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Medical Surveillance for Military Readiness

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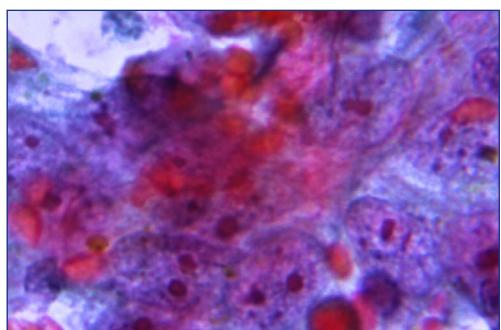
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14 [Trends in Cervical Cancer Screening Modality in the Active Component U.S. Military, 2013–2023](#)

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19 [Update: Infertility Among Active Component Service Women, U.S. Armed Forces, 2019–2023](#)

This update of infertility surveillance, analysis and reporting provides more recent estimates of infertility diagnosis incidence and prevalence of among active component U.S. service women. MSMR has published the incidence and prevalence of diagnosed female infertility among active component women since 2000, with assessments of annual rates of fertility testing since 2019.



26 [Brief Report: Association Between Recurring Headache and Selected Women's Health Issues Among U.S. Navy and Marine Corps Women: Cross-Sectional Results of the Annual Periodic Health Assessment, 2021](#)

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This cross-sectional study examines univariate associations of self-reported recurring headache with demographics and women's health characteristics.



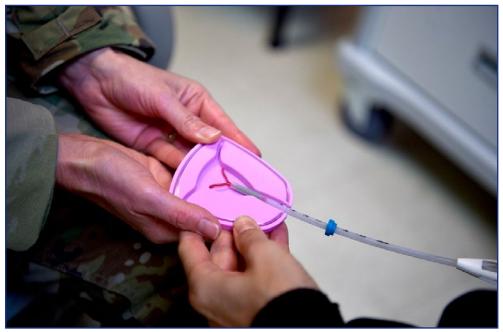
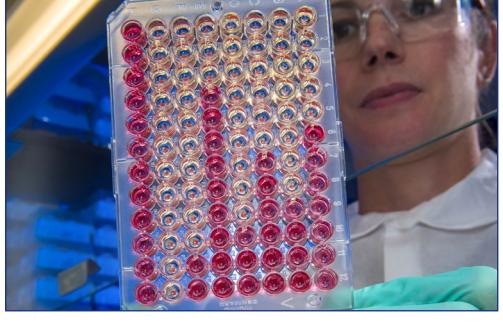
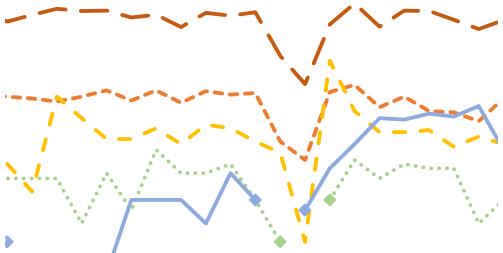
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Trends of Sepsis Hospitalizations Among Female Active Component U.S. Service Members, 2011–2022

Alexis A. McQuistan, MPH; Michael T. Fan, PhD; Sithembile L. Mabila, PhD, MSc

Studies of sepsis within the U.S. military population have consistently shown that rates of sepsis have increased over time. The observed higher incidence of sepsis in studies among women compared to men of the active component U.S. military population is of concern and warrants further evaluation, as it diverges from incidence typically observed in the U.S. general population. The objectives of this study were to examine cases of sepsis among active component U.S. service women between January 1, 2011 and December 31, 2022, compare them to active component men in the U.S. military, and identify factors associated with sepsis among female active component service members. In this study, female active component service members evinced higher rates (66.5 per 100,000 person-years) compared to males (36.7 per 100,000 person-years), with a rate of sepsis 1.9 times higher after adjusting for demographic and military-related factors. Rates of sepsis were higher among women with a history of co-morbidities.

What are the new findings?

Rates of sepsis hospitalizations among female active component service members have consistently been higher compared to male active component members. Female active component members had 1.9 times higher rates for hospitalization for sepsis compared to active component service men after adjusting for demographic and military-related factors.

What is the impact on readiness and force health protection?

Sepsis is a life-threatening condition that is costly to treat. Patients who survive sepsis may experience lasting impacts, such as long-term disability. Recovery from sepsis could lead to lost duty time, disability, or attrition among service members if the infection is severe. Identifying risk factors and prevention measures to reduce sepsis incidence and severity would improve force health protection.

Each year, approximately 1.7 million adults in the U.S. develops sepsis, and at least 250,000 adults who develop sepsis die.¹ It is estimated that 30–50% of hospitalization deaths are attributable to sepsis,^{1,2} and this estimate increases with increased disease severity.³ In a study of 750 million U.S. hospitalizations over a 22-year period, the rate of sepsis increased from 82.7 to 240.4 cases per 100,000 population from 1979 to 2000.⁴ From 2016 to 2019 the number of inpatient stays in the U.S. increased by 20.1% to 2.1 million, and with the emergence of COVID-19, the number increased again to 2.5 million.⁵ Sepsis imposes a great burden on the U.S. health care system, costing an estimated \$41.5 billion per year.⁶ Implementing and maintaining hospital sepsis prevention programs associated with reductions in mortality, lengths of hospital stay, and health care costs is imperative.^{1,7}

Studies of sepsis among the U.S. military population have consistently shown

increasing rates of sepsis over time. A 2013 study of sepsis in the active component U.S. military population from 2000 to 2012 found an overall incidence of 13.2 cases per 100,000 person-years (p-yrs) and a 570% increase between 2004 and 2012. Definitions and coding practices for sepsis changed during that period, which may have driven the large increase.⁸ A follow-up study in 2021 found that overall incidence among the active component was 39.8 per 100,000 p-yrs, and annual incidence of sepsis hospitalization increased by 64% from 2011 to 2019.⁹

Both the 2013 and 2021 studies presented evidence to suggest that sepsis rates were higher among women compared to men in the U.S. military, which is the inverse of trends seen in the general U.S. population.^{1,4} Neither study, however, was able to explain the reason for this difference. The 2021 study noted that, although infections specific to female service members were

seen, the numbers were not large enough to account for the differences.⁹ It also suggested that clinical variability in coding practices could be a factor if, for example, obstetricians were more likely than internal medicine physicians to diagnose sepsis among patients under their care.

The observed higher incidence of sepsis in previous studies among women of the active component U.S. military population is a concern that needs to be further evaluated. The previous studies raised questions about a possible growing threat to women's health in the military due to sepsis. The objectives of this study were to examine cases of sepsis between 2011 and 2022 among active component U.S. service women, compare them to active component men in the U.S. military population, and identify factors associated with sepsis among female active component service members.

Methods

This retrospective analysis included active component service members (ACSMs) from the Army, Air Force, Navy, and Marine Corps of the U.S. Armed Forces from January 1, 2011 through December 31, 2022. Data to evaluate sepsis were obtained from the Defense Medical Surveillance System (DMSS), the central repository of medical data for service members. DMSS collects inpatient administrative health records for care received at military hospitals and clinics as well as private sector care purchased through TRICARE. Demographic data obtained from DMSS

included sex, age category, race and ethnicity, service branch, occupation, geographic region, deployed status, and military rank; race and ethnicity were self-reported. Deployment status was determined by service member deployment at time of sepsis diagnosis or deployment within the prior 30 days. Deployments to unknown locations or bodies of water were not included.

International Classification of Diseases, 9th Revision (ICD-9) and 10th Revision (ICD-10) diagnostic codes were used to define incident cases of sepsis (Table 1). Septicemia was no longer listed in ICD coding following the October 2015 change to ICD-10 codes, with specific codes including causative organisms provided

instead. A case was defined as any hospitalization record with a sepsis diagnostic code in any diagnostic position. A 14-day gap in care incidence rule was applied; an individual could be included as a case more than once if more than 14 days elapsed between dates of consecutive incident case-defining encounters. Co-occurring conditions at time of sepsis hospitalization were identified by ICD-9 and ICD-10 codes from the incident sepsis encounter.

Additional encounter data for pregnancies and co-morbidities prior to sepsis diagnosis were also included (Table 2). Frequencies of sepsis cases among women who were pregnant within 280 days preceding their incident sepsis encounter

TABLE 1. Frequency of Case-Defining ICD Codes for Sepsis by Sex, Active Component U.S. Service Members, 2011–2022

| ICD Version | ICD Code | Description | Females | | Males | |
|--|----------|--|---------|------|-------|------|
| | | | No. | % | No. | % |
| ICD-9-coded encounters (2010–September 2015) | 003.1 | Salmonella septicemia | 1 | 0.1 | 5 | 0.1 |
| | 022.3 | Anthrax septicemia | 0 | 0.0 | 0 | 0.0 |
| | 038* | Septicemia | 447 | 46.6 | 1,767 | 49.0 |
| | 995.91 | Sepsis | 340 | 35.4 | 1,199 | 33.3 |
| | 995.92 | Severe sepsis | 80 | 8.3 | 392 | 10.9 |
| | 785.52 | Septic shock | 45 | 4.7 | 220 | 6.1 |
| | 998.02 | Post-operative septic shock | 0 | 0.0 | 6 | 0.2 |
| | 112.5 | <i>Candida</i> sepsis | 2 | 0.2 | 15 | 0.4 |
| Female-specific | | | | | | |
| ICD-10-coded encounters (October 2015–2022) | 670.2* | Puerperal sepsis | 45 | 4.7 | 0 | 0.0 |
| | A02.1 | Salmonella sepsis | 1 | 0.1 | 1 | 0.0 |
| | A22.7 | Anthrax sepsis | 0 | 0.0 | 0 | 0.0 |
| | A26.7 | Erysipelothrix sepsis | 0 | 0.0 | 0 | 0.0 |
| | A32.7 | <i>Listeria</i> sepsis | 0 | 0.0 | 1 | 0.0 |
| | A40* | Streptococcal sepsis | 32 | 2.2 | 140 | 3.8 |
| | A41* | Other sepsis | 1,003 | 70.2 | 2,889 | 77.4 |
| | A42.7 | Actinomycotic sepsis | 0 | 0.0 | 0 | 0.0 |
| | A54.86 | Gonococcal sepsis | 4 | 0.3 | 3 | 0.1 |
| | B37.7 | <i>Candida</i> sepsis | 2 | 0.1 | 12 | 0.3 |
| | R65.2* | Severe sepsis | 202 | 14.1 | 675 | 18.1 |
| | T81.12 | Post-procedural septic shock | 1 | 0.1 | 8 | 0.2 |
| Female-specific | | | | | | |
| | O03* | Sepsis following spontaneous abortion | 52 | 3.6 | 0 | 0.0 |
| | O04.87 | Sepsis following induced termination of pregnancy | 5 | 0.4 | 0 | 0.0 |
| | O07.37 | Sepsis following failed attempted termination of pregnancy | 6 | 0.4 | 0 | 0.0 |
| | O08.82 | Sepsis following ectopic and molar pregnancy | 6 | 0.4 | 0 | 0.0 |
| | O85 | Puerperal sepsis | 97 | 6.8 | 4 | 0.1 |
| | O86.04 | Sepsis following obstetric procedure | 18 | 1.3 | 0 | 0.0 |

*Asterisk indicates that any subsequent digit or character is included.

Abbreviations: ICD, International Classification of Diseases; No., number.

TABLE 2. Pregnancy-related and Co-Morbidity Diagnosis Codes

| Diagnosis | ICD-9 Codes | ICD-10 Codes |
|-----------------------------------|--|--|
| Pregnancy and childbirth | V22.0-V22.2, V23.*, V27.*, V72.42, 630*-679* | Z33*, Z34*, Z37*, Z32.01, O*, |
| Immune-compromising conditions | 042, 279*, 280*-289*, V42*, V58.65, 696*, 277.3*, 714.0*-714.3*, 555*, 556*, 558* | B20, D55*-D77*, D80*-D89*, Z94*, Z795*, L40*, M04*-M08*, K50*-K52* |
| Chronic kidney disease | 583*, 585*, 586*, 590.0*, 590.1*, 590.2, 590.8*, 590.9, 591, 593.3, 593.4, 593.5, 593.7* | N03*-N16*, N18*-N19* |
| Any cardiovascular disease | 393*-457* | I05*-I89*, Z95* |
| Hypertension | 401*-405*, 642* | I10*-I16*, O10*-O16* |
| Neoplasms | 140*-239* | C00*-D49* |
| Metabolic disease | 250*, 6480*, V58.67, 240*-246*, 264*-269*, 277.7 | E08*-E13*, O24*, Z794*, E00*-E07*, E50*-E64*, E88.81* |
| Any lung disease | 490*-519* | J40*-J99* |
| Chronic lower respiratory disease | 490*-492* | J40*-J44* |
| Substance use disorders | 304*, 305.1*-305.9*, 305.0*, 303.0*, 303.9*, 291.0, 291.81 | F10*-F16*, F18*-F19*, F17* |
| Alcohol use disorders | 303* | F10* |
| Chronic liver disease | 570*-573*, 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.59 | K70*-K77*, B18* |

* Asterisk indicates that any subsequent digit or character is included.

Abbreviation: ICD, International Classification of Diseases.

with a history of a listed comorbidity are described. Pregnancy-related encounters were defined using ICD-9/ICD-10 diagnosis codes (Table 2) in any diagnostic position during an inpatient, outpatient, or in-theater medical encounter or with a positive laboratory test result for human chorionic gonadotropin. Co-morbidities were identified based on prior associations with risk of sepsis and mortality risk from sepsis.^{1,10-12} Co-morbidity encounters were defined using ICD-9/ICD-10 diagnosis codes in any diagnostic position from an inpatient, outpatient, or in-theater medical encounters. Co-morbidities were assessed for a period of 365 days preceding the incident sepsis date for sepsis cases and prior history of co-morbidity among all female ACSMs. Each co-morbidity was evaluated separately.

To further evaluate sepsis incidence among women, body mass index (BMI) data were obtained from the Military Health System Data Repository (MDR) Clinical Data Repository (CDR) Vitals and MDR GENESIS Vitals. BMI was categorized as obese (≥ 30) and not obese (<30). BMI records within 280 days before or after an 'O'-coded (encounters related

to pregnancy) inpatient or outpatient encounter were excluded. Prior history of co-morbidities related to sepsis was defined as having at least 1 inpatient or outpatient encounter with a co-morbidity diagnosis in any diagnostic position.

Incidence rates were calculated as incident sepsis diagnoses per 100,000 p-yrs. Rates were calculated separately for female and male ACSMs. Rates among female ACSMs with a history of selected co-morbidities were calculated. Person-time contributions for each service member were determined from January 1, 2011 through December 31, 2022. Person-time was censored when a service member left the active component or at the end of the surveillance period. Incidence rate ratios (IRRs) and 95% confidence intervals (CIs) were calculated to compare sepsis rates between female and male ACSMs. An adjusted Poisson regression model (adjusted for race and ethnicity, age, service, grade, occupation) calculated adjusted IRRs comparing rates of sepsis among women and men. All analyses were conducted using SAS-Enterprise Guide (version 8.3).

Results

From January 1, 2011 through December 31, 2022, 6,588 incident cases of hospitalized sepsis occurred among 573,477 (16.8%) female and 2,841,317 (83.2%) male ACSMs. Female ACSMs accounted for 1,684 (25.6%) incident cases of hospitalized sepsis, while male ACSMs accounted for 4,904 (74.4%) incident cases of hospitalized sepsis between 2011 and 2022.

Table 1 summarizes the most commonly occurring sepsis diagnoses, stratified by sex. A case could be counted multiple times if the incident encounter featured more than 1 sepsis ICD-9/ICD-10 code. Among ICD-9-coded diagnoses, septicemia and sepsis were the most common diagnoses, accounting for 82% of sepsis-related diagnoses among both female and male sepsis cases. Puerperal sepsis was the only female-specific ICD-9 code and accounted for 4.7% of ICD-9 diagnoses. Among ICD-10-coded encounters, 77.4% of sepsis-related diagnoses among men were coded as "other sepsis" (A41'), which included sepsis due to an unspecified organism (A41.9) or *Escherichia coli*

(A41.51), and was the most common diagnosis in this category. The 'other sepsis' (A41*) code only accounted for 70.2% of sepsis diagnoses among women. Female-specific sepsis diagnoses accounted for 12.9% of ICD-10 sepsis diagnoses among women. Severe sepsis was diagnosed more frequently among men (18.1%) compared to women (14.1%).

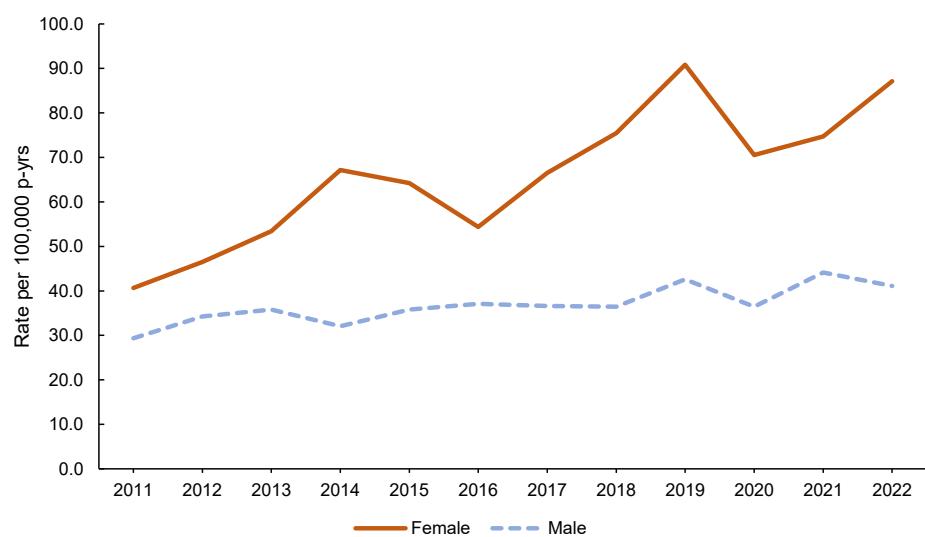
Figure 1 shows the incidence rates of sepsis per 100,000 p-yrs between 2011 and 2022, by sex. Female ACSMs consistently experienced higher rates of sepsis throughout the surveillance period. Among female ACSMs, incidence rates of sepsis peaked in 2019 (90.8 per 100,000 p-yrs) but began to trend upward again after 2020, registering 87.1 per 100,000 p-yrs in 2022. Women in nearly all demographic categories experienced higher rates of sepsis than men (**Table 3**) except in the recruit category, due to the small numbers of women. Crude rate ratios are provided that compare women to men.

Rates by age group for both sexes displayed a U-shaped pattern in which highest rates were in the under age 20 years (84.6 per 100,000 among females, 56.1 per 100,000 among males) and 45 years and older (81.6 per 100,000 among females; 72.3 per 100,000 among males) age groups in both sexes. The greatest difference between female and male sepsis cases was seen in the 20-24-year age group, in which women were 2.3 times (95% CI, 2.1, 2.6) more likely to have sepsis hospitalizations than men in the same group. Women had higher rates of sepsis compared to men in all racial and ethnic groups.

