180 days	8,201	15.2	2.49	1,691	15.9	1,527	15.3	1,553	14.8	1,743	15.5	1,687	14.7

[a]Rate per 10,000 person-years

FIGURE 3. Annual incidence rates of initial *Neisseria gonorrhoeae* infections, by service, active component, U.S. Armed Forces, 2010–2014

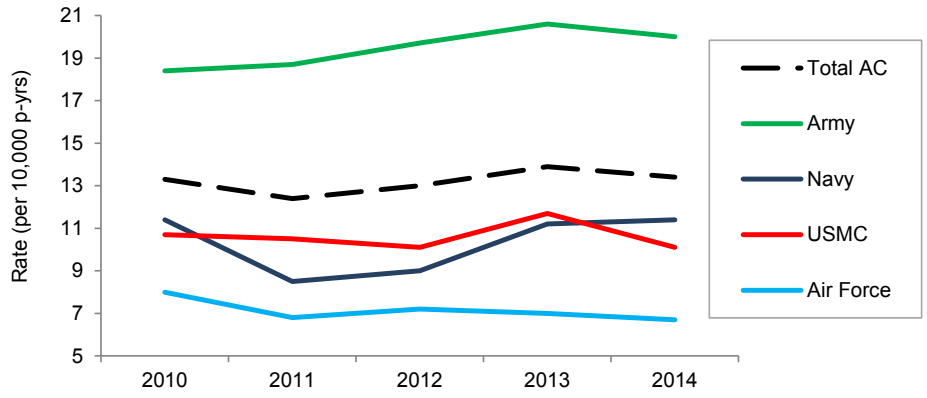


FIGURE 4. Annual incidence rates of initial *Neisseria gonorrhoeae* infections, by gender, active component, U.S. Armed Forces, 2010–2014

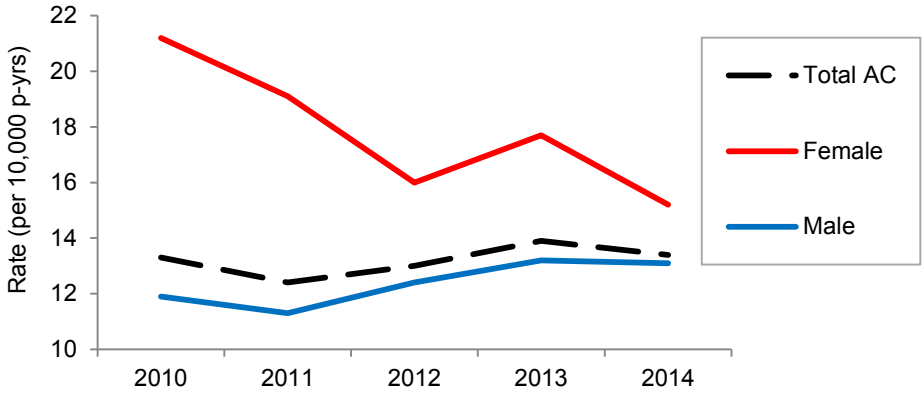


TABLE 4. Recurrent (repeat) *Chlamydia trachomatis* infections among active component service members with an initial infection between 2010 and 2014

No. of recurrent infections per service member	No. of service members with specified no. of recurrent infections	% of all service members who had an initial infection	Total no. of recurrent infections
0	56,738	85.5	0
1	8,023	12.1	8,023
2	1,319	2.0	2,638
3	248	0.4	744
4 or more	68	0.1	294
Total	66,396	100.0	11,699

seen nationally in the U.S., where, as previously mentioned, rates for males overtook rates for females in 2013.[1]

Finally, this report documents that, among active component service members who had an initial chlamydia or gonorrhea infection between 2010 and 2014, 15.0% of all cohort chlamydia infections and 11.1% of all gonorrhea infections were repeat infections. Given that active component members with a prior chlamydia or gonorrhea infection were excluded from the incident cohorts, but would likely have had repeat infections over the period, the actual proportion of overall active component infections accounted for by repeat infections would be greater than 15.0% and 11.1%. These proportions are consistent with the previously mentioned 2009 estimates for industrialized nation populations. However, notably, the proportion of chlamydia infections that were recurrent among active component service members was higher than those (7.2%–12.2% per year) reported in the *MSMR* for the 2000–2009 period.[10]

High-risk groups identified in this report are consistent with those identified in recent military reports. Soldiers, those less than 25 years of age, junior enlisted ranks, females, non-Hispanic blacks, single/never-married service members, and those with high school or less education had the highest crude rates of both initial chlamydia and gonorrhea infections. These same groups (with the exception of the education group and single/never-married service members) had highest adjusted risks of recurrent chlamydia infection. However, when all other factors were controlled for, relative risk was much lower across all categories for both types of repeat infection, and only the Army, junior enlisted ranks, and non-Hispanic black and Hispanic groups remained at statistically significant elevated risk of repeat gonorrhea infection.

The findings in this report are subject to several limitations. First, the use of ICD-9 codes alone, without requiring confirmatory laboratory results as the basis for a surveillance case definition, potentially increases the risk of misclassification due to miscoding. The use of reportable medical events in the case definition likely alleviates some of this potential bias, given the requirement for case confirmation prior to reporting. Second, members of the incident cohort were followed for varying amounts of time over the surveillance period, which likely results in underrepresentation of repeat infection counts and proportions. Finally, the definitions of incident and

TABLE 5. Recurrent (repeat) *Neisseria gonorrhoeae* infections among active component members with an initial infection between 2010 and 2014

No. of recurrent infections per service member	No. of service members with specified no. of recurrent infections	% of all service members who had an initial infection	Total no. of recurrent infections
0	8,186	89.6	0
1	809	8.9	809
2	114	1.2	228
3	20	0.2	60
4 or more	9	0.1	41
Total	9,138	100.0	1,138

recurrent (i.e., initial and repeat) infection in this report limit direct comparison to prior *MSMR* rate reporting. The definitions chosen also potentially bias the estimation of risk magnitude away from the null for younger age groups, given that service members with prior infections were excluded, and those members are likely to be older, with more years of service.