In every branch of service women also experienced higher rates of sepsis. The highest rates of sepsis for both women and men were in the Marine Corps, with female marines experiencing a rate of 87.2 per 100,000 p-yrs, while males experienced a rate of 46.1 per 100,000 p-yrs. The greatest difference in rates between the sexes was seen in the Navy, with 2.0 times (95% CI, 1.8, 2.3) the rate of sepsis hospitalization among female sailors compared to male sailors.

Among enlisted service members, rates were 1.9 times (95% CI, 1.8, 2.0) higher among women (72.4 per 100,000 p-yrs) than men. Among those in combat-specific occupations, rates were more than

FIGURE 1. Annual Rates of Sepsis Hospitalizations by Sex, Active Component, U.S. Armed Forces, 2011–2022



twice as high among women than men. Deployed service members had lower rates than those who did not recently deploy, but women had higher rates than men among both groups. Rates of sepsis among female recruits (43.0 per 100,000 p-yrs) were half that of male recruits (82.8 per 100,000 p-yrs). After accounting for the effects of age, race and ethnicity, service, grade, and occupation, the adjusted rate was nearly twice as high among female ACSMs as male ACSMs (**Table 4**).

Further descriptions of female sepsis cases are provided in **Tables 5–7**. The most frequent co-occurring infections for sepsis cases among female ACSMs are shown in **Table 5**. Among ICD-9-coded encounters, the most common infections were pyelonephritis, pneumonia with unspecified organism, unspecified urinary tract infection (UTI), and post-operative infection. Among ICD-10-coded encounters, the most common infections were acute pyelonephritis, unspecified UTI, COVID-19, unspecified *E. coli* infection, and unspecified pneumonia.

The most common co-occurring non-infectious diagnoses under ICD-9 coding were hypotension, acute kidney failure, unspecified anemia, hypo-osmolality and/or hyponatremia, and acute respiratory failure (**Table 6**). Among ICD-10-coded diagnoses, the most common non-infectious diagnoses were hypokalemia,

hypo-osmolality and hyponatremia, acute kidney failure, tubule-interstitial nephritis, and unspecified anemia.

The co-occurring diagnoses in **Tables 5** and **6** are limited to those occurring within the incident sepsis encounter. Among female ACSM sepsis cases, 1,187 cases had another health encounter that did not include a sepsis-related diagnosis, within 7 days prior to the incident sepsis hospitalization (data not shown). Seventy-seven cases were hospitalized in the 7 days preceding the incident sepsis encounter, and more than half (n=42, 55%) of those cases had primary diagnoses related to pregnancy, delivery, or postpartum care (data not shown).

Women were also assessed for co-morbid conditions in the year preceding sepsis diagnosis, defined as at least 1 diagnosis for a co-morbid condition within 365 days before the incident sepsis diagnosis (**Table 7**). Just over two-thirds, or 67.2%, of sepsis cases had health care encounters with at least 1 co-morbidity diagnosis (n=1,131), listed in **Table 7**, within 365 days preceding incident their sepsis diagnoses. Immune-compromising conditions were the most common (n=517, 30.7%), followed by chronic kidney disease (n=325, 19.3%), cardiovascular disease (n=315, 18.7%), neoplasms (n=271, 16.1%), and obesity (n=275, 16.3%). Slightly less than one-third, or 30.8%, of women

TABLE 3. Incidence of Sepsis by Sex, Active Component U.S. Service Members, 2011–2022

| Demographic Characteristics | Females | | Males | | Crude Rates | | |
|-----------------------------|---------|-------------------|-------|-------------------|-------------|---------|---------|
| | No. | Rate ^a | No. | Rate ^a | RR | 95% LCL | 95% UCL |
| Total | 1,684 | 66.5 | 4,904 | 36.7 | 1.8 | 1.7 | 1.9 |
| Age, y | | | | | | | |
| <20 | 158 | 84.6 | 483 | 56.1 | 1.5 | 1.3 | 1.8 |
| 20–24 | 630 | 75.7 | 1,360 | 32.3 | 2.3 | 2.1 | 2.6 |
| 25–29 | 349 | 55.5 | 932 | 29.6 | 1.9 | 1.7 | 2.1 |
| 30–34 | 234 | 58.4 | 695 | 32.4 | 1.8 | 1.6 | 2.1 |
| 35–39 | 160 | 59.9 | 635 | 40.2 | 1.5 | 1.3 | 1.8 |
| 40–44 | 86 | 64.0 | 427 | 47.7 | 1.3 | 1.1 | 1.7 |
| 45+ | 67 | 81.6 | 372 | 72.3 | 1.1 | 0.9 | 1.5 |
| Race and ethnicity | | | | | | | |
| White, non-Hispanic | 712 | 64.9 | 3,044 | 38.0 | 1.7 | 1.6 | 1.9 |
| Black, non-Hispanic | 384 | 60.1 | 658 | 34.5 | 1.7 | 1.5 | 2.0 |
| Hispanic | 330 | 74.9 | 692 | 35.2 | 2.1 | 1.9 | 2.4 |
| Other | 258 | 72.6 | 510 | 34.5 | 2.1 | 1.8 | 2.4 |
| Service branch | | | | | | | |
| Army | 531 | 62.1 | 1,824 | 36.1 | 1.7 | 1.6 | 1.9 |
| Navy | 495 | 67.8 | 1,051 | 33.2 | 2.0 | 1.8 | 2.3 |
| Air Force | 501 | 65.4 | 1,084 | 35.1 | 1.9 | 1.7 | 2.1 |
| Marine Corps | 157 | 87.2 | 945 | 46.1 | 1.9 | 1.6 | 2.2 |
| Rank | | | | | | | |
| Enlisted | 1,479 | 72.4 | 4,229 | 38.3 | 1.9 | 1.8 | 2.0 |
| Officer | 205 | 41.8 | 675 | 29.2 | 1.4 | 1.2 | 1.7 |
| Military occupation | | | | | | | |
| Combat-related | 51 | 83.8 | 823 | 37.4 | 2.2 | 1.7 | 3.0 |
| Motor transport | 56 | 72.1 | 156 | 40.2 | 1.8 | 1.3 | 2.4 |
| Pilot/air crew | 22 | 58.3 | 130 | 23.6 | 2.5 | 1.6 | 3.9 |
| Repair/engineering | 346 | 69.2 | 1,420 | 34.0 | 2.0 | 1.8 | 2.3 |
| Communications/intelligence | 572 | 69.1 | 888 | 33.9 | 2.0 | 1.8 | 2.3 |
| Health care | 299 | 61.9 | 366 | 40.3 | 1.5 | 1.3 | 1.8 |
| Other | 338 | 62.0 | 1,121 | 44.5 | 1.4 | 1.2 | 1.6 |
| Recruit status | | | | | | | |
| Yes | 24 | 43.0 | 227 | 82.8 | 0.5 | 0.3 | 0.8 |
| No | 1,660 | 67.0 | 4,677 | 35.7 | 1.9 | 1.8 | 2.0 |
| Education level | | | | | | | |
| High school or less | 1,078 | 74.9 | 3,331 | 37.7 | 2.0 | 1.9 | 2.1 |
| Some college | 266 | 71.2 | 611 | 39.9 | 1.8 | 1.5 | 2.1 |
| Bachelor's degree or more | 318 | 48.4 | 880 | 32.4 | 1.5 | 1.3 | 1.7 |
| Other/unknown | 22 | 34.8 | 82 | 28.7 | 1.2 | 0.8 | 1.9 |
| Marital status | | | | | | | |
| Single | 677 | 59.4 | 1,943 | 35.3 | 1.7 | 1.5 | 1.8 |
| Married | 812 | 70.8 | 2,720 | 37.0 | 1.9 | 1.8 | 2.1 |
| Other | 195 | 79.4 | 241 | 47.8 | 1.7 | 1.4 | 2.0 |
| Deployment status | | | | | | | |
| Yes | 16 | 24.2 | 115 | 21.2 | 1.1 | 0.7 | 1.9 |
| No | 1,668 | 67.6 | 4,789 | 37.4 | 1.8 | 1.7 | 1.9 |

Abbreviations: No., number; RR, rate ratio; LCL, lower confidence limit; UCL, upper confidence limit; y, years.

^aRate per 100,000.

had a pregnancy-related encounter within 280 days preceding an incident sepsis diagnosis.

Rates of sepsis among women with histories of hypertension, lung disease, immune-compromising conditions, alcohol abuse disorders, chronic liver disease, chronic kidney disease, neoplasms, obesity, and diabetes also were evaluated (Figure 2). Rates of sepsis were consistently higher among women with a history of comorbidities, with the highest rates among women with a history of chronic kidney disease (526.3 per 100,000 p-yrs), chronic liver disease (491.2 per 100,000 p-yrs), or diabetes (204.7 per 100,000 p-yrs).

Discussion

Between January 1, 2011 and December 31, 2022, female ACSMs experienced higher rates of sepsis compared to male ACSMs, consistent with previous studies of the U.S. military population.^{8,9} This difference in rates was true for all demographic groups analyzed except the recruit population. After adjusting for other demographic and military-related factors, female ACSMs still demonstrated higher rates than male ACSMs. While the difference in rates between sexes persists after adjustment, it cannot be ruled out that changes in 2016 in the clinical definitions of sepsis under Sepsis-3 may have had a greater impact on the rates in women than men.

Rates of sepsis were highest among the youngest and oldest age groups in both sexes. The highest rates of sepsis in active component women were seen in those of Hispanic race or ethnicity, marines, enlisted members, and service members in combat-related occupations. The highest rates of sepsis among active component men were seen in those of White, non-Hispanic race or ethnicity, marines, enlisted members, and service members in motor transport and health care occupations.

This study attempted to better understand descriptive characteristics of female ACSMs hospitalized with sepsis. Among co-occurring diagnoses with sepsis, kidney infections such as pyelonephritis and UTIs were the most frequent co-occurring

TABLE 4. Adjusted Incidence Rate Ratios of Sepsis Hospitalizations, Active Component U.S. Service Members, 2011–2022

| Demographic Characteristics | Adjusted IRR ^a | 95% CI |
|-----------------------------|---------------------------|---------|
| Sex | | |
| Female | 1.9 | 1.8–2.0 |
| Male | Reference | |
| Race and ethnicity | | |
| White, non-Hispanic | Reference | |
| Black, non-Hispanic | 0.9 | 0.8–0.9 |
| Hispanic | 0.9 | 0.9–1.0 |
| Other | 1 | 0.9–1.0 |
| Age, y | | |
| <20 | 1.3 | 1.2–1.5 |
| 20–24 | 0.9 | 0.9–1.0 |
| 25–29 | 0.9 | 0.8–1.0 |
| 30–34 | Reference | |
| 35–39 | 1.2 | 1.1–1.4 |
| 40–44 | 1.5 | 1.4–1.7 |
| 45+ | 2.5 | 2.2–2.8 |
| Service branch | | |
| Army | Reference | |
| Navy | 1.0 | 0.9–1.1 |
| Air Force | 1.0 | 0.9–1.1 |
| Marine Corps | 1.3 | 1.2–1.4 |
| Grade | | |
| Enlisted | 1.7 | 1.6–1.9 |
| Officer | Reference | |
| Military occupation | | |
| Combat-specific | Reference | |
| Communications/intelligence | 0.9 | 0.8–1.0 |
| Health care | 1.1 | 0.9–1.2 |
| Motor transport | 1.0 | 0.9–1.2 |
| Other | 1.1 | 1.0–1.2 |
| Pilot/air crew | 0.8 | 0.7–1.0 |
| Repair/engineering | 0.9 | 0.8–1.0 |

Abbreviations: IRR, Incidence rate ratio; CI, confidence interval, y, years.

^aAdjusted for sex, age, race and ethnicity, service, grade, occupation

conditions in incident sepsis encounters among women. Hospitalization rates for genitourinary disorders have consistently been higher among females in the active component, with a risk rate difference of 3.6 per 1,000 p-yrs reported in 2019.¹³ Trends in pyelonephritis and UTIs have not been assessed in the U.S. military population more recently than 2013¹⁴ and may warrant further study. Genitourinary diseases were also the second most frequent reason for a

health encounter in the week prior to sepsis diagnosis (n=372) (data not shown).

In 2 large multi-center cohorts (Kaiser Permanente Northern California and Ann Arbor Veterans Health Administration systems) that included over 46,000 patients, 45% of sepsis patients were seen by clinicians in the week preceding hospitalization, with sharp increases just prior to admission.¹⁵ In another study of patients in a Michigan Medicine center hospitalized

TABLE 5. Frequency Distribution of Co-Occurring Infections with Sepsis, Hospitalized Cases, Female Active Component U.S. Service Members, 2011–2022

| ICD-9 Code | Description | No. | % of Diagnoses |
|------------|---|-----|----------------|
| 59080 | Pyelonephritis, unspecified | 98 | 2.9 |
| 486 | Pneumonia, organism unspecified | 74 | 2.2 |
| 59010 | Acute pyelonephritis without lesion of renal medullary necrosis | 56 | 1.7 |
| 5990 | UTI, site not specified | 51 | 1.5 |
| 99859 | Other post-operative infection | 32 | 0.9 |
| 4149 | Other and unspecified <i>E. coli</i> | 22 | 0.6 |
| 64783 | Other specified infectious and parasitic diseases of mother, antepartum condition or complication | 20 | 0.6 |
| 64663 | Infections of genitourinary tract in pregnancy, antepartum condition or complication | 19 | 0.6 |
| 845 | Intestinal infection due to <i>C. diff.</i> | 11 | 0.3 |
| 340 | Streptococcal sore throat | 10 | 0.3 |

| ICD-10 Code | Description | No. | % of Diagnoses |
|-------------|--|-----|----------------|
| N10 | Acute pyelonephritis | 182 | 2.3 |
| N390 | Urinary tract infection, site not specified | 123 | 1.6 |
| Z20822 | Contact with and (suspected) exposure to COVID-19 | 103 | 1.3 |
| B9620 | Unspecified <i>E. coli</i> as cause of diseases classified elsewhere | 98 | 1.2 |
| J189 | Pneumonia, unspecified organism | 83 | 1.1 |
| B9689 | Other specified bacterial agents as cause of diseases classified elsewhere | 39 | 0.5 |
| U071 | COVID-19 | 38 | 0.5 |
| O753 | Other infection during labor | 27 | 0.3 |
| O411230 | Chorioamnionitis, third trimester, not applicable or unspecified | 26 | 0.3 |
| N739 | Female pelvic inflammatory disease, unspecified | 25 | 0.3 |

Abbreviations: ICD-9, International Classification of Diseases, 9th Revision; No., number; ICD-10, International Classification of Diseases, 10th Revision; UTI, urinary tract infection; *E. coli*, *Escherichia coli*; *C. diff.*, *Clostridium difficile*.

for sepsis, 10% of these patients were seen in a clinic within 1 day of admission.¹⁶ In the present study, 70% of individuals had a health care encounter in the week prior to sepsis hospitalization. Early interactions with medical providers can lead to improved outcomes from sepsis infections if symptoms are recognized early in treatment. Sepsis severity could not be assessed in this study, but if individuals who sought care prior to their sepsis diagnoses had lower morbidity and mortality related to sepsis, this could be evidence of good practices in sepsis care and management by providers. Encouraging care-seeking behavior for kidney and UTIs among women may reduce the number of infections that progress to sepsis by providing treatment earlier in the infection. Early identification of signs of sepsis and early interventions help

mitigate debilitating long-term effects from infection.

Co-morbid conditions were evaluated as potential risk factors for women. Chronic medical conditions have been shown to be associated with increased risk of sepsis and severity of sepsis due to their effects on the immune system or inflammation.^{10–12} In this study, women with prior history of chronic kidney disease and chronic liver disease had rates 13 times and 8 times, respectively, higher compared to women without prior history of those 2 co-morbidities. Previous population-based studies have shown strong associations between chronic kidney disease and risk of hospital admission and death from sepsis.¹¹ Liver dysfunction is not only a risk factor for sepsis but is also associated with multiple organ dysfunction and death due to

sepsis.¹⁷ Additional analyses of sepsis outcomes, such as severity of illness and mortality, among women service members with co-morbidities would be needed to better quantify risk.

This study is limited due to its use of administrative health records to identify sepsis hospitalizations. While administrative health records allow for large, population-based studies, it is possible that sepsis is under-coded in administrative health records.¹⁸ ICD coding errors are also possible in administrative health records, which may result in misclassification. Due to limitations with casualty data in DMSS, cause of death cannot be determined, and sepsis-related mortality could not be examined fully. Of note, 47 (2.9%) female ACSMs died after sepsis hospitalization, compared to 268 (5.7%) male ACSMs (data not shown).

TABLE 6. Frequency Distribution of Other Co-Occurring Diagnoses with Sepsis of Non-Infectious Conditions, Hospitalized Cases, Female Active Component U.S. Service Members, 2011–2022

| ICD-9 Code | Description | No. | % of Diagnoses |
|------------|-------------------------------------|-----|----------------|
| 2768 | Hypototassemia | 63 | 1.9 |
| 5849 | Acute kidney failure, unspecified | 57 | 1.7 |
| 2859 | Anemia, unspecified | 45 | 1.3 |
| 2761 | Hypo-osmolality and/or hyponatremia | 42 | 1.2 |
| 51881 | Acute respiratory failure | 39 | 1.2 |
| 27651 | Dehydration | 34 | 1.0 |
| 3051 | Tobacco use disorder | 34 | 1.0 |
| 5119 | Unspecified pleural effusion | 31 | 0.9 |
| 591 | Hydronephrosis | 28 | 0.8 |
| 2762 | Acidosis | 24 | 0.7 |

| ICD-10 Code | Description | No. | % of Diagnoses |
|-------------|--|-----|----------------|
| E876 | Hypokalemia | 174 | 2.2 |
| E871 | Hypo-osmolality and hyponatremia | 130 | 1.7 |
| N179 | Acute kidney failure, unspecified | 129 | 1.6 |
| N12 | Tubulo-interstitial nephritis, not specified as acute or chronic | 115 | 1.5 |
| D649 | Anemia, unspecified | 111 | 1.4 |
| E872 | Acidosis | 89 | 1.1 |
| E860 | Dehydration | 78 | 1.0 |
| J9601 | Acute respiratory failure with hypoxia | 75 | 1.0 |
| D509 | Iron deficiency anemia, unspecified | 57 | 0.7 |
| K5900 | Constipation, unspecified | 51 | 0.6 |

Abbreviations: ICD-9, International Classification of Diseases, 9th Revision; No., number; ICD-10, International Classification of Diseases, 10th Revision.

TABLE 7. Numbers and Percentages of Incident Sepsis Cases with Co-Morbidity Encounter, 365 Days Preceding Incident Diagnosis, Female Active Component U.S. Service Members, 2011–2022

| Prior Co-Morbidity | No. | % |
|-----------------------------------|-----|------|
| Pregnancy-related encounter | 519 | 30.8 |
| Immune compromising conditions | 517 | 30.7 |
| Chronic kidney disease | 325 | 19.3 |
| Any cardiovascular disease | 315 | 18.7 |
| Hypertension | 200 | 11.9 |
| Obesity | 275 | 16.3 |
| Neoplasms | 271 | 16.1 |
| Metabolic disease | 223 | 13.2 |
| Any lung disease | 223 | 13.2 |
| Chronic lower respiratory disease | 43 | 2.6 |
| Substance use disorders | 200 | 11.9 |
| Chronic liver disease | 85 | 5.1 |

Abbreviation: No., number

There were no deaths among women with pregnancy-related sepsis diagnoses during the surveillance period. Additional studies may be warranted to examine mortality outcomes related to sepsis in the military population. Treatment received, such as antibiotics or intravenous fluids, could not be quantified in this study.

Further insights into the differing rates of sepsis among female and male ACSMs may be obtained through chart review, which could help address concerns about misclassification of cases due to possible differences in diagnosis patterns by physicians. The underlying cause of sepsis may also provide clues behind the disparities as well if there are differences by sex. For example, if female ACSMs are more likely to develop sepsis from genitourinary sources than respiratory infections, there

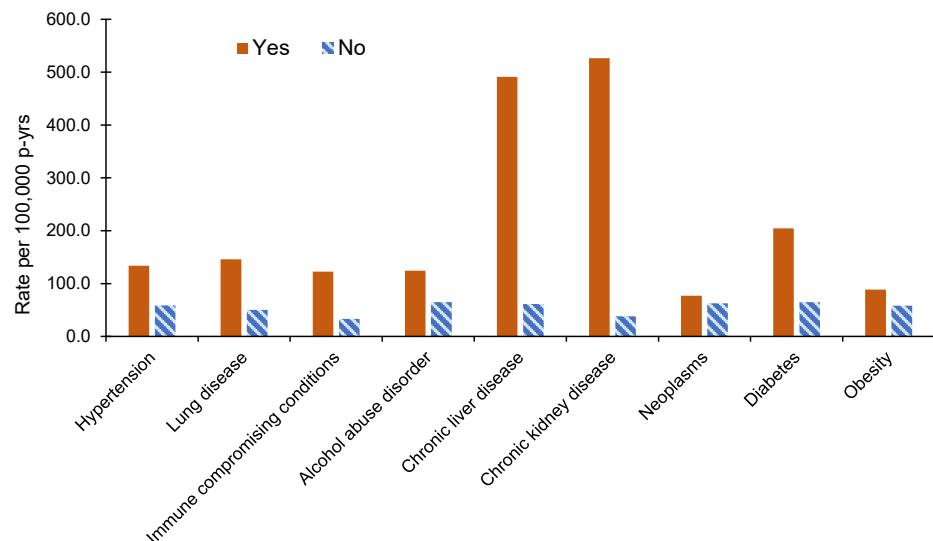
may be opportunities to promote health education about genitourinary infections, and for increased vigilance in monitoring these types of infections. Ensuring proper treatment and adherence to treatment with antibiotics of UTIs, for instance, may also play a role in reducing the progression to sepsis. Inadequate treatment of UTIs can lead to recurrence and spread of infection.¹⁹

The impact of COVID-19 on the decline in sepsis hospitalizations in 2020 remains unexplained. Sepsis rates in both men and women were higher in 2021 and 2022 compared to 2020, suggesting that some aspect of the early pandemic affected sepsis rates. It cannot be determined from this study whether that decline was due to changes in health care seeking-behavior or preventive measures implemented during the pandemic that reduced the prevalence of other infections. It has been noted that severe COVID-19 infections causing organ dysfunction may not have been coded as sepsis,²⁰ which could explain the 2020 decline.

Sepsis has been identified as a key area of focus for the Defense Health Agency (DHA)'s Critical Care and Trauma Clinical Community, which created DHA's Sepsis Working Group in 2021.²¹ The Sepsis Working Group issued a memorandum in 2025 that established a sepsis strategy in military hospitals and clinics that includes multi-disciplinary teams and a process for monitoring facility performance on sepsis-related quality measures. As efforts are made within the Military Health System to evaluate sepsis treatment and prevention strategies, this study demonstrates the importance of stratifying by sex in the study of sepsis in the military population.

Treatment and intervention strategies to prevent sepsis infections may differ by sex. Care-seeking behavior has also been shown to differ between male and female service members: Women tend to seek care at higher rates than men,²² which may have implications for differences in sepsis severity and mortality outcomes by sex, which could not be assessed in this study. Future work on sepsis in the U.S. military should include measures of severity including sepsis-related mortality and disease severity.

FIGURE 2. Incidence Rates of Sepsis by Co-Morbidity History, Female Active Component U.S. Service Members, 2011–2022



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Trends in Cervical Cancer Screening Modality in the Active Component U.S. Military, 2013–2023

Meghan Ginn, MD; Shauna L. Stahlman, PhD, MPH; Michael T. Fan, PhD; Symone Baker Miller, MD, MPH

Cervical cancer screening recommendations have evolved in the past 20 years. Several recent studies have reported on practice pattern changes in the U.S. in response to these guideline changes, but practice patterns have not yet been evaluated in the Military Health System (MHS). Data for active component service women were queried from the Defense Medical Surveillance System for relevant inpatient and outpatient encounter codes within the MHS between January 1, 2013 and December 31, 2023 to identify instances of cervical cancer screening and classify each by modality: cytology alone, HPV alone, and co-testing. Trends in the use of each were evaluated within age categories: younger than age 21 years, ages 21–29 years, ages 30–64 years. A total of 378,952 screening events were captured from 2013 through 2023. MHS practice patterns demonstrated a response to national guideline changes, including increased co-testing and evidence of increasing primary HPV screening among women aged 30–64 years. Cervical cancer screening in women younger than age 21 years markedly decreased following recommendations against screening in this age group. The overall trends in the MHS are similar to those reported in the U.S. general population.

What are the new findings?

Trends in use of each screening modality—cytology, primary HPV, and co-testing—for active component service women are shifting in response to changing national guidelines. There is emerging evidence of increasing primary HPV screening in women ages 30–64 years, especially after 2021.

What is the impact on readiness and force health protection?

Newer cervical cancer screening modalities that incorporate HPV testing, including the possibility of patient self-collected samples, allow for prolonged screening intervals and use in challenging health care settings. Full implementation will likely require significant investment in patient and provider education as well as laboratory processes, with several key questions that remain unanswered.

The U.S. has made noteworthy gains in reducing the incidence of cervical cancer, from 9.7 per 100,000 (age-adjusted) in 1999 to 7.4 per 100,000 in 2013.¹ New screening technology, namely human papillomavirus (HPV) testing, increased understanding of the pathophysiology of HPV-driven carcinoma, and the introduction of primary prevention through HPV vaccines, continue to drive changes in cervical cancer screening methods and recommendations.² National 2012 guidelines from both the U.S. Preventive Services Task Force (USPSTF) and the American Cancer Society (ACS) included testing for HPV concurrently with cytology ('co-test') for women aged 30–65 years, which allowed safe prolongation of screening intervals from 3 years to 5 years.^{3,4} Primary HPV screening, in which high-risk HPV (hrHPV) is tested first and cytology is performed as a reflex only if HPV is positive, was introduced for 30–65-year olds

in 2018 by the USPSTF and expanded to 25–65-year olds by the ACS in 2020.^{2,5} ACS guidelines notably recommended primary HPV as the preferred screening modality, with cytology and co-test acceptable if primary HPV is not available, a stance that has since been put forward for comment by the USPSTF in their draft 2024 cervical cancer screening guidelines.^{2,6} The first patient self-collected vaginal swabs for primary HPV screening were also approved in 2024 by the U.S. Food and Drug Administration, and large multi-site trials are currently underway to evaluate these swabs outside of clinical settings as true 'at home' screening tests for cervical cancer.^{7,8}

Implementation of new national cervical cancer screening guidelines is a massive undertaking, particularly when those guidelines require new testing modalities. Laboratories often must acquire and validate new equipment, workflows, and testing menus.^{2,9–11} Providers must understand,

agree with, and offer the new screening modalities to their patients, who then must accept their providers' recommendations.^{9,10} This large expenditure of both human and financial resources may not be immediately feasible.² Several studies have examined how quickly the updated screening guidelines are implemented, by analyzing trends in use of cervical cancer screening modalities over time, including Qin et al.'s 2021 study of nearly 10 million commercially insured women from 2013 through 2019.^{10,11} Qin et al. found that trends in co-test and cytology screening of 30–65-year olds aligned well with new guidelines but observed minimal uptake of primary HPV screening and some discrepancies in screening modalities of 21–29-year olds.¹¹

To our knowledge, these trends have not yet been investigated in the Military Health System (MHS). The MHS experiences the same resource management

challenges as the rest of U.S. health care. It must also overcome unique challenges posed by its patient population, some of whom undertake long assignments to remote and austere locations without infrastructure or medical providers necessary to support cytology screenings.¹² Applying the same methods of Qin et al. to the MHS, this report aims to reveal trends in cervical cancer screening modalities (primary HPV vs. cytology alone vs. co-test) in active component service members (ACSMs) as a response to changing national guidelines and compare trends to those of the U.S. population previously reported.

Methods

The Defense Medical Surveillance System (DMSS) was queried for inpatient and outpatient encounters within the MHS between January 1, 2013 and December 31, 2023 that included International Classification of Diseases (ICD), 10th and 9th revisions, Current Procedural Terminology (CPT), and Healthcare Common Procedure Coding System (HCPCS) codes listed in Appendix 2 of Qin et al. Inpatient encounters were included in the query to apply surveillance exclusion criteria (see below), in addition to avoiding unwitting omission of the rare inpatient screening events that met surveillance inclusion criteria. The surveillance period was chosen to capture changes following the 2012 addition of co-testing to national guidelines and include the most current available data.

The surveillance population included all female ACSMs in the Air Force (including Space Force after 2022), Army, Marine Corps, and Navy younger than 65 years, on continuous active component status for the entirety of the calendar year, with routine cervical cancer screening. To identify tests performed for routine cervical cancer screening, as opposed to diagnosis or follow-up to treatment, exclusions were made using ICD-10 / ICD-9 / CPT / HCPCS codes, mirroring those of Qin et al., with the sole addition of CPT code 57530 (trachelectomy). Service women were excluded from analysis if they had documented history of cervical

dysplasia or procedure for diagnosis or treatment of dysplasia, such as loop electrosurgical excision and cervical conization, or congenital or acquired absence of uterine cervix.

To maintain comparability with reported U.S. national trends, the modality definitions of Qin et al. were also utilized. Cervical cancer screening was classified as 'co-test' if DMSS documentation included both cervical cytology within the calendar year and hrHPV testing within 3 days preceding or 30 days after cytology. Screening was classified as 'cytology alone' if cervical cytology was performed within the calendar year but no hrHPV was documented within the guidelines of 'co-testing'. Finally, screening was classified as 'HPV alone' if at least 1 hrHPV test was documented in the calendar year but no cervical cytology was performed. The screening test categories were mutually exclusive, with individuals counted only once per year,

with prioritization for co-testing, followed by cytology alone and HPV alone. Individuals were further classified by demographics and age as recorded on the date of cervical cancer screening. Descriptive statistics were used to evaluate trends in use of each cervical screening modality over the duration of the surveillance period by age category, reported as a percentage of women within the surveillance population screened by each modality each year. Overall screening compliance (i.e., percentage of women 'up to date' at any given time) was not considered as an outcome.

Results

After exclusions, the surveillance population averaged 147,476 women in service each year, ranging from 123,828 in 2013 to 168,444 in 2021 (Tables 1 and 2).

TABLE 1. Study Population Demographics, Annual Average, 2013–2023

| | Average | |
|-------------------------|---------|------|
| | No. | % |
| Age, y | | |
| <21 | 15,094 | 10.2 |
| 21–24 | 46,487 | 31.5 |
| 25–29 | 41,308 | 28.0 |
| 30–39 | 34,740 | 23.6 |
| 40–49 | 8,584 | 5.8 |
| 50–64 | 1,264 | 0.9 |
| Service branch | | |
| Army | 48,563 | 32.9 |
| Navy | 44,949 | 30.5 |
| Air Force, Space Force | 43,038 | 29.2 |
| Marine Corps | 10,927 | 7.4 |
| Race and ethnicity | | |
| White, non-Hispanic | 62,909 | 42.7 |
| Black, non-Hispanic | 35,587 | 24.1 |
| Hispanic | 27,779 | 18.8 |
| Other | 18,497 | 12.5 |
| Unknown | 2,705 | 1.8 |
| Rank, grade | | |
| Junior enlisted (E1–E4) | 67,480 | 45.8 |
| Senior enlisted (E5–E9) | 51,289 | 34.8 |
| Warrant officer (W) | 862 | 0.6 |
| Junior officer (O1–O3) | 19,564 | 13.3 |
| Senior officer (O4–O10) | 8,281 | 5.6 |

Abbreviations: y, years; E, enlisted; W, warrant officer; O, officer.

TABLE 2. Testing Modality, Year of Surveillance and Age Group, Absolute Number and Relative Percent, 2013–2023

| Year | | 2013 | | 2014 | | 2015 | | 2016 | | 2017 | | 2018 | |
|------------------|--------------------|---------|------|---------|------|---------|------|---------|------|---------|------|---------|------|
| Population total | | 123,828 | | 127,446 | | 130,187 | | 133,938 | | 137,796 | | 147,760 | |
| Age group, y | Screening modality | No. | % |
| <21 | Total, age group | 12,130 | | 13,080 | | 12,865 | | 13,858 | | 14,965 | | 16,882 | |
| | Co-test | 6 | 0.1 | 4 | 0.0 | 3 | 0.0 | 6 | 0.0 | 9 | 0.1 | 7 | 0.0 |
| | Cyto | 371 | 3.1 | 307 | 2.4 | 214 | 1.7 | 210 | 1.5 | 201 | 1.3 | 206 | 1.2 |
| | HPV | 15 | 0.1 | 9 | 0.1 | 7 | 0.1 | 20 | 0.1 | 32 | 0.2 | 24 | 0.1 |
| 21–29 | Total, age group | 70,384 | | 74,123 | | 77,701 | | 80,714 | | 83,350 | | 89,381 | |
| | Co-test | 115 | 0.2 | 112 | 0.2 | 216 | 0.3 | 468 | 0.6 | 692 | 0.8 | 1,056 | 1.2 |
| | Cyto | 19,659 | 27.9 | 20,268 | 27.3 | 21,553 | 27.7 | 23,280 | 28.8 | 23,458 | 28.1 | 24,333 | 27.2 |
| | HPV | 74 | 0.1 | 52 | 0.1 | 96 | 0.1 | 94 | 0.1 | 158 | 0.2 | 123 | 0.1 |
| 30–64 | Total, age group | 41,314 | | 40,243 | | 39,621 | | 39,366 | | 39,481 | | 41,497 | |
| | Co-test | 808 | 2.0 | 1,015 | 2.5 | 1,195 | 3.0 | 1,628 | 4.1 | 2,014 | 5.1 | 2,364 | 5.7 |
| | Cyto | 9,542 | 23.1 | 9,417 | 23.4 | 8,725 | 22.0 | 7,934 | 20.2 | 7,007 | 17.7 | 6,685 | 16.1 |
| | HPV | 114 | 0.3 | 118 | 0.3 | 140 | 0.4 | 154 | 0.4 | 190 | 0.5 | 210 | 0.5 |
| Year | | 2019 | | 2020 | | 2021 | | 2022 | | 2023 | | | |
| Population total | | 155,605 | | 164,708 | | 168,444 | | 166,864 | | 165,661 | | | |
| Age group, y | Screening modality | No. | % |
| <21 | Total, age group | 17,782 | | 18,550 | | 17,245 | | 14,726 | | 13,946 | | | |
| | Co-test | 9 | 0.1 | 4 | 0.0 | 10 | 0.1 | 4 | 0.0 | 7 | 0.1 | | |
| | Cyto | 160 | 0.9 | 150 | 0.8 | 164 | 1.0 | 120 | 0.8 | 73 | 0.5 | | |
| | HPV | 10 | 0.1 | 7 | 0.0 | 5 | 0.0 | 9 | 0.1 | 7 | 0.1 | | |
| 21–29 | Total, age group | 93,884 | | 98,650 | | 101,170 | | 99,844 | | 96,543 | | | |
| | Co-test | 1,283 | 1.4 | 1,437 | 1.5 | 1,067 | 1.1 | 1,221 | 1.2 | 1,458 | 1.5 | | |
| | Cyto | 26,399 | 28.1 | 24,195 | 24.5 | 26,811 | 26.5 | 23,042 | 23.1 | 20,489 | 21.2 | | |
| | HPV | 161 | 0.2 | 192 | 0.2 | 227 | 0.2 | 339 | 0.3 | 464 | 0.5 | | |
| 30–64 | Total, age group | 43,939 | | 47,508 | | 50,029 | | 52,294 | | 55,172 | | | |
| | Co-test | 2,920 | 6.6 | 2,708 | 5.7 | 3,241 | 6.5 | 3,460 | 6.6 | 3,999 | 7.2 | | |
| | Cyto | 6,988 | 15.9 | 6,459 | 13.6 | 7,581 | 15.2 | 6,525 | 12.5 | 5,762 | 10.4 | | |
| | HPV | 281 | 0.6 | 351 | 0.7 | 439 | 0.9 | 784 | 1.5 | 1,212 | 2.2 | | |

Abbreviations: y, years; Cyto, cytology; HPV, human papillomavirus.

Distributions of age, race and ethnicity, branch of military service, and military rank within the surveillance population were consistent throughout the surveillance period. The largest proportions of the population were 21–29 years of age (59.5%), non-Hispanic White (42.7%), and enlisted (45.8%). Service distribution was nearly equal among the Army, Air Force, and Navy, with a much smaller proportion of Marine Corps members.

A total of 378,952 cervical cancer screenings were captured during the surveillance period, classified according to the methods described. An average of 34,450

screenings occurred each calendar year, ranging from 30,704 in 2013 to 39,545 in 2021 (Table 2). Cervical cancer screening in individuals younger than age 21 years declined steadily during the surveillance period, from 3.2% in 2013 to 0.6% in 2023 (Figure 1). The majority (83.1–95.9%) of screenings in the younger than age 21 group were classified as cytology. Among 21–29 year olds, use of cytology alone remained steady throughout most of the surveillance period (27.9% in 2013, 28.1% in 2019) but decreased after 2019, to 21.2% in 2023 (Figure 2). Co-test and HPV alone in the 21–29-year age group increased during

the surveillance period, but use of both remained low: In 2019, 1.5% of women ages 21–29 were screened by co-test, 0.5% were screened by HPV alone (Figure 2). Similar, but more pronounced, trends were observed in the 30–64-year age group (Figure 3). Use of cytology alone decreased by more than 50% (23.1% in 2013 to 10.4% in 2023) among 30–64 year olds, while co-test more than tripled over the surveillance period (2.0% to 7.2%). HPV alone also increased in this age group, with the most marked increase occurring after 2021 (0.3% in 2013, 0.9% in 2021, 2.2% in 2023) (Table 2, Figure 3).