TABLE 6. Risk of recurrent *Chlamydia trachomatis* infection among active component members with an incident infection between 2010 and 2014: risk of recurrence vs. no recurrence[a]

	No. of incident chlamydia infections	No. of cohort members with recurrence	Recurrence rate (per 10,000 p-yrs)	Multivariate rate ratio	95% CI	
Total	66,396	9,658	892.2			
Service						
Army	30,287	4,958	1032.9	1.45	1.37	1.54
Navy	13,853	1,767	807.1	Ref		
Air Force	14,456	2,004	736.7	1.02	0.95	1.09
Marine Corps	7,800	929	833.0	1.14	1.05	1.24
Age (years)						
17–19	9,534	2,122	1404.3	3.26	2.33	4.55
20–24	38,521	5,686	936.9	2.49	1.79	3.46
25–29	12,732	1,428	652.1	1.97	1.42	2.74
30–39	4,932	385	411.1	1.33	0.95	1.86
40+	677	37	311.5	Ref		
Rank						
Jr. enlisted	52,042	8,237	1010.3	1.49	1.27	1.74
Sr. enlisted	12,098	1,216	545.7	1.22	1.04	1.44
Officer	2,256	205	461.9	Ref		
Gender						
Female	23,482	4,468	1163.0	1.36	1.30	1.42
Male	42,914	5,190	743.2	Ref		
Race/ethnicity						
White, non-Hispanic	30,800	3,758	760.0	Ref		
Black, non-Hispanic	20,315	3,600	1073.3	1.31	1.25	1.37
Hispanic	8,405	1,278	933.7	1.18	1.10	1.26
Asian/Pacific Islander	2,145	326	881.1	1.19	1.06	1.33
American Indian/Alaskan Native	718	110	989.8	1.23	1.01	1.48
Other/unknown	4,013	586	866.8	1.18	1.07	1.29
Marital status						
Single, never married	43,533	6,905	994.6	1.15	1.09	1.21
Married	19,455	2,303	700.6	Ref		
Other/unknown	3,408	450	755.6	1.23	1.11	1.36
Education						
High school or less	58,630	8,803	930.8	1.05	0.96	1.14
Some college or greater	6,806	755	625.7	Ref		
Unknown	960	100	622.5	0.88	0.71	1.09
Re-deployment						
Less than 180 days	5,820	839	820.0	Ref		
More than 180 days	60,576	8,819	899.7	0.98	0.91	1.06

[a]Univariate and multivariate Poisson regression analysis was conducted. Multivariate results are presented.

TABLE 7. Risk of recurrent *N. gonorrhoeae* infection among active component members with an incident infection between 2010 and 2014: risk of recurrence vs. no recurrence[a]

	No. of incident gonorrhea infections	No. of cohort members with recurrence	Recurrence rate (per 10,000 p-yrs)	Multivariate rate ratio	95% CI	
Total	9,138	952	621.1			
Service						
Army	5,272	689	813.8	2.16	1.75	2.68
Navy	1,648	104	355.1	Ref		
Air Force	1,172	90	393.7	1.11	0.83	1.48
Marine Corps	1,046	69	419.0	1.15	0.85	1.57
Age (years)						
17–19	1,096	136	716.3	1.72	0.84	3.50
20–24	5,027	585	721.5	1.72	0.87	3.43
25–29	1,888	162	495.9	1.37	0.69	2.70
30–39	961	60	336.6	1.02	0.51	2.07
40+	166	9	330.9	Ref		
Rank						
Jr. enlisted	7,018	810	720.8	1.84	1.12	3.00
Sr. enlisted	1,828	122	350.9	1.16	0.70	1.93
Officer	292	20	326.1	Ref		
Gender						
Female	1,814	206	618.4	0.91	0.77	1.07
Male	7,324	746	621.8	Ref		
Race/ethnicity						
White, non-Hispanic	2,788	188	414.8	Ref		
Black, non-Hispanic	4,686	613	771.0	1.62	1.38	1.92
Hispanic	951	99	623.5	1.48	1.16	1.90
Asian/Pacific Islander	228	20	485.3	1.11	0.70	1.77
American Indian/Alaskan Native	76	5	387.5	1.09	0.45	2.64
Other/unknown	409	27	377.1	1.21	0.80	1.83
Marital status						
Single, never married	5,928	652	661.9	1.03	0.88	1.21
Married	2,782	258	547.2	Ref		
Other/unknown	428	42	550.9	1.21	0.87	1.69
Education						
High school or less	8,050	849	633.9	0.86	0.67	1.10
Some college or greater	966	89	519.2	Ref		
Unknown	122	14	636.8	1.04	0.59	1.83
Re-deployment						
Less than 180 days	937	101	591.7	Ref		
More than 180 days	8,201	851	624.8	1.09	0.88	1.34

[a]Univariate and multivariate Poisson regression analysis was conducted. Multivariate results are presented.

However, an analysis of true incident and recurrent chlamydia and gonorrhea infections among active component members may allow for better characterization of the burden and risk of these infections. For example, the steady and marked increase in new chlamydia infections shown in this report may partially represent increased case-finding due to screening practices. However, the fact that rates increased prominently among men and remained stable among women suggests an actual increase in incidence, given that men are not routinely screened. That, coupled with the notable decrease in new gonorrhea infection rates among women (while male rates increased slightly) and the lack of

statistically significant difference in gender-specific risk of recurrence, potentially supports reassessment of active component male STI screening—at least among high-risk groups.

At a minimum, continued efforts at strict compliance with United States Preventive Services Task Force chlamydia and gonorrhea screening recommendations[11] appear to be warranted. Implementation of Community Preventive Services Task Force evidence-based STI comprehensive risk reduction (CRR) strategies[12] could also be considered. CRR programs could be targeted at well-established active component high-risk groups, and, importantly, at members with initial chlamydia or gonorrhea infection, given the significant impact of repeat infection on the epidemiology of these conditions.

Disclaimer: The views expressed are those of the authors and do not necessarily reflect the official views of the Uniformed Services University of the Health Sciences or the Department of the Navy.