FIGURE 1. Percentage of Women Younger than Age 21 Years with Screening for Cervical Cancer, Any Modality, 2013–2023

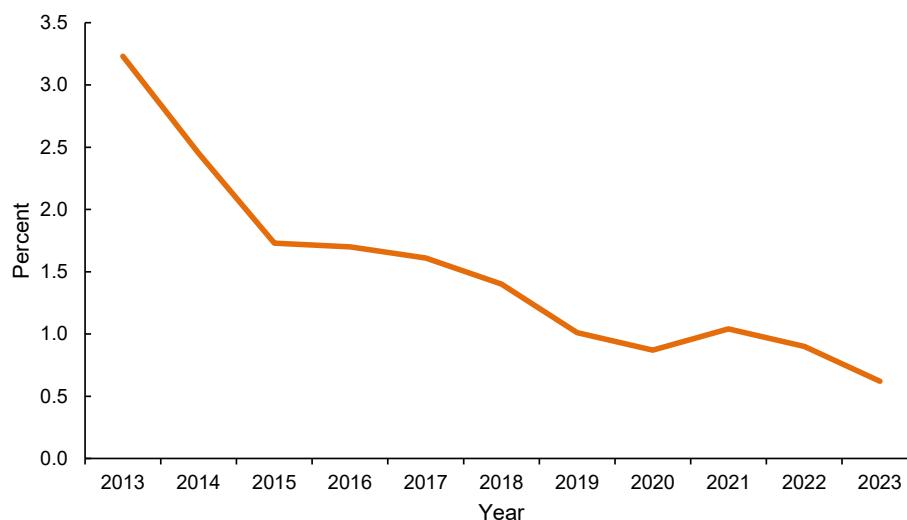
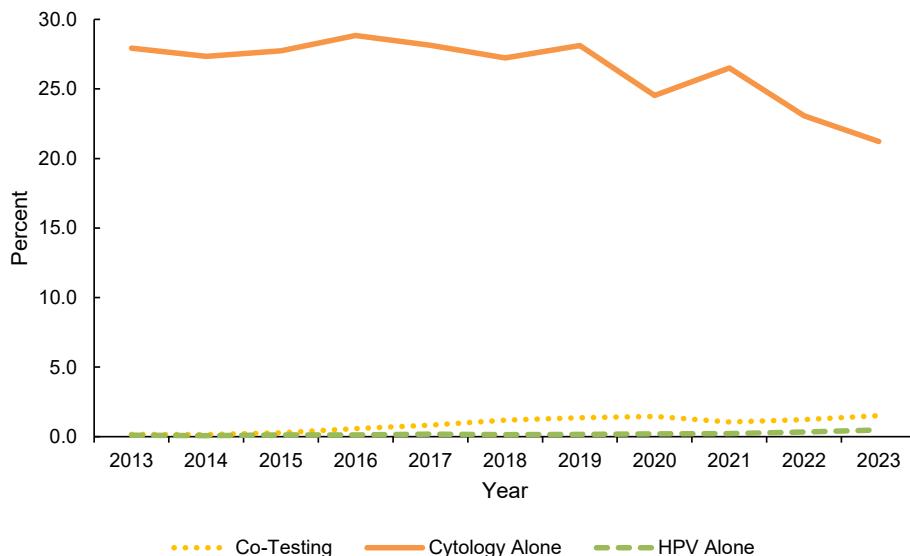


FIGURE 2. Percentage Use of Each Screening Modality for Cervical Cancer, Women Ages 21–29 Years, 2013–2023



Abbreviation: HPV, human papillomavirus.

Discussion

Understanding how practice patterns within the MHS change in response to guideline shifts is important because it reflects a myriad of factors influencing those changes such as provider education, patient and provider preference, and testing infrastructure, which may then inform how well the MHS is positioned to respond to future changes in screening guidelines.

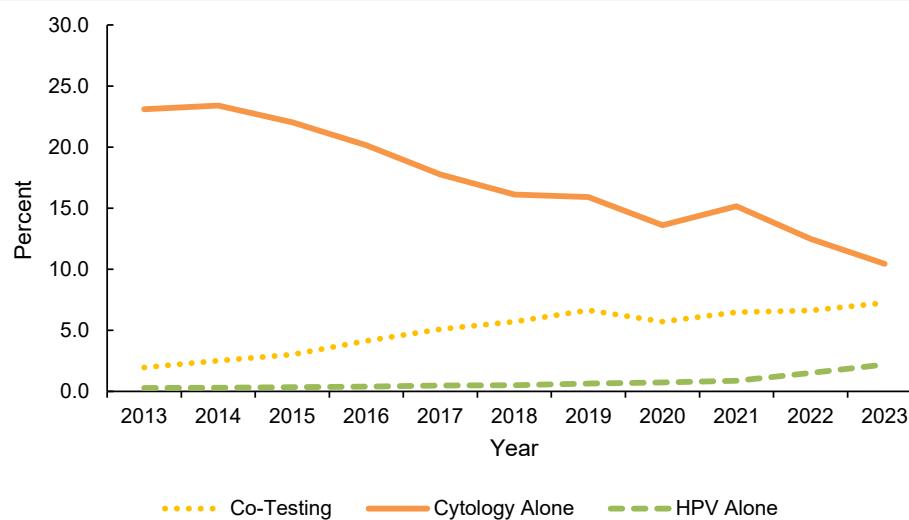
These results show that trends in the MHS are overall as expected in response to national guideline changes, and similar to trends in the U.S. reported by Qin et al. in 2021. Cervical cancer screening guidelines have recommended against screening women younger than age 21 years since 2012.⁴ Screening in this age group declined precipitously in the MHS, to 1.0% in 2019, well below the 9.0% reported in 2019 among women ages 18–20 years in the U.S. population.¹¹ Similarly, screening modalities in

women ages 30–64 years shifted in both the MHS and U.S. populations in response to the 2012 guideline updates, increasingly favoring co-testing as opposed to cytology alone. Interestingly, while use of cytology alone in 30–64 year old ACSMs declined throughout the surveillance period, it remained the more common modality over co-testing. In contrast, Qin et al. reported that co-testing overtook cytology alone between 2014 and 2015.¹¹ Whether this represents a difference in testing characteristics, including rates of squamous atypia or length of time between reporting of cytology and hrHPV results, or a true preference for cytology and reflex HPV over co-testing within the MHS, is unclear.

Qin et al., among others, have reported a decline in use of cytology for cervical cancer screening in individuals 21–29 years of age. Potential explanations have included genuinely decreased screening among recipients of the HPV vaccine who are now entering the screening pool, as well as an artificial decline in apparent use as a result of extended screening intervals from annually to every 3 years.¹¹ Among ACSMs, cervical cancer screening is required as part of individual medical readiness regardless of HPV vaccination status, making this an unlikely explanation for the decrease in cytology after 2020. The 2019 management guidelines of the American Society for Colposcopy and Cervical Pathology differ between patients younger than age 25 years and those aged 25–29 years with atypical squamous cells of undetermined significance (ASCUS) on cytology screening, with preference to HPV testing for further risk stratification in those aged 25–29 years.¹³ Data on the results of cervical cancer screening were not included in this analysis, and it is conceivable that a rise in ASCUS results among those 25–29 years of age caused an artificial decline in cytology percentages as ASCUS cytology results triggered reflex HPV and subsequent misclassification as 'co-test'.

This study has several limitations. As mentioned, the definitions of screening modality (co-test vs. cytology alone vs. HPV) were chosen to correlate with Qin et al., for comparison to national trends. There is likely misclassification among modalities, however, including abnormal cytology

FIGURE 3. Percentage Use of Each Screening Modality for Cervical Cancer, Women Ages 30-64 Years, 2013–2023



Abbreviation: HPV, human papillomavirus.

with reflex HPV misclassified as co-test, positive primary HPV with reflex cytology misclassified as co-test or cytology (depending on timing of cytology result), and co-test misclassified as cytology (if HPV is coded significantly before cytology result). Pathology data were not available at the time of this analysis, which precluded use of laboratory-generated data to validate or quantify degree of possible misclassification by medical encounter data. The surveillance period of this study overlaps with the COVID-19 pandemic, which may have affected screening rates during the pandemic years but would have unlikely influenced testing modality. Finally, the analysis was intended only for women undergoing routine screening, but women with a history of dysplasia may have been mistakenly included if that history was not documented within the electronic health record.

Future work should aim to confirm the trends reported here with validation by laboratory data. The performance characteristics of primary HPV screening in the ACSM population should be evaluated, including its cost effectiveness and negative predictive value in a population with a potentially higher rate of HPV infection.¹² Paradigm shifts in large-scale screening programs are gradual, and continued surveillance should be considered for further

evaluation and guidance of the process as practice patterns and guidelines continue to evolve.

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Infertility Among Active Component Service Women, U.S. Armed Forces, 2019–2023

This report presents the incidence and prevalence of diagnosed female infertility among active component U.S. service women. During 2019–2023, 8,154 active component women of childbearing potential were diagnosed with incident infertility, resulting in an overall incidence of 77.5 cases per 10,000 person-years (p-yrs). Incidence rates were highest among women in their 30s, non-Hispanic Black individuals, those in health care and pilot or air crew occupations, Army soldiers, and those who were married. From 2019 through 2023, the incidence rate of diagnosed female infertility decreased from 89.2 per 10,000 p-yrs to 69.5 per 10,000 p-yrs despite a concurrent increase in the rate of fertility testing. During the surveillance period, the average annual prevalence of diagnosed female infertility was 1.6%. Of the service women diagnosed with infertility for the first time during the surveillance period, 2,005 (24.6%) delivered live births within 2 years following their incident infertility diagnoses.

What are the new findings?

The incidence rate of diagnosed infertility among service women decreased by 22.1% during the surveillance period, coincident with an increase of 74.0% in the rate of fertility testing from 2019 through 2023.

What is the impact on readiness and force health protection?

The incidence rates of diagnosed infertility in the U.S. military reveal that there are subgroups of active component service members at higher risk. Further assessment of potential risk factors, such as health behaviors, physical as well as mental health conditions, along with occupational exposures, may be warranted. A rapid increase in annual fertility testing rates among active component service women also indicates a need for more comprehensive guidance to infertility service access and use.

For the purposes of public health data collection, the definition of infertility refers to the inability of couples to conceive a pregnancy after 1 year or more of unprotected sex.¹ Female infertility is commonly classified into several major etiological categories, including infertility associated with ovulatory dysfunction, tubal disease, uterine and cervical factors, and other or unspecified causes.² Ovulation disorders are estimated to account for one-third of infertility cases, most often caused by polycystic ovary syndrome (PCOS).^{3,4} Other causes of infertility include hypothalamic-pituitary hormone imbalances, endometriosis, and primary ovarian insufficiency (i.e., premature menopause).⁵

Advanced maternal age may also contribute to infertility, due to declining egg quality and diminished ovarian reserves.⁶ Approximately 20% of women in the U.S.

now have their first child after age 35 years.⁵ Data reported by the Department of Defense Birth and Infant Health Registry also indicate a trend toward delayed childbearing in military women. From 2003 to 2014, the percentages of active component women who delivered live births sharply increased among those aged 30–34 (12.5–21.7%) and 35–39 (5.4–8.5%) years.⁷

Many modifiable lifestyle factors, such as age when starting a family, nutrition, weight, and psychological stress, can have substantial effects on fertility.⁸ Approximately half of military service women choose to postpone pregnancy or starting a family while in service.⁹ Occupational and environmental hazards such as radiation, repetitive motions, and injury require more research within military populations for associations with infertility.¹⁰ The increasing numbers and durations of wartime deployments have been associated with

increasing rates of menstrual disorders and infertility in active component service women.¹¹

MSMR has reported the incidence and prevalence of diagnosed female infertility among active component service women in the U.S. Armed Forces since 2000.¹² Annual rates of fertility testing have also been assessed since 2019.¹³ From 2013 to 2018, the incidence of diagnosed female infertility decreased from 85.1 per 10,000 p-yrs to 63.6 per 10,000 p-yrs, despite a concurrent increase in the rate of fertility testing.¹³

This report continues prior MSMR surveillance reporting to provide more recent estimates of the incidence and prevalence of infertility diagnoses, descriptions of specific types of diagnosed infertility, and measures of concurrent rates of fertility testing services among active component service women in the U.S. Armed Forces from 2019 through 2023.

Methods

The surveillance population consisted of all active component service women of childbearing potential who served in the Army, Navy, Air Force, or Marine Corps at any time from January 1, 2019 through December 31, 2023. Women of childbearing potential were defined as women ages 17-49 years without any history of hysterectomy or permanent sterilization. History of hysterectomy or permanent sterilization was defined by a qualifying diagnostic or procedural code for hysterectomy or permanent sterilization in any position of an inpatient or outpatient record. These diagnostic and procedural codes have been previously described.^{14,15} All data used for these analyses were abstracted from records routinely maintained in the Defense Medical Surveillance System (DMSS) for health surveillance purposes.

An incident case of infertility was defined by at least 2 outpatient medical encounters with an infertility diagnosis (International Classification of Diseases, 9th Revision [ICD-9] code 628.*; International Classification of Diseases, 10th Revision [ICD-10] code N97.*¹) in the first or second diagnostic position or by an inpatient encounter with an infertility diagnosis in the first diagnostic position. An individual could be counted as a case of infertility only once. The incident date was the date of the first qualifying medical encounter. The type of infertility—either anovulation, tubal origin, uterine origin, other, or unspecified—was assigned from the specific diagnostic codes of the inpatient or outpatient encounter record during military service; however, if an individual had

multiple types of infertility, the specific type diagnosed in the earliest incident was utilized (**Table 1**).

For incidence calculations, person-time denominators were censored at the time of the first hysterectomy or permanent sterilization diagnosis, or when the service member turned 50 years of age, or at the time of the first infertility diagnosis, whichever occurred first. The incidence rate was calculated per 10,000 person-years (p-yrs).

To be counted as a prevalent case of infertility, the woman of childbearing potential had to 1) be in active component military service during the calendar year of interest, 2) qualify as an incident case of infertility in the year of interest or any year prior (including before 2013), and 3) have an inpatient or outpatient encounter for any infertility type in any diagnostic position during the year of interest. The denominator for prevalence calculations was the total number of women of childbearing potential in active component service during that year. Prevalence rates were calculated per 10,000 persons.

The burden of medical encounters for infertility was analyzed by calculating the total number of inpatient and outpatient encounters with a primary diagnosis of infertility among all active component service women (including both prevalent and incident cases of infertility). The total numbers of individuals affected and the total number of hospital bed days for infertility were also calculated according to standard MSMR burden methodology.¹⁶

The rate of fertility testing among all active component women, not just women of childbearing potential, was also measured for the surveillance period. Fertility testing was defined by the presence of an

inpatient or outpatient encounter with a diagnosis of fertility testing (ICD-9: V26.21; ICD-10: Z31.41) in any diagnostic position. One test per person per day was counted. The denominator was person-time for all female active component service members during the surveillance period.

Finally, incident infertility cases were followed for up to 2 years to measure subsequent live birth deliveries. Live birth deliveries were defined by having a hospitalization with a live birth delivery-related diagnosis code—ICD-9, V27* (excluding V271, V274, V277) and ICD-10, Z37* (excluding Z371, Z374, Z377)—in any diagnostic position.

Results

Incidence

During the surveillance period, 8,154 active component women of childbearing potential were diagnosed with infertility for the first time, corresponding to a crude overall incidence rate of 77.5 per 10,000 p-yrs (**Table 2**). Infertility of 'unspecified' origin accounted for the most common diagnosis (29.0 per 10,000 p-yrs), followed by 'other specified' origin (26.2 per 10,000 p-yrs), and anovulation (13.7 per 10,000 p-yrs). Infertility of tubal origin (6.6 per 10,000 p-yrs) and uterine origin (2.0 per 10,000 p-yrs) represented less common diagnoses for active component women. While the annual incidence of diagnosed infertility (of any origin) decreased by 22.1% during the surveillance period, infertility of unspecified and uterine origin did not follow an overall decline;

TABLE 1. ICD-9/ICD-10 Codes for Female Infertility

| ICD-9 | ICD-10 | Description |
|---------------------|--------|--|
| 628.0 | N97.0 | Infertility associated with anovulation |
| 628.2 | N97.1 | Infertility of tubal origin (block, occlusion, stenosis of fallopian tubes) |
| 628.3 | N97.2 | Infertility of uterine origin (congenital anomaly of uterus, non-implantation) |
| 628.1, 628.4, 628.8 | N97.8 | Infertility of other specified origin (pituitary-hypothalamic, cervical or vaginal, age-related, etc.) |
| 628.9 | N97.9 | Infertility of unspecified origin |

Abbreviations: ICD, International Classification of Diseases.

these 2 infertility types followed the general downward trend in 2019 and 2020, thereafter increasing through 2023 (Figure 1).

Overall rates of incident infertility diagnoses increased with age, peaking for women ages 35-39 years (159.2 per 10,000 p-yrs) (Table 2). While incident infertility diagnoses for women under age 40 years followed a general decline for the overall surveillance period, rates of incident infertility for those aged 40-44 years remained relatively stable. Among women ages 45-49 years, the incident infertility rate declined to 7.5 per 10,000 p-yrs in 2022, thereafter increasing to 18.4 per 10,000 p-yrs in 2024 (Figure 2). For this oldest age group (40-49 years), infertility due to 'other specified' origin accounted for the highest rate of diagnosis (34.1 per 10,000 p-yrs), whereas 'other specified' and unspecified origins accounted for approximately equal rates (55.0 and 54.7 per 10,000 p-yrs, respectively) for women aged 30-39 years, and unspecified infertility accounted for the highest rate of diagnosis (20.1 per 10,000 p-yrs) in women 20-29 years of age (Figure 3).

Overall incidence rates of infertility diagnoses of any type were highest among non-Hispanic Black service women (89.3 per 10,000 p-yrs) compared to women in other race and ethnicity groups (Table 2); this finding is consistent for each type of infertility diagnosis, with the exception of anovulation (Figure 4). Active component service women of other or unknown racial and ethnic groups accounted for the highest rates of infertility due to anovulation (16.9 per 10,000 p-yrs), followed by non-Hispanic White (14.2 per 10,000 p-yrs) and Hispanic (12.7 per 10,000 p-yrs) service women.

Overall rates of incident infertility diagnoses were highest among service women in the Army (92.0 per 10,000 p-yrs) and lowest in the Marine Corps (45.3 per 10,000 p-yrs), although it should be noted that these findings present rates that were unadjusted for age (Table 2). Senior enlisted women had higher incidence rates than junior enlisted personnel, and senior officers had higher rates than junior officers. Compared to other occupations, service women in health care occupations had the highest incidence of diagnosed

TABLE 2. Incidence of Infertility by Type, Demographic and Military Characteristics, Active Component Service Women of Childbearing Potential, U.S. Armed Forces, 2019-2023

| | No. | Rate ^a |
|----------------------------------|-------|-------------------|
| Total | 8,154 | 77.5 |
| Type of infertility | | |
| Anovulation | 1,437 | 13.7 |
| Tubal origin ^b | 694 | 6.6 |
| Uterine origin ^c | 211 | 2.0 |
| Other specified origin | 2,761 | 26.2 |
| Unspecified origin | 3,051 | 29.0 |
| Age, y | | |
| <20 | 61 | 6.9 |
| 20-24 | 1,533 | 40.8 |
| 25-29 | 2,276 | 83.2 |
| 30-34 | 2,347 | 143.0 |
| 35-39 | 1,535 | 159.2 |
| 40-44 | 382 | 96.7 |
| 45-49 | 20 | 14.7 |
| Race and ethnicity | | |
| White, non-Hispanic | 3,314 | 75.5 |
| Black, non-Hispanic | 2,162 | 89.3 |
| Hispanic | 1,499 | 68.0 |
| Other/unknown | 1,179 | 78.3 |
| Service branch | | |
| Army | 2,959 | 92.0 |
| Navy | 2,365 | 75.1 |
| Air Force | 2,296 | 74.6 |
| Marine Corps | 354 | 45.3 |
| Coast Guard | 169 | 60.9 |
| Space Force | 11 | 68.5 |
| Rank | | |
| Junior enlisted (E1-E4) | 2,492 | 50.1 |
| Senior enlisted (E5-E9) | 3,311 | 92.3 |
| Junior officer (O1-O3, W01-W03) | 1,554 | 106.4 |
| Senior officer (O4-O10, W04-W05) | 797 | 160.0 |
| Military occupation | | |
| Combat-specific ^d | 200 | 60.5 |
| Motor transport | 221 | 62.1 |
| Pilot/air crew | 167 | 96.6 |
| Repair/engineering | 1,333 | 63.4 |
| Communications/intelligence | 2,645 | 81.2 |
| Health care | 2,016 | 113.4 |
| Other/unknown | 1,572 | 62.4 |
| Marital status | | |
| Married | 5,973 | 136.0 |
| Unmarried | 1,456 | 28.2 |
| Other | 725 | 74.8 |

Abbreviations: No., number; y, years.

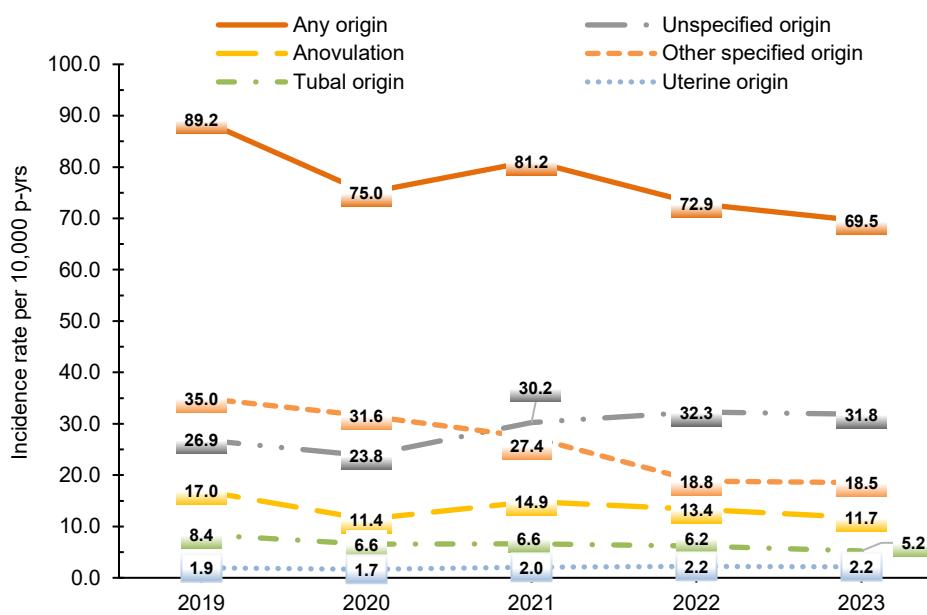
^aRates per 10,000 person-years.

^bBlock, occlusion, or stenosis of fallopian tubes.

^cStructural abnormality of uterus or non-implantation; includes fibroids.

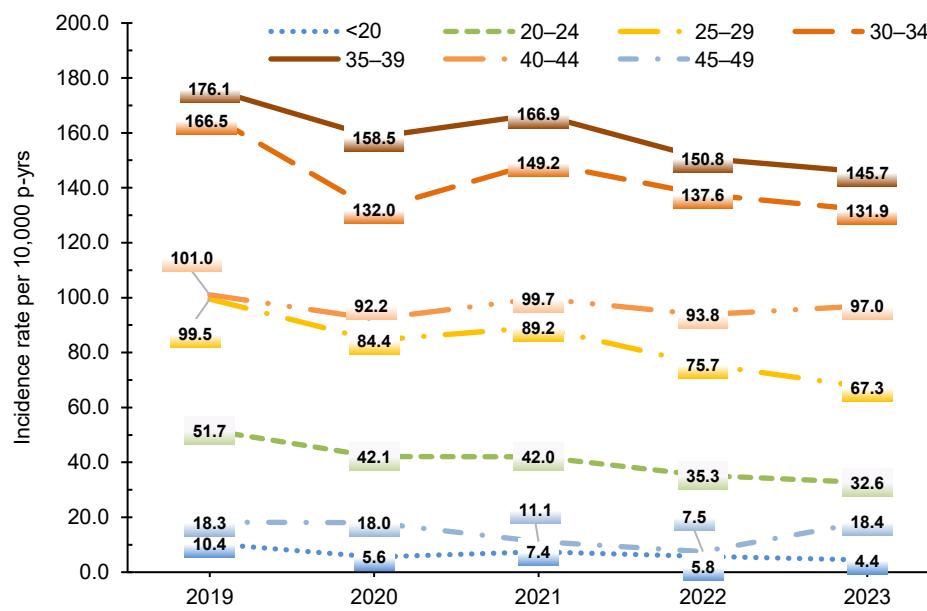
^dIncludes infantry/artillery/combat engineering/armor.

FIGURE 1. Annual Incidence Rates of Female Infertility Diagnoses, Active Component Service Women of Childbearing Potential, 2019–2023



Abbreviations: P-yrs, person-years.

FIGURE 2. Annual Incidence Rates of Female Infertility Diagnoses by Age Group, Active Component Service Women of Childbearing Potential, 2019–2023



Abbreviations: P-yrs, person-years.

infertility (113.4 per 10,000 p-yrs), and were followed by pilots and air crew (96.6 per 10,000 p-yrs). The rate of incident infertility diagnoses among married service women was nearly 5 times the rate of unmarried service women.

Prevalence

In 2023, the prevalence of diagnosed female infertility of any type was 152.7 per 10,000 persons, translating to 1.5% of the female active component population that

year. This figure decreased by approximately 11% during the surveillance period, down from 171.5 per 10,000 persons (or 1.7%) in 2019. Two types of infertility increased during the surveillance period: Prevalence of infertility of uterine origin increased by 30.0% (from 4.0 to 5.2 per 10,000 persons) and infertility of unspecified origin rose by 26.8% (from 37.8 to 47.9 per 10,000 persons) from 2019 through 2023 (Figure 5).

Burden

There were 66,918 total medical encounters and 31 hospital bed days recorded for female infertility during the surveillance period (data not shown). Annual numbers of medical encounters during which infertility was reported as a primary (first-listed) diagnoses and numbers of individuals affected by infertility remained relatively stable during the period, declining from 13,935 medical encounters in 2019 to 12,925 medical encounters in 2023 (Figure 6).

Fertility testing

During the surveillance period, annual rates for female fertility testing increased 74.0%, from 87.2 per 10,000 p-yrs in 2019 to 151.7 per 10,000 p-yrs in 2023 (Figure 7).

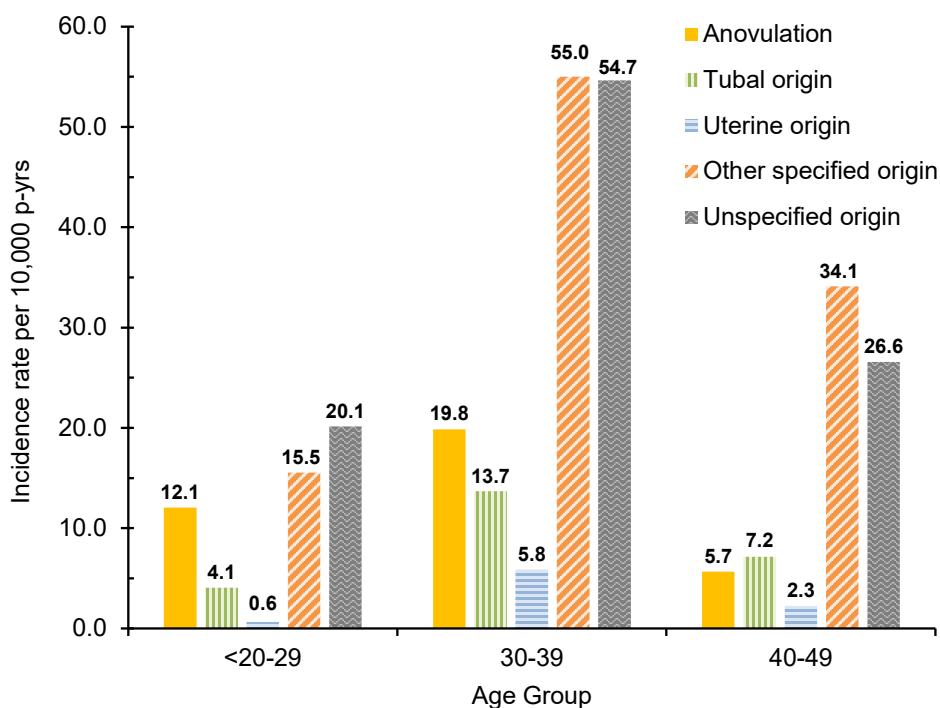
Live births after infertility diagnosis

Of the 8,154 service women diagnosed with infertility for the first time during the surveillance period, 666 (8.2%) were hospitalized for a live birth within 1 year following incident their infertility diagnoses (data not shown). In total, 2,005 (24.6%) women were hospitalized for a live birth within 2 years after an incident infertility diagnosis.

Discussion

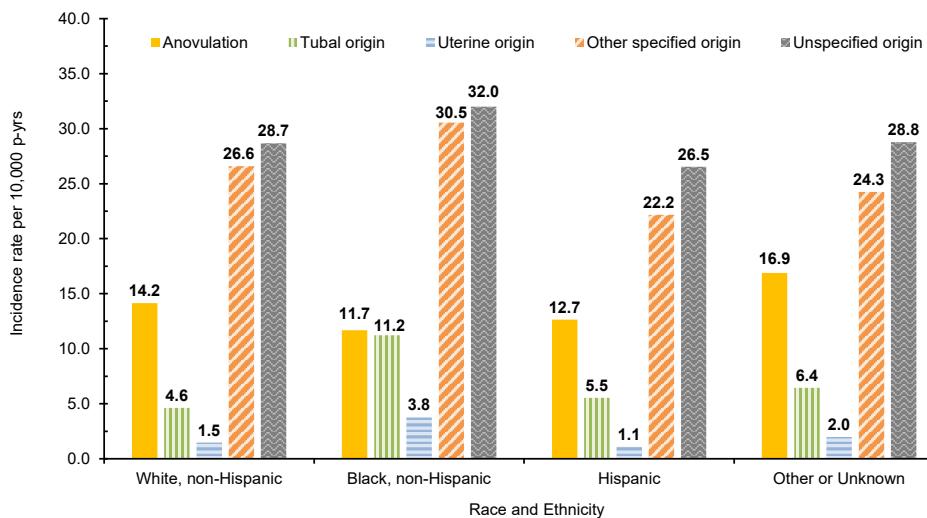
The crude overall incidence rate of diagnosed infertility among active component service women during the 2019–2023 surveillance period (77.5 per 10,000 p-yrs) remained slightly below the 2013–2018 incidence rate (79.3 per 10,000 p-yrs) previously reported, despite increased fertility

FIGURE 3. Incidence Rates of Female Infertility Diagnoses by Type and Age Group, Active Component Service Women of Childbearing Potential, 2019–2023



Abbreviations: P-yrs, person-years.

FIGURE 4. Incidence of Infertility by Type and Race and Ethnicity, Active Component Service Women of Childbearing Potential, U.S. Armed Forces, 2019–2023



Abbreviations: P-yrs, person-years.

testing.¹³ Over 70% of incident infertility cases were diagnosed as ‘other specified’ or unspecified origin, limiting descriptions of the types of causes of infertility. While annual incidence rates of diagnosed infertility (of any origin) decreased by 22.1% during the surveillance period, the rate of unspecified infertility increased by nearly 34% from 2020 through 2023. This

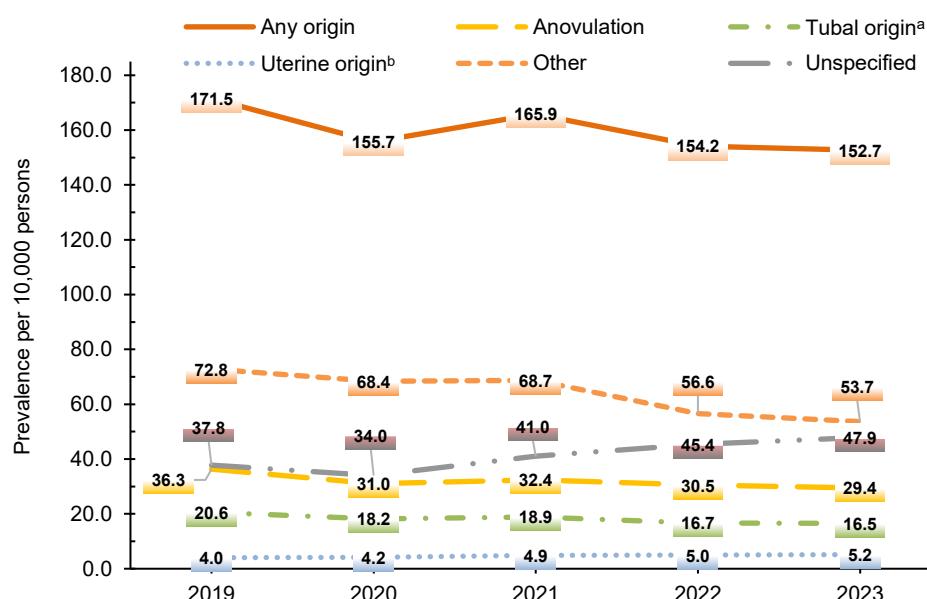
increasing trend in unspecified diagnoses, coupled with a sustained proportion of cases diagnosed as ‘other’ origin, may warrant further study to better elucidate the specific types of causes of infertility; however, current ICD-10-CM coding does not provide a greater level of detail beyond the unspecified and ‘other’ diagnoses.

The demographic results reported herein are broadly similar to prior surveillance reports focused on active component service women, with the highest rates of female infertility diagnosed among Army soldiers, women of non-Hispanic Black race or ethnicity, and individuals aged 30–39 years. Between 2000 and 2012, active component service women ages 30–34 years accounted for the highest rates of diagnosed infertility, but the highest rates shifted to women ages 35–39 years from 2013 to 2018. This finding has persisted through this surveillance period, 2019–2023, in which women ages 35–39 years accounted for the highest rates of diagnosed infertility, followed closely by women aged 30–34 years. The comparison of age-stratified rates for infertility of uterine origin are also notable for women in their 30s. While the overall incidence rate of women diagnosed with infertility of uterine origin remained minimal during the surveillance period, the age-stratified rate (5.8 per 10,000 p-yrs) for women aged 30–39 years from 2019 to 2023 is elevated beyond the comparable age-specific rate reported for 2013–2018, at 2.9 per 10,000 p-yrs.¹³

Notably, fertility testing for active component service women increased by 74.0%, exceeding the increasing trend (30.0%) described in the prior surveillance period.¹³ The current report also approximates that one-quarter (24.6%) of women had live births within 2 years following their incident infertility diagnoses, increasing from one-fifth (20.7%), previously reported for 2013–2018.¹³

Over the last 3 decades, development of new medications, testing, and treatment strategies for infertile women have increased at a rapid pace.¹⁷ Women in active military service may receive diagnostic services to identify physical causes of infertility and some medically necessary treatments (e.g., hormonal therapy, corrective surgery, antibiotics). TRICARE does not currently cover assisted reproductive technology services (ART), except for service-related infertility.¹⁸ ART services are available on a ‘first-come, first-serve’ basis at greatly reduced cost, offered at 8 military hospitals with obstetrical/gynecological reproductive endocrinology and infertility graduate medical education programs.^{18,19}

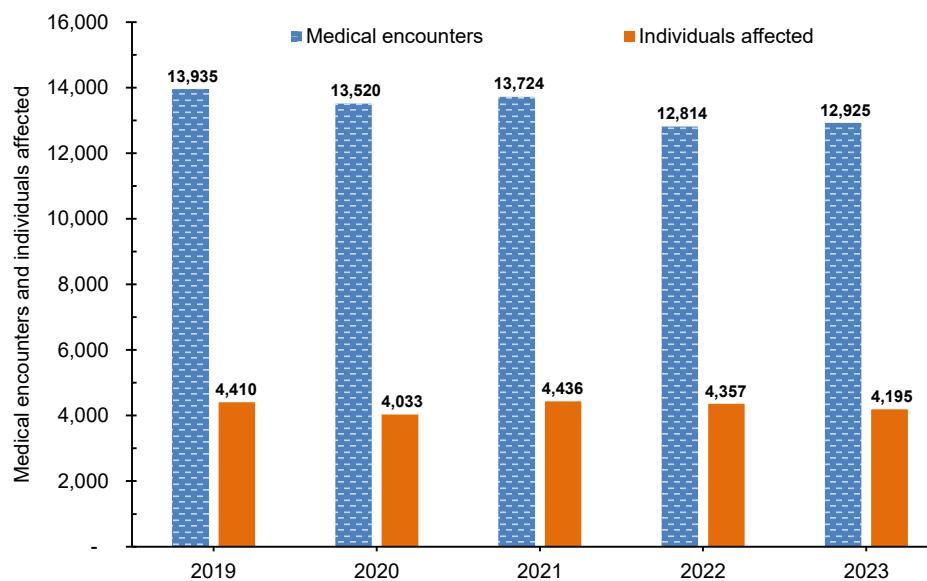
FIGURE 5. Prevalence of Infertility by Type, Active Component Service Women of Childbearing Potential, U.S. Armed Forces, 2019–2023



^aBlock, occlusion, or stenosis of the fallopian tubes.

^bStructural abnormality of the uterus or nonimplantation (includes fibroids).

FIGURE 6. Numbers of Medical Encounters for Infertility and Numbers of Individuals Affected, Active Component Service Women, 2019–2023



Access to these infertility services may vary, depending on a range of factors such as current duty station location, career stage, cost of services, command climate, and current policy.²⁰ As testing services become more commonly used, analyses related to the use, safety, efficacy and quality of infertility treatments may be warranted, based

on guidelines from the Centers for Disease Control and Prevention's National Public Health Action Plan for the Detection, Prevention and Management of Infertility.¹⁰

The results presented in this report should be interpreted as estimates defined from administrative diagnostic codes, which are methodologically different from

studies that use self-reported survey tools. Furthermore, administrative diagnostic codes may underestimate the true incidence and prevalence of infertility. The prevalence estimates from this report (1.5–1.7%) remain far below self-reported data from the Department of Defense Women's Reproductive Health Survey (15.2%),⁹ due to inherent methodological differences in comparing survey data with diagnostic codes from electronic health records.