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REFERENCES

1. Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2013*. Atlanta: U.S. Department of Health and Human Services; 2014.
2. Centers for Disease Control and Prevention. Chlamydia–CDC Fact Sheet. www.cdc.gov/std/chlamydia/stdfact-chlamydia.htm. Last updated 12 December 2014. Accessed on 2 November 2015.
3. Centers for Disease Control and Prevention. Gonorrhea–CDC Fact Sheet. www.cdc.gov/std/gonorrhea/stdfact-gonorrhea.htm. Last updated 14 December 2014. Accessed on 2 November 2015.
4. Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2012*. Atlanta: U.S. Department of Health and Human Services; 2013.
5. Sanchez J, Agan B, Tsai A, et al. Expanded Sexually Transmitted Infection Surveillance Efforts in the United States Military: A Time for Action. *Mil Med*. 2013;178(12):1271–1280.
6. Armed Forces Health Surveillance Center. Sexually transmitted infections, active component, U.S. Armed Forces, 2000–2012. *MSMR*. 2013;20(2):5–10.
7. Centers for Disease Control and Prevention. 2015 Sexually Transmitted Diseases Treatment Guidelines: Chlamydial Infections. www.cdc.gov/std/tg2015/chlamydia.htm. Last updated 4 June 2015. Accessed on 4 November 2015.
8. American College of Obstetricians and Gynecologists. Committee Opinion No. 645: Dual therapy for gonococcal infections. *Obstet Gynecol*. 2015;126:e95–e99.
9. Hosenfeld CB, Workowski KA, Berman S, et al. Repeat infection with chlamydia and gonorrhea among females: a systematic review of the literature. *Sex Transm Dis*. 2009;36(8):478–489.
10. Armed Forces Health Surveillance Center. Brief report: Recurrent chlamydia diagnoses, active component, 2000–2009. *MSMR*. 2010;17(8):15–17.
11. U.S. Preventive Services Task Force. Final Recommendation Statement: Gonorrhea and Chlamydia: Screening, September 2014. www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/chlamydia-and-gonorrhea-screening. Last updated September 2014. Accessed on 2 November 2015.
12. Community Preventive Services Task Force. Preventing HIV/AIDS, Other STIs, and Teen Pregnancy: Group-Based Comprehensive Risk Reduction Interventions for Adolescents. www.thecommunityguide.org/hiv/riskreduction.html. Last updated 23 February 2015. Accessed on 2 November 2015.

Incidence of *Chlamydia trachomatis* Infections and Screening Compliance, U.S. Army Active Duty Females Under 25 Years of Age, 2011–2014

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Reported chlamydia infection rates among active duty U.S. Army females less than 25 years old declined by 20% from 2011 to 2014 (11,028 infections per 100,000 person-years [p-yrs] to 8,793 infections per 100,000 p-yrs, respectively). An overall decline in the proportions of high-risk female soldiers tested for chlamydia occurred during the same period, declining from a high of 85% in 2011 to a low of 71% in 2012, with an increase to 80% in 2014. Chlamydia laboratory testing volume also decreased from 2011 to 2013 but the test positivity rate remained stable at 6.0%–6.4%. By using projected incidence rates based on 100% of at-risk women being screened with a stable laboratory positivity rate, there was an estimated 15% decline in chlamydia incidence from 2011 to 2014 (12,794 to 10,991 infections per 100,000 p-yrs, respectively). Surveillance for chlamydia infections must include consideration of screening program performance in addition to passive reporting.

Chlamydia trachomatis is the most commonly reported bacterial infection in the U.S.[1] Previous studies have documented high incidence rates among members of the U.S. military, especially Army soldiers.[2,3] High-risk groups for infection include individuals less than 25 years old, females, ethnic minorities, those in low socioeconomic status, residents of the Southern U.S., and persons engaging in high-risk behaviors such as drug use. Among those infected, women are more affected by repeat or undetected infections due to potential reproductive sequelae. Untreated infections can lead to pelvic inflammatory disease, a major cause of infertility, ectopic pregnancy, and chronic pelvic pain.[1] Consequently, most chlamydia screening programs have targeted women.

Because the vast majority of chlamydia infections are asymptomatic, screening programs are crucial. Annual chlamydia screening for sexually active females less than 25 years old was ranked by the National Commission on Prevention Priorities as one of the 10 most beneficial and cost-effective prevention strategies.[4] Currently, the U.S. Preventive Services Task Force recommends that sexually active women aged 24 years and younger receive annual chlamydia screening.[5] The U.S. Army follows this guidance.[6] The first screening opportunity occurs during Advanced Individual Training, where testing is provided to trainees who have progressed from basic military training (BMT). The recommended age for annual chlamydia screening can vary to include sexually active women less than 26 years old. The U.S. Navy, which provides medical services for the Navy and Marine Corps, currently uses this cut point for annual chlamydia screening; however, the first opportunity for screening, which occurs in BMT, is provided to all female trainees.[7] The U.S. Air Force provides annual screening for women that begins with screening of all female trainees during the first week of BMT.[8] Thereafter, Centers for Disease Control and Prevention (CDC) guidelines are followed.[9]

The U.S. Army consists of primarily young, healthy, sexually active people with high chlamydia infection rates, so chlamydia screening programs are supported and encouraged.[1–3] The infections identified are reported in the military's Disease Reporting System-internet (DRSi), in accordance with DoD reporting guidelines.[10] Reporting of chlamydia cases among Army active duty (AD) soldiers using DRSi, for the period 2008–2014, was found to represent approximately 90% of diagnosed chlamydia cases recorded in the Military Health System (MHS).[11] A decline in the reported incidence of chlamydia infections from 2011 to 2014 prompted a review of the female soldier chlamydia screening program to identify artifactual contributions.