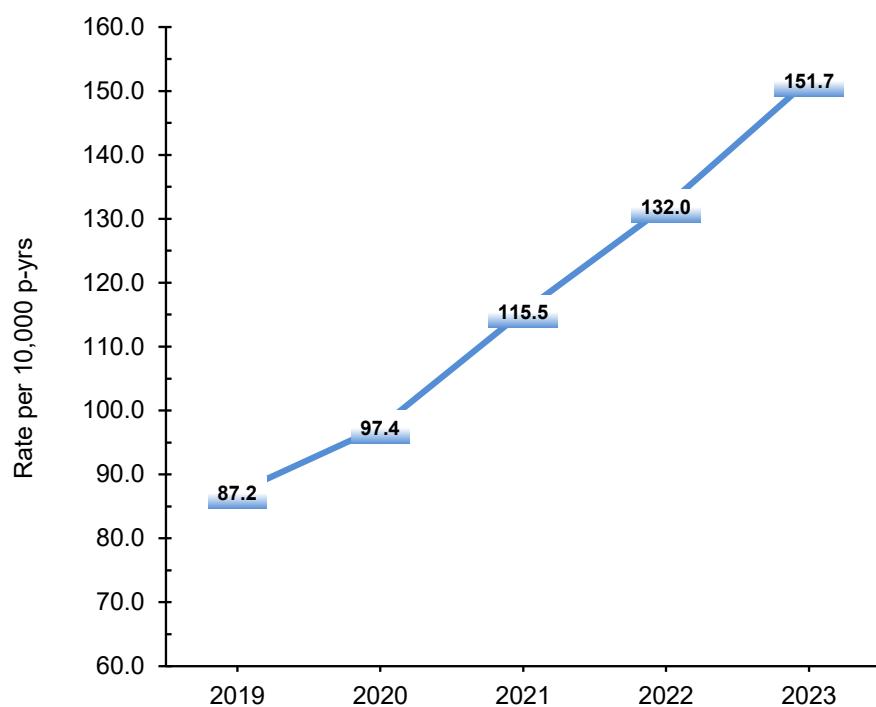
Additional limitations may be present in this report. The percentage of women who gave birth following incident infertility diagnoses is likely underestimated, as women who gave birth after leaving military service are not captured. Furthermore, this analysis did not explicitly capture recurrent pregnancy loss (ICD-9: 629.81, 646.3*; ICD-10: N96, O26.2*), which could be considered a type of infertility. Some individuals diagnosed with recurrent pregnancy loss may have received a diagnosis of unspecified infertility, however, and would have been included in this analysis.

Despite these limitations, this report provides an update on the incidence and prevalence of diagnosed infertility among active component U.S. service women. The standardized measurement of diagnosed infertility provides a basis for reviewing trends and comparing rates by socio-demographic variables, in addition to further assessing suggested risk factors,¹ such as health behaviors (e.g., alcohol or tobacco use), physical and mental health conditions (sexually transmitted infections, obesity, depression, cancer), and occupational exposures. Furthermore, the rapidly increasing rates of fertility testing among active component service women indicates need for further studies to more comprehensively describe infertility service access and use.

Disclaimer

The views and opinions expressed herein are those of the authors and do not necessarily reflect those of the U.S. Government nor any of its agencies.

FIGURE 7. Annual Rates of Fertility Testing, Active Component Service Women of Childbearing Potential, U.S. Armed Forces, 2019–2023



Abbreviations: P-yrs, person-years.

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Association Between Recurring Headache and Selected Women's Health Issues Among U.S. Navy and Marine Corps Women: Cross-Sectional Results of the Annual Periodic Health Assessment, 2021

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Recurring headache, a broad term that includes chronic migraine as well as other headache diagnoses, is a major cause of lost duty time among U.S. military women.¹ Migraine, in particular, is as much as 3 times more prevalent among women and is the headache type most affected by changes in estrogen levels that may result from biological processes (e.g., menopause, pregnancy) or use of exogenous hormones (e.g., hormonal contraceptives).²

Although prior studies have compared recurring headache among male and female service members,³⁻⁵ few have focused on the association of recurring headache with women's health issues.⁶ Furthermore, the availability of treatments for certain headache diagnoses, such as use of contraceptives to treat migraine without aura, suggests that studies of recurring headache and women's health issues could inform targeted health care strategies.⁷

This cross-sectional study of self-reported "recurring headaches/migraines," referred to in this report as "recurring headache," focused on 2 specific aims: 1) examining univariate associations of recurring headache with demographics and women's health characteristics and 2) examining age-specific associations of recurring headache with menstrual-related issues.

Methods

Data for this cross-sectional study were drawn from the 2021 Periodic Health Assessment (PHA).⁸ The PHA is a standardized, annual health assessment for all

military services that assesses individuals' medical readiness. The PHA is comprehensive and collects data on survey items related to chronic medical conditions such as recurring headache and women's health issues.

The PHA Data Sharing Agreement restricted analyses to U.S. Navy and Marine Corps personnel through 2021. Because a new version of the PHA questionnaire was introduced mid-2021, assessments in this study included those completed from August through December 2021. The main outcome was recorded as a closed question prompt on the PHA that asks for self-reported experience of "recurring headaches / migraines" within the prior year. The PHA asks survey participants, "Since your last PHA, have you experienced any of the following health conditions that either required medical care or impacted your duty performance (or both) and if so, what is your status?"

To examine recurring headache status (regardless of medical care or performance), we dichotomized answers to 'yes' or 'no.' Women's health variables of interest were hypothesized determinants (or surrogates for determinants) of recurring headache, reflecting putative relevance to estrogen-associated migraine: pregnancy history, contraceptive methods, history of total hysterectomy (as a surrogate for oophorectomy), post-menopausal status, and menstrual-related issues.² Women's health questions and possible answers from the PHA are displayed in Table 1. Demographics included age (in years), pay grade (% enlisted), number of deployments (% ≥ 1), service branch (% Marine Corps or Navy), service component (% active duty

or reserve), and "temporary profile or temporary limited duty" (LIMDU/TLD) status (% 'yes').

To examine distributions of demographics for women's health characteristics—Aim 1—we displayed percentages among women with or without self-reported recurring headache. *P*-values were computed from t-tests or Chi-square tests. For Aim 2, to examine age-specific associations of recurring headache with menstrual-related issues (i.e., responding 'yes', or endorsing heavy and/or irregular menstrual cycles/pain or pre-menstrual syndrome), we used log-binomial regression to test interaction terms for statistical significance, defined as *p* < 0.05. Estimates were stratified into 4 age groups: 18–29, 30–39, 40–49, and 50–64 years. Age-specific prevalence ratios (PRs) and 95% confidence intervals (CIs) were estimated from log-binomial regression of the probability of recurring headache.

Results

Overall, 17,629 women who completed the 2021 PHA were included in this study. The prevalence of self-reported recurring headache was 23.0%. Table 1 demographics show that women with self-reported recurring headache were more likely than women without self-reported recurring headache to be older, enlisted, deployed at least once, active duty, or on LIMDU/TLD. Associations with women's health variables suggest that those with recurring headache, compared to those without, were more likely to endorse "[are] or may be pregnant,"

TABLE 1. Distribution of Demographic and Women's Health Characteristics of Respondents, With and Without Self-Reported Recurring Headaches or Migraine, Annual Periodic Health Assessment, Female U.S. Navy and Marine Corps Service Members, 2021

| Characteristics | Recurring Headaches or Migraine | | | | P-value ^a |
|--|---------------------------------|------|------------------|------|----------------------|
| | No (n=13,570) | % | Yes (n=4,059) | % | |
| Age, y ^b | No. | % | No. | % | |
| 18–24 | 5,324 | 39.2 | 1,008 | 24.8 | |
| 25–29 | 3,278 | 24.2 | 968 | 23.8 | |
| 30–34 | 2,159 | 15.9 | 786 | 19.4 | |
| 35–39 | 1,446 | 10.7 | 635 | 15.6 | |
| 40+ | 1,360 | 10.0 | 662 | 16.3 | |
| Pay grade | | | | | <0.0001 |
| Enlisted | 10,348 | 76.3 | 3,456 | 85.1 | |
| Deployments, n | | | | | <0.0001 |
| ≥ 1 | 4,143 | 30.5 | 1,507 | 37.1 | |
| Service branch | | | | | 0.7785 |
| Marine Corps | 2,418 | 17.8 | 716 | 17.6 | |
| Navy | 11,152 | 82.2 | 3,343 | 82.4 | |
| Component | | | | | <0.0001 |
| Active | 10,906 | 80.4 | 3,501 | 86.3 | |
| Reserves | 2,658 | 19.6 | 558 | 13.7 | |
| Temporary profile or LIMDU/TLD | | | | | <0.0001 |
| Yes | 1,066 | 7.9 | 674 | 16.6 | |
| “Which of the following best describes you?” | | | | | <0.0001 |
| I am or may be pregnant | 645 | 4.8 | 240 | 5.9 | |
| I was pregnant or just delivered within the past 6 months | 609 | 4.5 | 217 | 5.3 | |
| I was pregnant or delivered 6–12 months ago | 423 | 3.1 | 198 | 4.9 | |
| I am not pregnant now, and was not pregnant or delivered in the past 12 months | 11,893 | 87.6 | 3,404 | 83.9 | |
| “Since your last PHA, what contraceptive methods, if any, have you and your partner(s) been using to prevent pregnancy? Mark all that apply” | | | | | |
| Long term IUD (including copper or progesterone) or implant, yes | 3,231 | 23.8 | 894 | 22.0 | 0.0459 |
| Injectable—every 3 months, yes | 200 | 1.5 | 63 | 1.6 | 0.9229 |
| Daily—birth control pills, yes | 1,937 | 14.3 | 493 | 12.1 | 0.0022 |
| Monthly—contraceptive patch/vaginal ring, yes | 296 | 2.2 | 111 | 2.7 | 0.1171 |
| Emergency contraception (such as Plan B), yes | 481 | 3.5 | 126 | 3.1 | 0.3879 |
| “Have you had a total hysterectomy (uterus and cervix removed)?” | | | | | <0.0001 |
| Yes | 161 | 1.2 | 132 | 3.3 | |
| “Are you postmenopausal and no longer experiencing menstrual cycles?” | | | | | <0.0001 |
| Yes | 457 | 3.4 | 156 | 3.8 | |
| “Do you have heavy and/or irregular menstrual cycles/pain or premenstrual syndrome (PMS)?” | | | | | <0.0001 |
| Yes, but I am in treatment and having no problems | 766 | 5.6 | 313 | 7.7 | |
| Yes, and I am having ongoing issues | 2,119 | 15.6 | 1,359 | 33.5 | |
| No | 10,150 | 74.8 | 2,150 | 53.0 | |
| Missing | 535 | 3.9 | 237 | 5.8 | |

Abbreviations: n, number; No., number; y, years; LIMDU, limited duty; TLD, temporary limited duty; PHA, Periodic Health Assessment; IUD, intrauterine device; PMS, pre-menstrual syndrome.

^a P-values are for the χ^2 test of independence for categorical variables.

^b Values of age among respondents with no recurring headache do not sum to 100% because 3 respondents were age 17 years.

history of total hysterectomy, or postmenopausal status. The occurrence of menstrual-related issues was strongly associated with recurring headache, particularly among those who endorsed ongoing issues. Notably, univariate associations showed that women with recurring headache were less likely to report using a long-term intrauterine device (IUD) (22.0% vs. 23.8%, $p=0.0459$) or daily birth control pills (12.1% vs. 14.3%, $p=0.0022$).

As shown in **Table 2**, age-specific associations of recurring headache with menstrual-related issues were stronger among women in the younger age groups, particularly those who endorsed ongoing issues. P -values for each interaction term of age (as a continuous covariate) and menstrual-related issues ("Yes, but in treatment and no issues" or "Yes, but having ongoing issues") were $p=0.6313$ and $p=0.0711$, respectively. PRs and 95% CIs of recurring headache among women with ongoing menstrual-related issues (compared with no issues) were 2.4 (2.2, 2.6); 2.3 (2.1, 2.5); 1.7 (1.5, 2.0); and 3.1 (1.4, 7.0)—among women ages 18–29, 30–39, 40–49, and 50–64 years, respectively. Among women 50–64 years of age, wider CIs likely reflected a smaller sample in this age group.

Discussion

This study indicated a high prevalence of self-reported recurring headache (23.0%) during a 5-month period in 2021 among U.S. Navy and Marine Corps women. This study's numbers approximate 2011 findings from the Millennium Cohort Study, which included female U.S. active duty, reserve, and Guard members (n=12,409), and reported provider-diagnosed migraine or recurrent severe headache occurrence within the past year among 20.9% or 22.3% of military women, respectively.⁹ These estimates are higher than the female general population's annual prevalence (17%)¹⁰ but lower than lifetime migraine prevalence (30.1%) among female veterans.³

Although this study could not differentiate between specific headache diagnoses, noted associations with estrogen-related health characteristics suggest that a substantial proportion of women may be at risk for estrogen-associated migraines upon clinical evaluation.² This cross-sectional study could not establish temporal relationships between variables of interest, and our findings have limited

ability to support causal inference. Nevertheless, the lower prevalence of recurring headache among women in treatment for menstrual-related issues warrants consideration of whether individuals reporting ongoing menstrual-related issues could benefit from hormonal contraception or other hormone-related treatments of estrogen-associated headache,¹¹ which is consistent with the literature.^{2,12}

This work adds to the literature on recurring headache among women in the U.S. Navy and Marine Corps. Limitations of this preliminary study include an inability to differentiate between diagnostic subtypes of headache, absence of covariates of interest not recorded by the PHA, and cross-sectional analysis that precludes causal inference. Strengths of this work include its large sample size and estimation of age-specific prevalences. Additional work is needed to understand patterns of headache and migraine among U.S. military women, but this study highlights the importance and relevance of women's health issues in female service members with recurring headache.

TABLE 2. Age-Specific Prevalence and Prevalence Ratios of Self-Reported Recurring Headaches or Migraines, by "Heavy and/or Irregular Menstrual Cycles/Pain or Premenstrual Syndrome," Annual Periodic Health Assessment, Female U.S. Navy and Marine Corps Service Members, 2021

| Age Group | "Heavy or Irregular Menstrual Cycles, Pain, or PMS?" ^a | Total (n) | Recurring Headache or Migraine Cases (n) | Prevalence (%) | Prevalence Ratio ^b | 95% CI |
|-----------|---|-----------|--|----------------|-------------------------------|-----------|
| 18–29 | No | 7,592 | 1,071 | 14.1 | 1.0 | Reference |
| | Yes, but in treatment and no issues | 629 | 145 | 23.1 | 1.6 | 1.4–1.9 |
| | Yes, but having ongoing issues | 2,208 | 733 | 33.2 | 2.4 | 2.2–2.6 |
| 30–39 | No | 3,635 | 787 | 21.7 | 1.0 | Reference |
| | Yes, but in treatment and no issues | 320 | 120 | 37.5 | 1.7 | 1.5–2.0 |
| | Yes, but having ongoing issues | 943 | 467 | 49.5 | 2.3 | 2.1–2.5 |
| 40–49 | No | 1,003 | 283 | 28.2 | 1.0 | Reference |
| | Yes, but in treatment and no issues | 117 | 45 | 38.5 | 1.4 | 1.1–1.7 |
| | Yes, but having ongoing issues | 308 | 151 | 49.0 | 1.7 | 1.5–2.0 |
| 50–64 | No | 67 | 9 | 13.4 | 1.0 | Reference |
| | Yes, but in treatment and no issues | 13 | 3 | 23.1 | 1.7 | 0.5–5.5 |
| | Yes, but having ongoing issues | 19 | 8 | 42.1 | 3.1 | 1.4–7.0 |

Abbreviations: n, number; PMS, pre-menstrual syndrome; CI, confidence interval.

^aService members with missing responses to "heavy and/or irregular menstrual cycles/pain or premenstrual syndrome" are excluded from table totals.

^bPrevalence ratios and 95% CIs are from age group stratified log-binomial regression of the probability of recurring headache.

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Long-Acting Reversible Contraception and Unintended Pregnancy Among U.S. Active Duty Service Members, 2017–2018

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Long-acting reversible contraception (LARC) includes forms of birth control that offer strong combinations of efficacy, safety, and convenience, such as subdermal implants and intrauterine devices (IUDs).¹ In the U.S., LARC use is estimated to be twice as prevalent among active duty service members (ADSMs) compared with the general population (23.0% vs. 10.4%).^{2,3} The number of active duty LARC users increased by 19.0% between 2016 and 2019, from 50,365 to 59,942.²

While unintended pregnancy following LARC placement is rare (<1.0%),^{1,4} there is a paucity of research among ADSMs, a population in which unintended pregnancy has major implications for military readiness.⁵ This descriptive study examined demographic, military, and medical characteristics of unintended pregnancies diagnosed after LARC placement in U.S. ADSMs, including pregnancies due to LARC failure as well as pregnancies undetected at time of LARC placement.

Methods

This study utilized medical encounter data from the Military Health System Data Repository, military personnel data from Defense Manpower Data Center (DMDC), as well as data abstracted from patient electronic health records (EHRs). Medical encounter data included care received at either military or civilian facilities coded with International Classification of Diseases (ICD) and Current Procedural Terminology (CPT) codes. Data were linked using the unique Electronic Data Interchange Personal Identifier assigned to each ADSM.

The study population included confirmed cases of unintended pregnancy diagnosed after LARC placement. Suspected cases were first screened from medical encounter data; this group included ADSMs who had LARC placement at a military clinic in 2017 or 2018 (ICD-10 diagnosis code Z30.430; ICD-10 procedure codes 0UH[9,C]xHZ; CPT codes 11981, 58300), indication of pregnancy within 12 months after placement (ICD-10 diagnosis codes Z32.01, Z[33,34,36].x, O[03,09,20].x, O26.3), and no indication of LARC removal or re-insertion prior to pregnancy (ICD-10 diagnosis codes Z30.43[2,3]; ICD-10 procedure codes 0UPDxHZ; CPT codes 11976, 11982-83, 58301). Suspected cases were confirmed using information abstracted from patient EHRs; all cases had no records of LARC removal prior to pregnancy diagnosis and were described as unintended pregnancies.

Cases were categorized into 2 types, based on estimated timing of conception relative to placement: LARC failure or undetected pregnancy at placement. Date of conception was calculated by adding 2 weeks to the date of last menstrual period (LMP), as obtained from patient self-reporting or pregnancy ultrasound records.⁶ Estimated dates of conception occurring more than 1 week after LARC placement were considered LARC failures, while all others were estimated to be already pregnant at LARC placement.

All variables were abstracted from patient EHRs except for race and ethnicity, marital status, education, rank, and service branch, which were derived from DMDC files from the month of LARC placement. Characteristics were assessed overall and by outcome type (LARC failure or undetected pregnancy at placement) using descriptive and summary statistics. Statistical analysis

was completed using SAS Enterprise Guide, version 8.3.

Institutional Review Board approval for this study was obtained from the Naval Health Research Center (protocol NHRC.1999.0003) and informed consent was waived per 32 Code of Federal Regulations §219.116(d).

Results

Initial screening identified 466 ADSMs with suspected pregnancy within 1 year following LARC placement that occurred in 2017 or 2018. After EHR review, 76 (16.3%) cases were confirmed as unintended pregnancies, of which 42 (55.3%) occurred in ADSMs who experienced LARC failure and 34 (44.7%) were among those with undetected pregnancy at LARC placement. Most cases had determined LMP from patient self-reporting at time of LARC placement versus ultrasound dating (72.4 vs. 27.6%; data not shown).

Most cases occurred among ADSMs aged 18–24 years at LARC placement (55.3%), married (52.6%), and of enlisted military rank (94.7%) (Table 1). Compared with patients who experienced LARC failure, those with undetected pregnancy at placement were younger and more likely of non-Hispanic Black race or ethnicity, junior enlisted rank, in the Army, and never previously pregnant. Most LARC failures occurred among patients with an IUD (88.1%), while nearly all patients already pregnant at placement received a subdermal implant (91.2%) (Table 2). Overall, almost all cases (94.7%) had completed a pregnancy test prior to LARC placement. Almost half of cases (43.4%) ended in a non-live birth outcome.

TABLE 1. Demographic, Military and Clinical Characteristics of U.S. Active Duty Service Members with LARC Placement in 2017–2018 and Diagnosed Unintended Pregnancy in the Following Year, Overall and by Outcome Type

| Characteristics ^a | All Unintended Pregnancies | | Outcome Type | | | |
|--------------------------------------|----------------------------|------|--------------|------|-----------------------------------|------|
| | | | LARC Failure | | Undetected Pregnancy at Placement | |
| | No. | % | No. | % | No. | % |
| Total | 76 | — | 42 | — | 34 | — |
| Age, y | | | | | | |
| 18-24 | 42 | 55.3 | 21 | 50.0 | 21 | 61.8 |
| 25-34 | 21 | 27.6 | 12 | 28.6 | 9 | 26.5 |
| ≥35 | 13 | 17.1 | 9 | 21.4 | 4 | 11.8 |
| Mean ± SD | 25.2 ± 5.6 | | 26.9 ± 6.3 | | 23.2 ± 3.9 | |
| Median (IQR) | 23 (21-29) | | 24 (23-32) | | 23 (20-25) | |
| Race and ethnicity | | | | | | |
| Hispanic | 17 | 22.4 | 10 | 23.8 | 7 | 20.6 |
| Black, non-Hispanic | 25 | 32.9 | 10 | 23.8 | 15 | 44.1 |
| White, non-Hispanic | 24 | 31.6 | 16 | 38.1 | 8 | 23.5 |
| All other groups ^b | 10 | 13.2 | 6 | 14.3 | 4 | 11.8 |
| Marital status | | | | | | |
| Married | 40 | 52.6 | 24 | 57.1 | 16 | 47.1 |
| Unmarried | 36 | 47.4 | 18 | 42.9 | 18 | 52.9 |
| Education | | | | | | |
| Less than bachelor's degree | 68 | 89.5 | 35 | 83.3 | 33 | 97.1 |
| Bachelor's degree or greater | 8 | 10.5 | 7 | 16.7 | 1 | 2.9 |
| Military rank | | | | | | |
| Junior enlisted (E1-E3) | 29 | 38.2 | 10 | 23.8 | 19 | 55.9 |
| Enlisted (E4-E9) | 43 | 56.6 | 28 | 66.7 | 15 | 44.1 |
| Officer | 4 | 5.3 | 4 | 9.5 | 0 | 0.0 |
| Service branch | | | | | | |
| Army | 29 | 38.2 | 12 | 28.6 | 17 | 50.0 |
| Navy | 23 | 30.3 | 19 | 45.2 | 4 | 11.8 |
| Air Force | 14 | 18.4 | 7 | 16.7 | 7 | 20.6 |
| Marine Corps | 10 | 13.2 | 4 | 9.5 | 6 | 17.6 |
| Gravidity | | | | | | |
| 0 | 29 | 38.2 | 10 | 23.8 | 19 | 55.9 |
| 1+ | 47 | 61.8 | 32 | 76.2 | 15 | 44.1 |
| Parity | | | | | | |
| 0 | 31 | 40.8 | 12 | 28.6 | 19 | 55.9 |
| 1+ | 45 | 59.2 | 30 | 71.4 | 15 | 44.1 |
| Body mass index (kg/m ²) | | | | | | |
| <18.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 18.5-24.9 | 26 | 34.2 | 14 | 33.3 | 12 | 35.3 |
| 25.0-29.9 | 31 | 40.8 | 14 | 33.3 | 17 | 50.0 |
| ≥30.0 | 19 | 25.0 | 14 | 33.3 | 5 | 14.7 |
| Patient medical history | | | | | | |
| Cesarean section | 9 | 11.8 | 7 | 16.7 | 2 | 5.9 |
| Diabetes | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Fibroids | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Hypertension | 1 | 1.3 | 1 | 2.4 | 0 | 0.0 |
| Obesity | 14 | 18.4 | 9 | 21.4 | 5 | 14.7 |
| Pelvic inflammatory disease | 2 | 2.6 | 0 | 0.0 | 2 | 5.9 |
| Sexually transmitted infection | 6 | 7.9 | 3 | 7.1 | 3 | 8.8 |
| LARC expulsion | 3 | 3.9 | 3 | 7.1 | 0 | 0.0 |

Abbreviations: LARC, long-acting reversible contraception; y, years; SD, standard deviation; IQR, interquartile range; E, Enlisted; kg, kilogram; m, meter.

^aRefers to patient characteristics at time of LARC placement.

^bAll other race and ethnicity groups include American Indian or Alaska Native (overall n=2), Asian or Pacific Islander (n=3), those with more than 1 race or ethnicity reported (n=4), and those with missing data (n=1).

In this study of unintended pregnancies diagnosed after LARC placement, the majority of cases occurred among young, enlisted ADSMs; about half of cases were unmarried, and one-third were never previously pregnant. These characteristics generally suggest a patient population with reduced social support and limited independence from the military, which providers should be aware of when offering LARC-related care.

The American College of Obstetricians and Gynecologists guidelines state that implants and IUDs can be placed any time during the menstrual cycle if there is reasonable certainty a patient is not pregnant.¹ This study found only 34 instances in which providers were unable to detect or reasonably rule out pregnancy at contraceptive initiation, suggesting some variation in recommended practice guidelines,^{1,7} or incomplete or inaccurate dating of patients' recent sexual histories or LMPs, albeit rare.

To be reasonably certain a patient is not pregnant at LARC placement, providers should follow the pregnancy checklist recommended by the Centers for Disease Control and Prevention, as these criteria are highly accurate in ruling out pregnancy (i.e., negative predictive value of 99–100%).⁷ Editing checks within EHRs (e.g., re-entering dates to facilitate patient recall and avoid entry errors) and improved patient-provider communication (e.g., through shared decision-making vs. traditional provider-driven model^{8,9}) can also help promote optimal LARC selection and timing of placement.

While calculation of a formal LARC failure rate was outside the scope of this study, only 42 failures were identified over the 2-year period, most of which were among patients with IUDs. This number is small and consistent with existing evidence that shows extremely high effectiveness (i.e., failure rates <1.0%) of LARC methods.^{1,4}

Study limitations include potential misclassification of outcome type (LARC failure or undetected pregnancy at placement), as date of LMP was most often

TABLE 2. LARC Placement and Pregnancy Characteristics Among U.S. Active Duty Service Members with LARC Placement 2017–2018 and Diagnosed Unintended Pregnancy in the Following Year, Overall and by Outcome Type

| Characteristics | All Unintended Pregnancies | | Outcome Type | | | |
|--|----------------------------|------|--------------|------|-------------|------|
| | No. | % | No. | % | No. | % |
| Total | 76 | — | 42 | — | 34 | — |
| LARC type | | | | | | |
| Implant | 36 | 47.4 | 5 | 11.9 | 31 | 91.2 |
| Hormonal IUD | 23 | 30.3 | 20 | 47.6 | 3 | 8.8 |
| Copper IUD | 17 | 22.4 | 17 | 40.5 | 0 | 0.0 |
| Placement characteristics | | | | | | |
| Pregnancy test prior to placement | 72 | 94.7 | 39 | 92.9 | 33 | 97.1 |
| Postpartum placement ^a | 6 | 7.9 | 5 | 11.9 | 1 | 2.9 |
| Days from last menses to placement | | | | | | |
| ≤ 7 days | 12 | 15.8 | 12 | 28.6 | 0 | 0.0 |
| > 7 days | 64 | 84.2 | 30 | 71.4 | 34 | 100 |
| Placement provider type | | | | | | |
| Certified nurse midwife | 12 | 15.8 | 7 | 16.7 | 5 | 14.7 |
| Nurse practitioner | 17 | 22.4 | 9 | 21.4 | 8 | 23.5 |
| Physician | 42 | 55.3 | 24 | 57.1 | 18 | 52.9 |
| Physician assistant | 3 | 3.9 | 1 | 2.4 | 2 | 5.9 |
| Other or unknown | 2 | 2.6 | 1 | 2.4 | 1 | 2.9 |
| Months from most recent delivery to placement^b | | | | | | |
| Mean ± SD | 25.1 ± 36.8 | | 23.1 ± 38.1 | | 29.5 ± 35.0 | |
| Median (IQR) | 6 (2-33) | | 2 (2-25) | | 12 (4-47) | |
| Confirmatory imaging of LARC | | | | | | |
| Retention | 12 | 15.8 | 10 | 23.8 | 2 | 5.9 |
| Expulsion | 13 | 17.1 | 13 | 31.0 | 0 | 0.0 |
| Perforation | 1 | 1.3 | 1 | 2.4 | 0 | 0.0 |
| No imaging records available | 50 | 65.8 | 18 | 42.9 | 32 | 94.1 |
| Months from placement to pregnancy identification | | | | | | |
| Mean ± SD | 4.5 ± 3.8 | | 7.1 ± 3.1 | | 1.3 ± 1.4 | |
| Median (IQR) | 4 (1-7) | | 7 (5-10) | | 1 (0-2) | |
| Pregnancy outcome | | | | | | |
| Live birth | 43 | 56.6 | 26 | 61.9 | 17 | 50.0 |
| Stillbirth | 1 | 1.3 | 1 | 2.4 | 0 | 0.0 |
| Ectopic pregnancy | 5 | 6.6 | 3 | 7.1 | 2 | 5.9 |
| Spontaneous abortion | 12 | 15.8 | 7 | 16.7 | 5 | 14.7 |
| Elective or therapeutic abortion | 15 | 19.7 | 5 | 11.9 | 10 | 29.4 |

Abbreviations: LARC, long-acting reversible contraception; IUD, intrauterine device; SD, standard deviation; IQR, interquartile range.

^aPostpartum placement was defined as those occurring within 6 weeks after delivery.

^bThis measure included 42 service members with a known prior delivery.

derived from patient self-reporting at time of LARC placement rather than ultrasound dating. Available EHRs lacked information on how a provider ruled out pregnancy at LARC placement (other than performing a pregnancy test) or determined or corrected LMP from ultrasound records, further hindering LMP estimate reliability. Among the 466 ADSMs screened for unintended pregnancy following LARC placement, only 16.3% were confirmed cases, demonstrating

the value of EHR use to identify true unintended pregnancies. Remaining cases were not confirmed due to various circumstances (e.g., no pregnancy, LARC removal before pregnancy). Limited resources did not allow for abstraction of LARC placements with no pregnancy; therefore, this study could not determine whether certain characteristics were associated with an increased risk for unintended pregnancy or LARC failure.

The consequences of unintended pregnancy can be significant for ADSMs, their support systems, and service units (e.g., extended non-deployability). If unintended pregnancy occurs while in a military theater of operation, increased costs incur due to medical evacuation and personnel replacement. Independent of deployment status, unintended pregnancy also results in quality of life adjustments for ADSMs as well as their unit personnel, with potential effects on ADSM retention, mission readiness, and unit cohesion.⁵ Active duty status may also influence a service member's decision to maintain a pregnancy. Ongoing efforts to improve contraceptive access, use, and reliability are critical for preserving operational readiness and career advancement opportunities among this population, while also decreasing health care expenditures.

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The study protocol was approved by the Naval Health Research Center Institutional Review Board in compliance with all applicable federal regulations governing protection of human subjects. Research data were derived from an approved Naval Health Research Center Institutional Review Board protocol, NHRC.1999.0003.

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Contraceptive Use Trends from the Periodic Health Assessment Among Female Active Duty U.S. Sailors and Marines, 2018–2023

Brooke K. Rodriguez, MPH; Katherine R. Gonzales, MPH; Sarah C. Kelsey, MPH

This Surveillance Snapshot highlights trends in birth control methods among female active duty U.S. sailors and marines. Birth control methods are self-reported during annual Periodic Health Assessments (PHAs) of active duty U.S. service members. This analysis captures data on birth control use including long-acting reversible contraceptives (LARCs), short-acting reversible contraceptives (SARCs), intrauterine devices (IUDs), implants, barrier methods, emergency contraception, sterilization, fertility awareness, or lack of use among individuals not actively taking steps to prevent pregnancy. These findings offer insights into active duty females' preferences and behaviors beyond clinical data and may inform Defense Health Agency (DHA) policies for enhancing female force readiness.

This analysis examined responses to question 22 on PHA DD Form 3204, versions 1 and 2, for calendar years 2018–2023.¹ The population included active duty female sailors and marines, ages 18–52 years. Version 2 of the form was introduced in August 2021 and retained the contraceptive questioning structure of version 1, allowing women to select why they may not be taking steps to prevent pregnancy. Contraceptive variables and free-text responses were used to determine prevalence of LARCs, SARCs, and other pregnancy prevention methods, which included infertility or sterilization (of the service member or partner), condom use, abstinence, fertility awareness methods, and pregnancy or breastfeeding. Alternatively, respondents could select a response indicating that pregnancy prevention was not needed (e.g., same sex partner[s], intention to conceive).

Among all PHAs completed and certified with medical provider signature (n=277,633), only 24.3% (n=67,430) included responses to assessment items on contraceptive methods. Among women with a response indicating at least 1 birth control

method during the study period, the Figure illustrates the distribution of birth control methods by type. Self-reported SARC and condom use decreased from 34.6% to 18.1%, and 30.1% to 15.5%, respectively, from 2018 to 2023. Self-reported LARC use showed an upward trend, rising from 19.6% in 2018 to 31.0% in 2023. During the study period, the percentage of active duty women reporting same-sex relationships increased from 0.6% to 1.8%, but remained below 2%; abstinence increased from 0.3% to 2.8%, but remained below 3%; infertility increased from 8.0% to 9.0%; cycle tracking and family planning increased from 1.8% to 3.6%. Breastfeeding as a method to prevent pregnancy remained consistently low during the period of analysis, never exceeding 2.8% of responses. PHAs with free-text responses to 'other' contraceptive methods (n=1,713), which could not be classified into the categories described, were excluded from the analysis.

It is important to note that PHA data consist of self-reported physical health information and do not represent actual diagnoses, or prescriptions written, filled, or taken. Nevertheless, this information has value, providing insights into reproductive health trends affecting force readiness and resilience, for informed health care strategies.

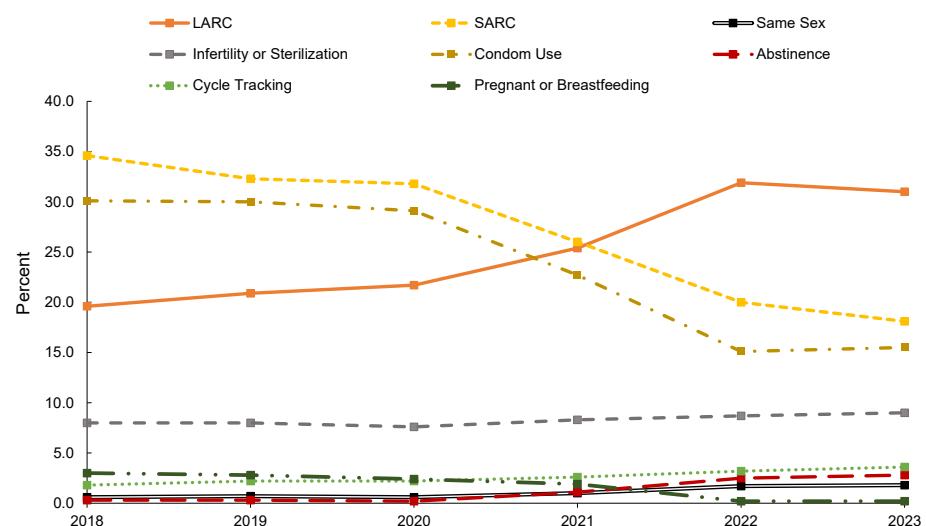
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FIGURE. Prevalence of Birth Control Method, Reported on Periodic Health Assessments, Active Duty Sailors and Marines, 2018–2023



Abbreviations: PHA, Periodic Health Assessment; LARC, long-acting reversible contraception; SARC, short-acting reversible contraception.

Optimizing Female Warfighter Health and Performance in Environmental Extremes

Gabrielle E. W. Giersch, PhD; Karleigh E. Bradbury, PhD; Nisha Charkoudian, PhD

The ongoing non-combat threats of extreme environmental exposure—including heat, cold, high altitudes, and subterranean areas—have always been important focuses for research and development of effective countermeasures, both within the military as well as other domains requiring prolonged outdoor activity. Over the past decade, the increased frequency of weather phenomena associated with climate change—such as extreme heat waves, violent storms, catastrophic flooding—have brought the biomedical risks and gaps in knowledge associated with extreme environmental exposure into sharper focus, both in the biomedical literature and mainstream media.^{1,2}

In military medicine, threats due to environmental exposure are particularly relevant, as small units and dismounted warfighters are often directly exposed to a given set of extreme environmental conditions. Until the past decade, much of the military medical literature on environmental stressors relied on data collected primarily from men. With women representing a growing percentage of the military force, both in the U.S. and around the world, it is increasingly necessary to understand the physiological and pathophysiological responses of both sexes for optimizing the health of all warfighters, in mission-critical scenarios as well as training.

The environmental physiology community, including the U.S. Army Research Institute of Environmental Medicine (USARIEM) and many academic laboratories and research teams, have recently increased focus on the female warfighter, to improve knowledge and awareness of individualized risk management for individuals exposed to extreme terrestrial environments.³⁻⁸ This editorial provides an update

on the state of the science to aid military medical providers' understanding of where and when sex-specific considerations in environmental exposure risk are necessary and—equally importantly—are not.

Threats of Extreme Environmental Exposure

Heat Stress

Heat-related illnesses remain a major threat to warfighters, with 2,000 or more individuals each year experiencing mild forms of heat illness, and approximately 500 individuals experiencing exertional heat stroke (EHS), which is the most severe, and potentially fatal, heat illness. It was previously assumed that women are at an increased risk for heat-related illnesses compared to their male counterparts,^{9,10} without appropriate evidence.