METHODS

Chlamydia incidence estimates among non-deployed AD Army soldiers during 2011–2014 were extracted from the Public Health 360 (PH360) dashboard.[12] PH360 incident chlamydia infections were identified from case reports submitted through the DRSi. A 30 day gap-in-care rule was used to define incident infections; any case reported more than 30 days after a previous report indicated a new infection. Person-year (p-yr) estimates obtained from the Defense Medical Surveillance System (DMSS), Silver Spring, MD, were used to develop the PH360 incidence estimates and were adjusted to remove time deployed to theaters of operations. In-theater case reports were likewise excluded from the analyses. Chlamydia screening estimates among sexually active female soldiers less than 25 years old were obtained from the Military Health System Population Health Portal (MHSPHP).[13] MHSPHP estimates were restricted to sexually active Army AD women less than 25 years old who were continuously enrolled in the MHS TRICARE Prime for each 12-month calendar year evaluated.[14]

Laboratory test data for chlamydia were provided by the Navy and Marine Corps Public Health Center, Portsmouth, VA, using Health Level 7 (HL7)-formatted records extracted from the MHS Composite Healthcare System (CHCS). Laboratory records for Army beneficiaries tested during

2011–2013 were examined. The numbers of tests done and the annual percentages testing positive were determined. To assess the potential effect decreased screening may have had on reported incidence, incidence projections were generated based on the assumptions of 100% screening compliance and a stable percentage of the screened population having a positive chlamydia test.

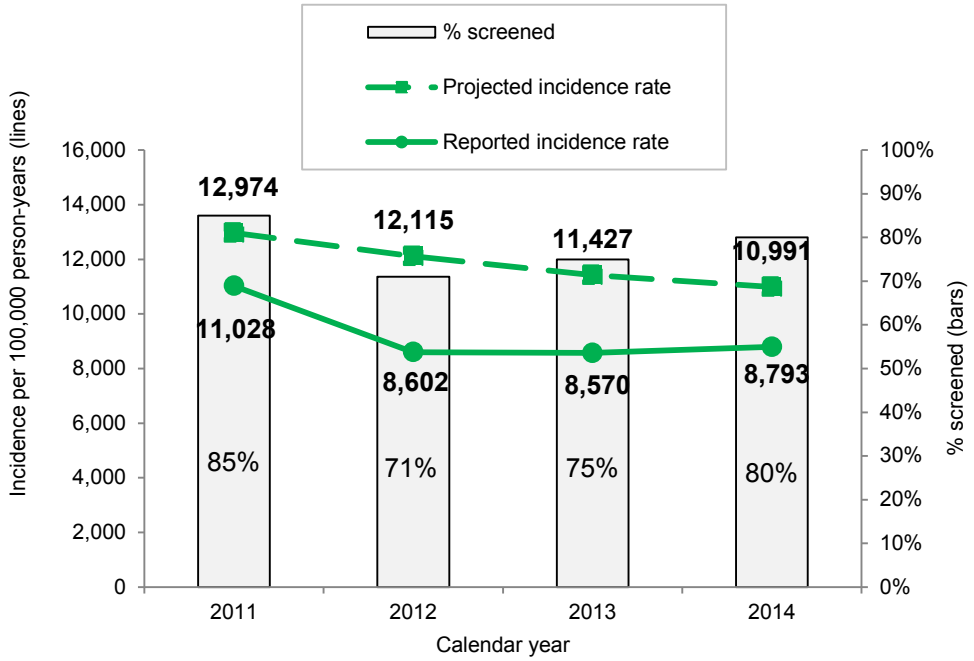
RESULTS

The overall incidence of reported chlamydia among all Army AD soldiers declined from a high of 1,884 infections per 100,000 p-yrs in 2011 to a low of 1,678 infections per 100,000 p-yrs in 2014 (data not shown). Observed incidence rates among female AD soldiers were roughly 3.5 times higher than their male counterparts. A modest 2% decline in incidence rates among male AD soldiers occurred from 2011–2014 (range: 1,298–1,278 infections per 100,000 p-yrs), while rates among AD females decreased 24% (range: 5,412–4,114 infections per 100,000 p-yrs). The decrease among females less than 25 years old was 20%, declining from 11,028 infections per 100,000 p-yrs in 2011 to 8,793 infections per 100,000 p-yrs in 2014 **(Figure 1)**. Analysis of HL7 laboratory records revealed a drop in overall Army chlamydia testing volume, decreasing by 30% from approximately 154,901 tests certified in 2011 to 107,740 certified in 2013. However, the proportion testing positive remained stable at 6.0%–6.4% (data not shown).

Based on the stability of chlamydia laboratory test positivity, projected incidence rates were extrapolated for the targeted female screening group with the assumption of 100% screening compliance. Projected incidence rates were approximately 29% higher on average, corresponding to an average of 620 new cases identified each year. Projections reflected an overall decrease of 15% during 2011–2014 (declining from 12,794 to 10,991 infections per 100,000 p-yrs), as compared to the 20% decrease observed for crude reported rates **(Figure 1)**.

Reductions in reported chlamydia incidence for women less than 25 years old correlated with changes in chlamydia screening rates and decreased chlamydia testing volume. Chlamydia screening estimates for Army AD females less than 25 years old peaked in 2011 at 85% but decreased in 2012 to a low of 71%, before rising to 80% in 2014. Although screening rates exceeded the Healthy People 2020 national goals for women enrolled in commercial healthcare plans (61% and 75% for women aged 16–20 and 21–24 years, respectively), surpassing to a greater extent the actual 2013 screening compliance for these groups (42% and 51% for women 16–20 and 21–24 years, respectively),[15] there remains room for improvement. Considerable variation in compliance was observed across U.S. Army installations (range: 35%–95%); disparities in screening compliance improved during the study period, with the lowest installation screening compliance increasing from 35% in 2011 to 67% in 2014 **(Figure 2)**.

FIGURE 1. Reported and projected incidence rates of chlamydia infections and chlamydia screening compliance, Army active duty females less than 25 years old, 2011–2014[a]



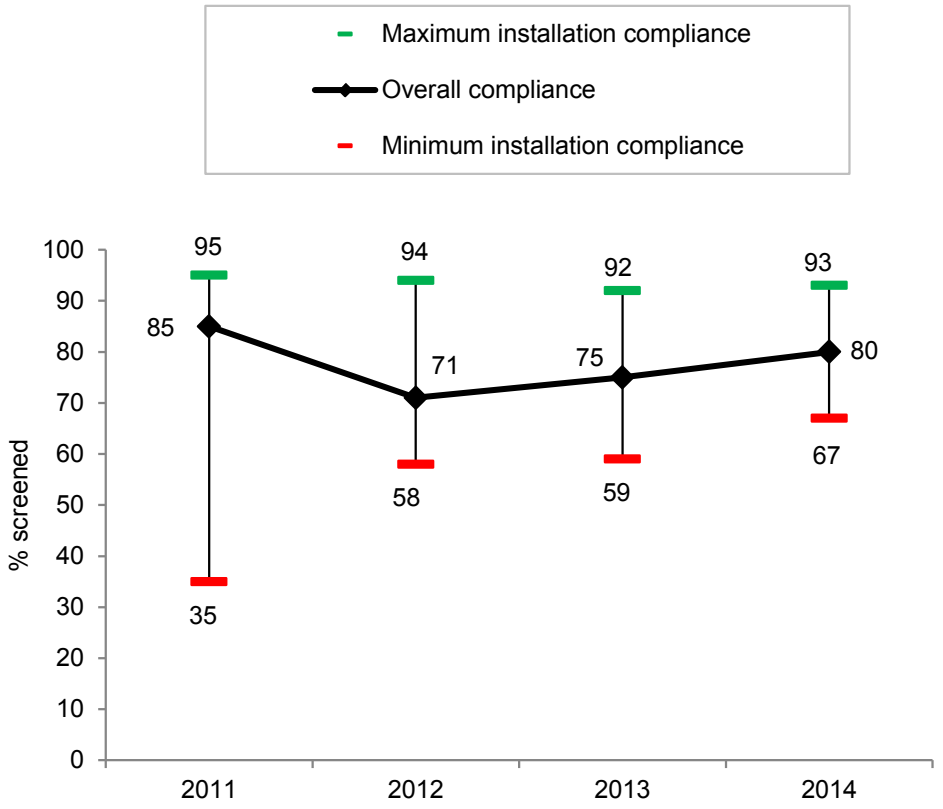
[a]Projected Incidence = Incidence expected if 100% of female soldiers under 25 years of age were screened, assuming a stable proportion of chlamydia laboratory test positivity.

DISCUSSION

During the surveillance period, reported chlamydia incidence decreased among AD soldiers. However, declines in screening of women less than 25 years old, the targeted demographic group for chlamydia screening, were of concern. Among this group, trends in reported chlamydia incidence rates coincided with screening compliance estimates. The most substantial drop for both reported incidence and screening occurred in 2012. A similar but considerably greater downward trend for the volume of chlamydia laboratory tests performed was observed, while the test positivity remained stable. Taken together, this information supported concerns that the decline in the incidence of chlamydia infections could be related to a decline in screening of women at risk. Incidence projections reflecting the expected incidence at 100% screening of at-risk women provided a more comprehensive estimation of the true incidence of chlamydia infections in U.S. Army female soldiers aged 24 years and younger. Benefits of multi-sourced data fusion are that it provides insight into possible surveillance artifacts and can help pinpoint areas for improvement. The notable drop in laboratory testing volume, for example, should be explored further, given that it exceeded what can be explained by decreased screening alone.

Within the Army, men make up approximately 85% of the chlamydia infection at-risk population, with nearly 40% being less

FIGURE 2. Chlamydia screening compliance: Proportions of active duty Army females less than 25 years old who were screened, by year, 2011–2014[a]



[a]Ranges reflect the range of screening compliance across Army installations.

than 25 years old. Given the predominance of asymptomatic infections in men, the large proportion of male soldiers in a high-risk age group, and decreased testing costs, consideration should be given to screening this group when resources are available.[16–18] The CDC has recommended that male military members less than 30 years old be considered for screening, and initial cost effectiveness studies support providing screening for male recruits.[16,18] However, the primary focus of chlamydia screening programs should remain on women who are at risk of serious sequelae.

Although screening proportions for Army women are relatively high, improved capture of the targeted screening group would potentially identify more than 600 currently unreported infections per year, reduce transmission, and prevent costly reproductive complications. Modeling chlamydia incidence through screening compliance proportions and laboratory testing provides a means to estimate the actual infection rate in the targeted screening population. However, determining the true incidence through 100% testing of high-risk females remains a goal to be achieved.

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REFERENCES

1. Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance, 2013*. Atlanta, GA: U.S. Department of Health and Human Services; December 2014.
2. Jordan NN, Lee SE, Nowak G, Johns NM, Gaydos JC. *Chlamydia trachomatis* reported among U.S. active duty service members, 2000-2008. *Mil Med*. 2011;176(3):312–319.
3. Gaydos CA, Howell MR, Quinn JC, McKee JKT Jr, Gaydos JC. Sustained high prevalence of *Chlamydia trachomatis* infections in female Army recruits. *Sex Transm Dis*. 2003;30(7):539–544.
4. Maciosek MV, Coffield AB, Edwards NM, et al. Priorities among effective clinical preventive services. Results from a systematic review and analysis. *Am J Prev Med* 2006;31(1):52–61.
5. U.S. Preventive Services Task Force. Final Recommendation Statement: Chlamydia and Gonorrhea: Screening. December 2014.
6. Bloom MS, Hu Z, Gaydos JC, Brundage JF, Tobler SK. Incidence rates of pelvic inflammatory disease diagnoses among Army and Navy recruits: potential impacts of chlamydia screening policies. *Am J Prev Med*. 2008;23(6):471–477.
7. Manual of the Medical Department U.S. Navy NAVMED P-117. Section V. Article 15-112. References and Resources and annual health assessment Recommendations for Active Duty Women. 16 December 2013.
8. 559th Medical Operations Squadron Operating Instruction 44-6. Gonorrhea and Chlamydia Screening and Evaluation. 5 August 2014.
9. Air Force Instruction 48-105. Surveillance, Prevention, and Control of Disease and Conditions of Public Health or Military Significance. 15 July 2015.
10. Armed Forces Health Surveillance Center. Armed Forces Reportable Medical Events Guidelines and Case Definitions, March 2012. www.afhsc.mil/Home/ReportableEvents.
11. Hurt L, Ying S. Completeness and timeliness of reporting of notifiable medical conditions, active component, U.S. Armed Forces, 2008–2014. *MSMR*. 2015;22(11):8–21.
12. Patient Administration Systems and Biostatistics Activity. PH360: Public Health 360.
13. Military Health System Population Health Portal MHSPHP.
14. Healthcare Informatics Division, AF/SG6H. Chlamydia Screening. March 2014.
15. Healthy People 2020. Sexually Transmitted Diseases. Objectives STD-4.1–STD4.2.www.healthypeople.gov/2020/topics-objectives/topic/sexually-transmitted-diseases/objectives. Accessed on 22 Feb 2016.
16. Nevin RL, Shuping EE, Frick KD, Gaydos JC, Gaydos CA. Cost and effectiveness of chlamydia screening among male military recruits: Markov modeling of complications averted through notification of prior female partners sexually transmitted diseases. *Sex Transm Dis*. 2008;35(8):705–713.
17. Cecil JA, Howell MR, Tawes JJ, Gaydos JC, McKee KT, Jr, Quinn TC, Gaydos CA: Features of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection in male Army recruits. *J Infect Dis*. 2001.184(9):1216–1219.
18. Centers for Disease Control and Prevention. Male Chlamydia Screening Consultation, Atlanta, GA, March 28–29, 2006: Meeting Report, May 22, 2007. www.cdc.gov/std/chlamydia/ChlamydiaScreening-males.pdf. Accessed on 23 February 2016.

Brief Report

Associations Between Antecedent Bacterial Vaginosis and Incident Chlamydia and Gonorrhea Diagnoses, U.S. Army Females, 2006–2012

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Bacterial vaginosis (BV) is a common vaginal condition in women of reproductive age.[1] In women with BV, the most frequent symptom is an excessive vaginal discharge that may appear white or gray with a strong fishy odor often noticed after sexual intercourse. The etiology of this condition is still unknown, but researchers believe that BV occurs when *Lactobacillus spp.*, the predominant species in healthy vaginal flora, is replaced by other organisms such as *Gardnerella vaginalis*. Over the past two decades, numerous studies have reported that BV is associated with chlamydia and gonorrhea infection.[2] There is also evidence that the severity of BV as measured by the Nugent score is strongly associated with these common bacterial infections.[3] The Nugent score, a reproducible and reliable method, is a scoring system on Gram-stained smears of vaginal secretions; a score of 7–10 is considered diagnostic of BV.[1] Recently, a cohort study has determined a temporal relationship between BV and chlamydia/gonorrhea in both directions, whereby BV facilitates acquisition of both of these sexually transmitted infections (STIs) and these STIs are associated with the development of BV.[4]

In the U.S. military, chlamydia and gonorrhea constitute two of the three most commonly reported STIs.[5] The highest rates for these infections occur among young females in the U.S. Army, of black race/ethnicity, and among service members from the Southern U.S. In the U.S. military, the incidence of BV and the associations between BV and chlamydia and gonorrhea infection are unclear. This report presents preliminary findings of an association between BV and these STIs from a 7-year analysis of diagnostic encounters among U.S. Army females.

METHODS

Using military surveillance data from the Defense Medical Surveillance System (DMSS), a nested case-control study was conducted to determine the degree of association between BV and chlamydia or gonorrhea infection. All female active duty U.S. Army personnel with a diagnosis of chlamydia (ICD-9: 099.41 or 099.5) or gonorrhea (ICD-9: 098.0x, 098.1x, 098.4x, or 098.8x), in either the first or second diagnostic position of an outpatient or inpatient encounter reported between January 2006 and December 2012 were selected as either "chlamydia cases" or "gonorrhea cases," respectively. Each chlamydia or gonorrhea case was randomly matched by age (±1 year) with 10 controls from the population of female soldiers who had never had a chlamydia or gonorrhea diagnosis. Controls had to be serving in the Army at the time of diagnosis of the case to which they were matched. Selection of controls employed risk-set sampling with replacement. Female service members with a diagnosis of BV (ICD-9: 616.10, vaginitis and vulvovaginitis, unspecified) in either the first or second diagnostic position of an outpatient or inpatient encounter recorded at any time prior to a diagnosis of chlamydia or gonorrhea were classified as "BV cases." Behavioral risk factor information such as number of lifetime sexual partners, sexual preferences, condom use patterns, and other high-risk sexual behaviors was not available.

Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated using conditional logistic regression to determine the association between BV and subsequent chlamydia and gonorrhea diagnosis. Reported p-values less than 0.05 were considered statistically significant, and analyses were carried out using Stata (Stata Corp LP, College Station, TX).

RESULTS

During the study period, 37,149 chlamydia cases and 4,987 gonorrhea cases were identified (**Table 1**). Among chlamydia cases, the prevalence of antecedent BV diagnosis was 21.4%, compared to 15.6% for their controls. Additionally, the highest BV prevalences among chlamydia cases were observed among women whose marital status was "other" or married, or who were black or Hispanic. Moreover, among the chlamydia controls, the highest antecedent BV prevalences were in women with "other" marital status or of black race/ethnicity. After adjustment, BV was significantly associated with a subsequent chlamydia diagnosis (AOR = 1.52, $p < 0.001$). Interestingly, the strongest adjusted associations were observed among single and white women soldiers.

Among gonorrhea cases, the prevalence of antecedent BV diagnosis was 34.7% compared to 22.2% for their controls. Highest antecedent BV prevalences were noted among other marital status and married women, and among those of

TABLE 1. Prevalence of antecedent bacterial vaginosis (BV) diagnosis (in %) and association with subsequent chlamydia and gonorrhea infection, U.S. Army females, 2006–2012

	Cases		Controls		Regression analysis	
	No.	Prevalence of BV (%)	No.	Prevalence of BV (%)	AOR	95% CI
			Chlamydia			
Overall	37,149	21.4	371,490	15.6	1.52	1.48–1.57
Race/ethnicity						
White	14,827	16.5	193,291	12.2	1.47	1.40–1.55
Black	12,753	29.1	77,712	26.2	1.22	1.16–1.29
Hispanic	4,990	19.9	51,949	14.9	1.35	1.21–1.51
Other[a]	3,961	15.7	41,236	11.4	1.35	1.17–1.56
Missing	618	27.2	7,302	19.3	1.60	0.84–3.06
Marital status						
Single	25,371	16.6	238,865	11.2	1.62	1.56–1.69
Married	9,373	29.3	118,436	22.3	1.44	1.36–1.52
Other	2,387	40.9	13,993	33.7	1.36	1.16–1.59
Missing	18	38.9	196	15.3	Undefined	
			Gonorrhea			
Overall	4,987	34.7	49,870	22.2	2.44	2.28–2.60
Race/ethnicity						
White	1,136	26.1	25,096	14.4	2.32	1.97–2.73
Black	2,838	39.4	11,571	31.8	1.56	1.40–1.73
Hispanic	525	32.0	6,777	18.5	2.12	1.55–2.89
Other[a]	391	27.1	5,426	13.6	2.65	1.76–3.98
Missing	97	41.2	1,000	24.2	0.97	0.19–4.92
Marital status						
Single	3,257	28.2	30,369	13.8	2.70	2.46–2.96
Married	1,370	44.2	17,107	25.6	2.20	1.94–2.51
Other	352	57.1	2,367	40.6	1.65	1.15–2.37
Missing	8	62.5	27	22.2	Undefined	

AOR = adjusted odds ratio, for race/ethnicity, marital status, and overall; CI = confidence interval.

[a]American/Indian/Alaska Native, Asian/Pacific Islander, and Other

black race/ethnicity. After adjustment, BV was significantly associated with a subsequent gonorrhea diagnosis (AOR = 2.44, $p < 0.001$). The analysis also revealed that the strongest adjusted associations between BV and gonorrhea were noted for women with single marital status and women whose race/ethnicity was "Other."

DISCUSSION

Preliminary findings from this nested case-control study among Army females appear to indicate that antecedent BV may constitute a biological risk factor for subsequent chlamydia and gonorrhea infection in the U.S. Army. In other words, women diagnosed with BV were 1.5 and 2.4 times more likely to have a subsequent diagnosis of chlamydia or gonorrhea, respectively. Similar estimates have been recently published for 645 female patients at a sexually transmitted disease clinic in Alabama.[4] Interestingly, the association of antecedent BV with incident chlamydia or gonorrhea was higher among Hispanic women compared to black women. This finding cannot be explained by the data available; thus, additional studies are required to explain this disparity. However, it is hypothesized that differences in the composition of bacterial vaginal flora among race/ethnicity groups might help to explain this disparity, in addition to differences in sexual risk behaviors.[6,7]

The preliminary results of this study also revealed that among single women, the association of chlamydia or gonorrhea with BV was stronger compared to married women. Based on a recent military study, unmarried and young women service members were more likely than married women to engage in high-risk sexual behaviors such as multiple lifetime sexual partners, low condom use, and sex while under the influence of drugs or alcohol.[8] These sexual behaviors may explain the strong association between BV and incident chlamydia and gonorrhea diagnosis among single women. It is also possible that the military's chlamydia screening program implemented in 1999, which involves the mandatory annual screening for infection of all active duty females younger than 25 years of age, may have had some effect on this relationship. Thus, it may be that younger, single women in service are screened more frequently, so, there may have been a potential bias toward finding an association in this group as opposed to older, married women.

In conclusion, these preliminary results indicate that among U.S. Army females, BV is associated with an increased risk of subsequent chlamydia and gonorrhea diagnoses, and that stronger associations were observed among single women. It is important to note that it is likely that the associations described herein were significantly affected by the limitations of ICD-9 codes as indicators of BV; many "BV cases" may have been misclassified and may have actually been cases of other types of vaginitis such as candidiasis or noninfectious vaginitis. Thus, laboratory-based studies which use objective clinical measures of BV (such as pH, assessment for clue cells and amine odor in wet smear) or the standardized Nugent criteria (which consider presence of *Lactobacilli*, *Gardnerella*, *Bacteroides* or curved gram-negative bacilli, and assessment for clue cells) would more specifically address associations between BV and these common bacterial infections in the U.S. military.

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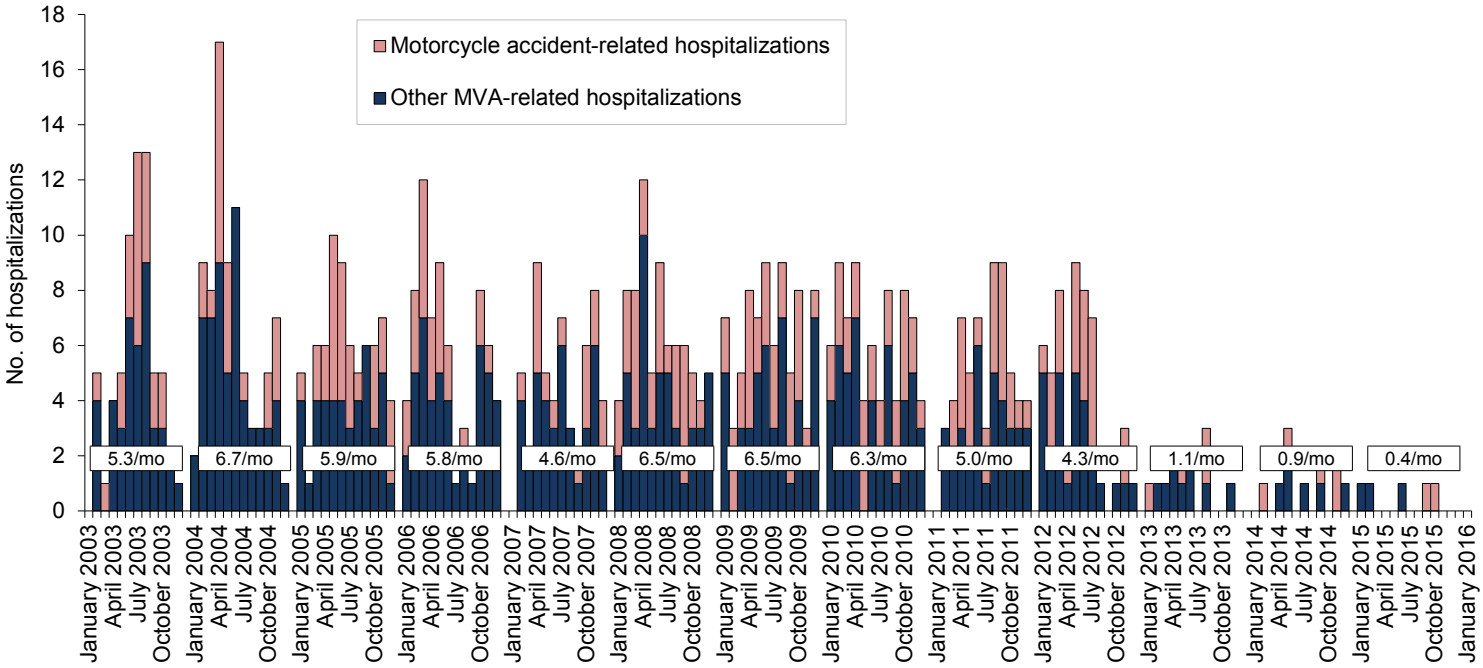
REFERENCES

1. Kenyon C, Colebunders R, Crucitti T. The global epidemiology of bacterial vaginosis: a systematic review. *Am J Obstet Gynecol*. 2013;209(6):505–523.
2. Wiesenfeld HC, Hillier SL, Krohn MA, Landers DV, Sweet RL. Bacterial vaginosis is a strong predictor of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infection. *Clin Infect Dis*. 2003;36(5):663–668.
3. Allsworth JE, Peipert JF. Severity of bacterial vaginosis and the risk of sexually transmitted infection. *Am J Obstet Gynecol*. 2011;205(2):113.e1–113e6.
4. Gallo MF, Macaluso M, Warner L, Fleenor ME, Hook EW 3rd, Brill I, et al. Bacterial vaginosis, gonorrhea, and chlamydial infection among women attending a sexually transmitted disease clinic: a longitudinal analysis of possible causal links. *Ann Epidemiol*. 2012;22:213–220.
5. Armed Forces Health Surveillance Center. Sexually transmitted infections, active component, U.S. Armed Forces, 2000–2012. *MSMR*. 2013;20(2):5–10.
6. Hickey RJ, Zhou X, Pierson JD, Ravel J, Forney LJ. Understanding vaginal microbiome complexity from an ecological perspective. *Transl Res*. 2012;160(4):267–282.
7. Royce RA, Jackson TP, Thorp Jr JM, Hillier SL, Rabe LK, Pastore LM et al. Race/ethnicity, vaginal flora patterns, and pH during pregnancy. *Sex Transm Dis*. 1999;26(2):96–102.
8. Stahlman S, Javanbakht M, Cochran S, Hamilton AB, Shoptaw S, Gorbach PM. Self-reported STIs and sexual risk behaviors in the U.S. military: how gender influences risk. *Sex Transm Dis*. 2014;41(6):359–364.

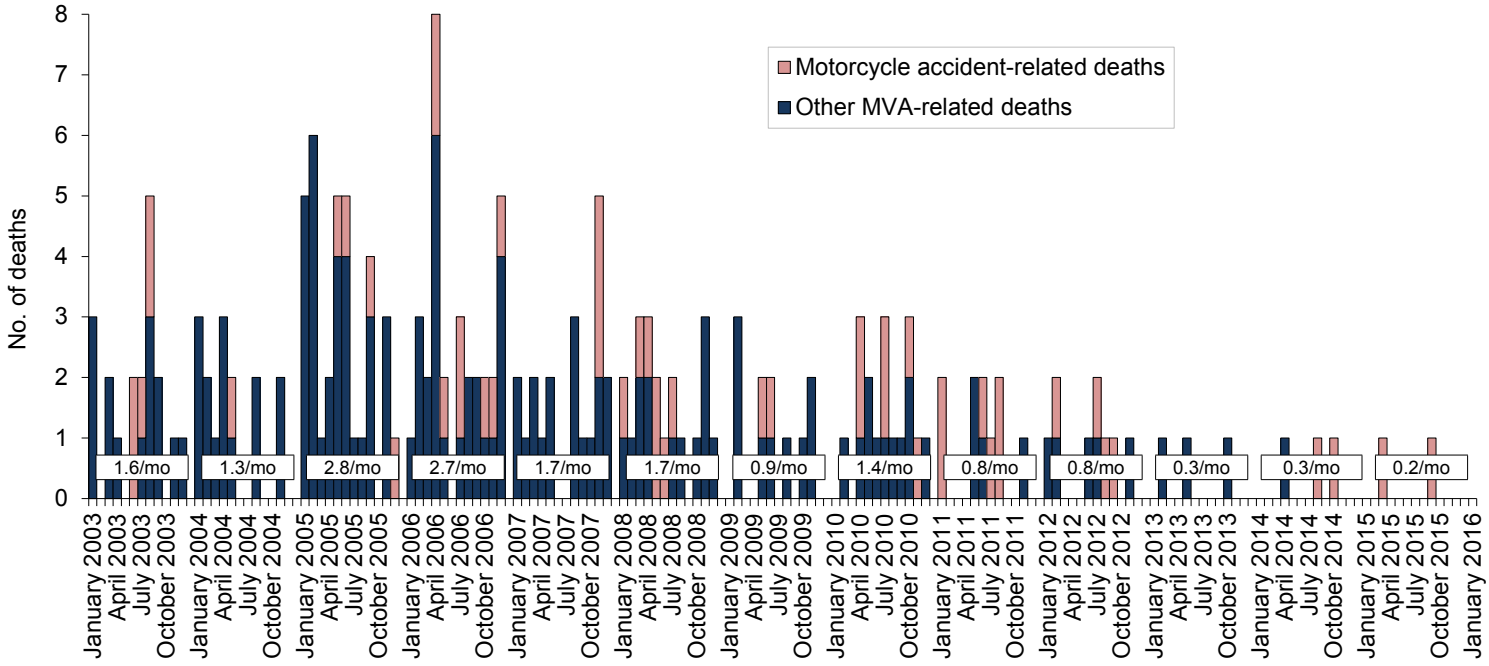
Deployment-related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003–January 2016 (data as of 22 February 2016)

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)



Reference: Armed Forces Health Surveillance Center. Motor vehicle-related deaths, U.S. Armed Forces, 2010. *MSMR*. 2011;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.

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