Recently, the Thermal and Mountain Medicine Division of USARIEM evaluated epidemiological data, using a case-control analysis, from an Army-wide analysis of EHS, the most severe form of heat illness, and found no differences in risk of EHS between men and women.^{11,12} While sex-related differences for EHS risk are not apparent, recent evidence suggests potential differences in organ damage between men and women following EHS. In a cohort of EHS cases from Fort Benning, the Thermal and Mountain Medicine Division of USARIEM also found that biomarkers of end organ damage were lower in women compared to men, despite similar highest recorded body temperatures.¹³ This may suggest that women suffer less damage than men from EHS of similar severity, but more research is needed to fully elucidate

physiological mechanisms to support that hypothesis.

Risk for developing other less severe, heat-related illnesses has recently been evaluated. Kazman et al. (2024) reported an increased risk for "mild" heat illness (i.e., heat exhaustion) in recruits,¹⁴ but more research to elucidate the mechanism for this potential difference is warranted. In the yearly heat illness active updates from MSMR, men and women consistently demonstrate similar rates of reported heat exhaustion, including heat injury (diagnosed as heat exhaustion with evidence of end organ damage).

While risk of heat-related illness does not appear to be affected by sex, relatively low-impact differences in thermoregulation between men and women exist. Namely, and likely the most effective, are the physical differences between men and women, where women are, on average, smaller with larger body surface area to mass ratio (BSA:mass⁻¹), which can enhance heat dissipation in some environments.¹⁵ This may provide women with a relative advantage in certain situations where heat dissipation is not impeded by clothing or the surrounding environment. Situations in which heat dissipation capacity is impeded, or work rate is very high (i.e., load carriage occurs), instead could turn women's BSA:mass⁻¹ into a disadvantage; lower lean body mass carrying an absolute load in clothing with less evaporative capacity leads to greater thermal stress. Additionally, there is evidence to suggest lower sweating rate in women at very high work loads,^{16,17} which may affect military personnel when performing ruck marches or runs, but also may not yield significant differences in total heat loss or core temperature responses, despite less sweat produced.¹⁸

Female sex hormones also have pronounced effects on the thermoregulatory system, as previously thoroughly described,¹⁹ but those hormonal or menstrual cycle differences do not seem to affect body temperature following exercise, when evaluated in a meta-analysis.²⁰ Contraceptive status did appear to influence esophageal temperature during exercise,²¹ with progestin-only contraceptive users experiencing higher core temperatures at baseline and throughout exercise, which may suggest that type of contraceptive influences thermoregulatory response in women.

Besides physiological differences, there are also well-described behavioral differences in thermoregulation between men and women, including pacing²² and behavioral thermoregulation.²³ Behavioral mechanisms may be more effective than physiological mechanisms for thermoregulation²⁴ and should be considered for future research in addition to practical prevention strategies.

Cold Stress

Female-specific responses during cold stress are less well-understood. Female sex hormones and cold stress responses have been thoroughly reviewed,⁷ with findings indicating that estradiol may enhance cutaneous vasodilatory responses²⁵⁻²⁷ and progesterone observed to shift the core temperature threshold to higher temperatures,^{25,28} which may affect shivering onset and sensitivity^{29,30} (although that finding varies in the literature,³¹ without consistent methodologies in reported investigations). Interestingly, if elevated progesterone concentrations, like those observed in the luteal phase of the menstrual cycle, do influence shivering onset, it is likely such effect is due to elevated core temperatures observed with high progesterone and would not influence risk of injury, impaired performance, nor loss of dexterity during cold stress.

Manual dexterity decreases with cold stress, and cold-induced vasodilation, a reflex that opens the blood vessels to the extremities to provide blood flow, likely occurs to prevent freezing cold injuries.³² Women have been shown to have lower finger temperatures than men, with no differences in cold-induced vasodilation or

dexterity measures between sexes,³³ but sex hormones were not evaluated systematically in that investigation.

The impacts of estradiol and progesterone, particularly with fluctuations that occur not only during the menstrual cycle, but throughout reproductive lifespan as well as with contraceptive use, require further investigation.

Women do appear to have a greater prevalence of Raynaud's phenomenon,^{34,35} but there is currently not evidence to suggest specific influence of female sex hormones or menstrual cycle phases on Raynaud's prevalence or severity.³⁶ Raynaud's phenomenon may pose an increased risk in developing freezing cold injuries such as frostbite.³⁷

The physical differences that largely govern differences between men and women in heat stress may also affect cold stress, with greater subcutaneous fat potentially providing insulation in women³⁸ and greater average BSA:mass⁻¹ potentially increasing heat loss in cold environments. It is unclear if these physical differences influence risk of injury or decreased performance during cold stress.

High Altitude Stress

It is well-established that humans experience myriad physiological responses upon exposure to high terrestrial altitude due to associated decrease in partial pressure of oxygen (PO₂).³⁹ The decrease in PO₂ is the primary cause of the decrements in both physical and cognitive performance⁴⁰ that occur with altitude exposure.

Both acute and chronic responses to hypoxia occur with a primary goal of increasing oxygen delivery throughout the body. Acute responses include, but are not limited to, increases in heart rate, ventilation, diuresis, and sympathetic nervous system activity.^{3,41} Longer-term adaptations, known as acclimatization, include increases in hemoglobin mass, alterations in substrate utilization (e.g., enhanced carbohydrate metabolism), and improvements in capillary O₂ extraction.⁴⁰ The current literature presents some sex differences in physiological variables such as ventilation and hemoglobin mass at sea level baseline, but these differences do not appear to

influence acute physiological responses to altitude nor the process of acclimatization in women.⁴¹

Ventilation has been shown to be influenced by sex and female sex hormones.⁴² Progesterone is a ventilatory stimulant that acts on both the peripheral and central chemoreceptors to increase ventilation⁴¹ and, concomitantly, lower partial pressures of end tidal CO₂ (PETCO₂). Higher ventilation and lower PETCO₂ have been reported in women in comparison to men, as well as during the luteal versus follicular phase of the menstrual cycle.⁴³ Despite the presence of progesterone, there are no sex differences in the acute hypoxic ventilatory response⁴³ or in the time course of ventilatory acclimatization.⁴⁴

One potential limitation for females at altitude is an increased work of breathing. Women experience increased work of breathing compared to men, even when corrected for body and lung size,⁴⁵ a result of smaller airways that increase air flow resistance during ventilation.⁴⁶ This physiological difference between sexes may be of particular importance during load carriage at altitude, when increased work of breathing intensifies due to increased thoracic resistance caused by the external load.

Increased work of breathing for a specific ventilation is caused by elevated oxygen demand and greater respiratory muscle use.^{47,48} In situations when respiratory muscle metabolic rates are increased, blood flow is redistributed to the diaphragm and other respiratory muscles because of increased sympathetic nerve activity, concomitant with vasoconstriction to blood vessels of other active or inactive muscles (i.e., respiratory muscle metaboreflex). Recent work has demonstrated attenuated sympathetic responses in women to increases in inspiratory muscle work, both at rest⁴⁹ and during exercise,⁵⁰ but the implications of these findings for blood flow redistribution during high levels of respiratory muscle work (i.e., during load carriage at altitude), and whether women are at a disadvantage due to increased work of breathing, are unknown.^{51,52}

High altitude illness is an important risk consideration for those ascending in altitude. The most common high altitude illness is acute mountain sickness

(AMS), which occurs when individuals rapidly ascend to altitudes to 2,500 meters or higher, with symptom prevalence and severity increasing with higher elevations.^{53,54} Symptoms of AMS often include nausea, dizziness, fatigue, headache, and gastrointestinal distress. Other, but less common, altitude-associated illnesses include high altitude cerebral and pulmonary edemas (HACE and HAPE, respectively). One formative study reported that men may be more likely to develop AMS,⁵⁵ but other reports suggest that women may be at a greater risk⁵⁶—or that there are no differences between the sexes.⁵³ Additional research to investigate potential sex differences in high altitude illness risk, while also exploring potential mechanisms, are needed.

Subterranean and Hypercapnic Environments

Environments with elevated levels of carbon dioxide, which can result in hypercapnia, are an environmental stressor that recently has gained interest in the military community, after relatively little research. In normal ambient air, the concentration of carbon dioxide (CO₂) is very low (~0.034%), but in certain situations such as subterranean environments (including underground tunnels and buildings),⁵⁷ or when individuals are wearing personal protective equipment,⁵⁸ CO₂ concentration can be as high as 7%.⁵⁹ Small increases in ambient CO₂ can cause symptoms such as decreased focus, fatigue, and weakness, as well as increased levels of anxiety, but higher concentrations (10-15%) can lead to unconsciousness and suffocation within minutes of exposure, with further increases resulting in death.⁶⁰

Similar to hypoxia, hypercapnia triggers a robust ventilatory response.^{61,62} Several investigations have sought to distinguish sex differences during ventilatory response to increased CO₂, known as hypercapnic ventilatory response (HCVR). Some investigations have reported a greater HCVR in men, but when corrected for body size—including body mass index, body surface area, and lung size—those differences no longer exist.^{63,64} While HCVR appears to be similar in both sexes, the ventilatory threshold for increase in ventilation is lower in women.⁶⁵

Previous studies have explored the influence of increased CO₂ on both physical⁵⁹ and cognitive performance,⁶⁶ but those studies included few women. Sex differences in physiological responses to increased CO₂ remains to be investigated.

Editorial Comment

With the increased proportional and absolute numbers of women in the U.S. military, it is vital to better understand female physiological responses to, and unique requirements for, environmental extremes. Continued research should seek to investigate these potential sex differences to ensure suitable policy recommendations for both women and men in uniform.

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Enhancing Military Women's Health and Readiness Through Targeted Research Initiatives

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Health and wellness are vital aspects of military mission readiness. The Congressionally Directed Medical Research Programs (CDMRP), a funding organization within the Defense Health Agency (DHA), supports research on over 90 different diseases, conditions, and topics that are directed by Congress. The CDMRP's vision is to transform health care through innovative and impactful research.

The CDMRP has implemented multiple initiatives to enhance women's health since its inception in 1992. Military women's health care needs and experiences differ from those of male service members, in addition to those of civilian women. Women who served in the military have a higher risk or incidence of some conditions compared to the civilian population, including breast cancer,¹ multiple sclerosis,² dementia,³ and eating disorders.⁴ Better prevention, diagnosis, and treatment ensure mission readiness not only as it relates to the service members' health, but for the health and well-being of their families as well.⁵

To achieve its vision, the CDMRP adheres to a mission of responsibly managing collaborative research that discovers, develops, and delivers health care solutions for service members, veterans, their families, and the American public. In fiscal years 2022-2023, the CDMRP funded approximately \$979.1 million in women's health research across many different conditions and topics that affect women exclusively, disproportionately, or differently (**Table**).

This editorial provides an overview of the CDMRP and its women's health research initiatives, including the directive on Inclusion of Women and Minorities as Subjects in Clinical Research and the directive on Sex as a Biological Variable in Research.

The editorial also describes efforts to prioritize women's health research and highlights examples of relevant CDMRP-funded studies to advance military women's health research.

CDMRP Women's Health Initiatives—Past to Present

Women's health is a foundational element of the CDMRP. The breast and ovarian cancer research programs established by the U.S. Congress in 1993 and 1997, respectively, provided funding that contributed to U.S. Food and Drug Administration (FDA)-approved drugs in addition to improved diagnostic approaches, prognostic tests, and changes in clinical practice. Those advancements continue to benefit service members and beneficiaries throughout the Military Health System (MHS).

Over the past 30 years, women's health research funded by the CDMRP has expanded to include Alzheimer's disease, autoimmune disorders (e.g., lupus, rheumatoid arthritis, scleroderma, celiac disease), cardiovascular disease, endometriosis, various cancers, sleep disorders, and chronic fatigue syndrome. Patients, survivors, and caregivers—including active duty service members and veterans—add critical perspectives and a sense of urgency within every aspect of the CDMRP's program cycle, serving as full voting members on both peer review panels as well as programmatic panels that contribute to funding decisions, program priorities, and investment strategies.

Consistent with *The Belmont Report*⁶ and Congressional legislation, inclusion

of women and minorities in clinical studies funded or supported by the CDMRP has been emphasized. Since 2009, the CDMRP's funding opportunity announcements have contained language encouraging the inclusion of women and minorities in clinical trials so the burdens and benefits of participating in clinical research may be applied to all affected populations. The CDMRP collaborated with partners at the National Institutes of Health (NIH) Office of Research on Women's Health, a leader in women's health research initiatives, to develop 2 important directives to ensure results from CDMRP-funded studies benefit both men and women from affected populations. These directives mirror policies already established by the NIH^{9,10} and incorporate their many years of lessons learned.

The first directive, in 2020, requires inclusion of women and minorities, as appropriate for a study's objectives, in all clinical research studies funded by the CDMRP, including clinical trials.⁷

In 2024, the CDMRP took its women's health initiatives a step further by implementing its directive requiring researchers to consider sex as a biological variable in their research designs and reporting, including pre-clinical studies with animal models.⁸ Failure to account for sex as a biological variable may undermine research rigor, transparency in participant population selection, and generalizability of research findings.

In fiscal year 2024 funding opportunities, the CDMRP began explicitly encouraging research on health areas and conditions that affect women uniquely, disproportionately, or differently from men. This research should relate anticipated findings to improvements in women's health

TABLE. CDMRP Investments in Women's Health Research, Fiscal Years 2022–2023

| Research Topic | Investment (millions) | Number of Awards |
|--|-----------------------|------------------|
| Breast cancer | \$264.8 | 159 |
| Neurological disorders | \$178.6 | 140 |
| Psychological health | \$106.9 | 49 |
| Gynecological cancers | \$103.3 | 128 |
| Other ^a | \$94.1 | 56 |
| Autoimmune disorders | \$67.1 | 73 |
| Other cancers | \$50.9 | 65 |
| Cardiovascular diseases | \$37.7 | 17 |
| Alzheimer's disease | \$26.3 | 23 |
| Pain | \$20.2 | 15 |
| Musculoskeletal disorders | \$13.7 | 11 |
| Sensory system disorders | \$8.8 | 10 |
| Gynecological and reproductive disorders | \$6.5 | 9 |
| Grand Total | \$979.1 | 755 |

^aIncludes diabetes, fragile X syndrome, Gulf war illness, neurofibromatosis, pancreatitis, Rett syndrome, toxic exposures, tuberous sclerosis complex.

outcomes or advancements in knowledge for women's health. Several programs have made targeted efforts to prioritize women's health as a focus area. The Peer Reviewed Orthopaedic Research Program, for example, offered a funding mechanism specifically to support research on orthopaedic injuries affecting women in combat roles.

Groundbreaking research is underway to advance military women's health throughout the many programs managed by the CDMRP. Three current CDMRP-funded studies advancing research for prevention and treatment of important conditions—breast cancer, pelvic pain, and post-traumatic stress disorder (PTSD)—with unique effects on military women are described in the following section.

CDMRP-funded Study Highlights

Breast Cancer Risk and Polycyclic Aromatic Hydrocarbons

Breast cancer is the most common non-skin cancer in women and the deadliest cancer in women under age 40 years,^{11,12} and its incidence rate in women aged 40–59 years is higher among active duty service members than in the general population. In 2020, the CDMRP's Breast Cancer

Research Program funded a research project totaling \$3.1 million to address the challenge of identifying determinants of breast cancer initiation, risk, and susceptibility among female active duty service members. Cumulative environmental exposures have been identified as a potential factor that may contribute to the difference in breast cancer rates among women of similar ages in military service and the civilian population.¹

Investigators Celia Byrne, PhD, at the Uniformed Services University of the Health Sciences, and Mary Beth Terry, PhD, at Columbia University Medical Center, are partnering in a case-control study utilizing the Department of Defense (DOD) Cancer Registry in addition to serum samples and data from the DOD's Armed Forces Health Surveillance Division (AFHSD). These investigators aim to quantify exposure to environmental contaminants called polycyclic aromatic hydrocarbons and evaluate breast cancer risk associated with exposures to such contaminants for female active duty service members. The study will also evaluate whether genetic variations affect susceptibility to environmental exposures.

If successful, findings from this study will identify specific exposures that contribute to breast cancer risk, leading to further understanding of the biological factors involved in breast cancer incidence.

Pelvic Pain Conservative Care in Female Service Members

Chronic pelvic pain, defined as persistent or recurrent pain perceived to be in and around the pelvis that lasts for at least 6 months that is not attributable to cancer,^{13,14} disproportionately affects female service members. The disproportionate occurrence of chronic pelvic pain in female service members may result from higher incidence of hip and pelvic injuries, inadequate urogenital hygiene in deployed environments, or sexual trauma.^{15,16}

The CDMRP's Peer Reviewed Orthopaedic Research Program funded a \$2.5 million research project in 2024 to assess clinical effectiveness and physiological efficacy of 3 physical therapy treatments for chronic pelvic pain in female service members. This clinical trial, led by Shane Koppes, PhD, at Baylor University, will randomly assign 300 women with chronic pelvic pain to 3 treatment groups. The study will test the hypothesis that field-expedient interventions are superior to usual care and not inferior to the highest or 'gold standard' of care. These interventions could enable injured female service members to remain on the battlefield or on mission without need for evacuation or medical discharge.

In addition to potential changes in clinical care guidelines, the study team aims to develop a clinical decision tool to predict subgroups of women with chronic pelvic pain who are most likely to benefit from emerging field-expedient care and differentiate those requiring 'gold standard' intravaginal specialist care.

Post-Traumatic Stress Disorder Prevention and Treatment with Microbiome-based Therapies

Women, service members, and veterans are more likely to develop PTSD than the general population, and there is an urgent need to identify more effective interventions.^{17,18} To address this need, in 2023 the CDMRP's Traumatic Brain Injury and Psychological Health Research Program awarded \$6.3 million to Brigham and Women's Hospital, for Yang-Yu Liu, PhD, to examine and target the relationship between PTSD and the gut microbiome, employing both human and animal studies.

Dr. Liu aims to develop a synbiotic therapeutic of prebiotics and probiotics to reduce PTSD symptoms. The study utilizes existing data and resources from the large, well-characterized cohort of women in the Nurses' Health Study II.¹⁹ This CDMRP-funded study's 4 research projects will 1) differentiate the gut microbiomes in women who have experienced PTSD, trauma, or resilience, 2) reveal causation between PTSD and gut microbiome using a novel computational method, 3) quantify the effect of trauma exposure on the gut microbiome and neuronal activity in mice, and 4) test the efficacy of microbiome-based therapeutics in reversing stress-induced behavioral alterations in mice.

If successful, this effort will provide foundational evidence for microbiome-targeted interventions for PTSD treatment for improved life quality and function among women and others affected by PTSD.

Editorial Comment

Many more CDMRP-funded women's health-related studies are complete or ongoing. Results from these funded studies will continue to advance the medical profession's understanding and ability to prevent, assess, and treat diseases and conditions that affect military women's readiness. Prioritizing research on the diseases and conditions that affect women uniquely, disproportionately, or differently, considering sex as a biological variable in all stages of research while ensuring appropriate representation of the diverse affected populations in clinical research, will accelerate medical solutions for all military women and enhance mission readiness. The CDMRP's ongoing commitment to women's health research will contribute to research advancements that will benefit not only service members, but their families, veterans, and the American public at large.

To learn more about the CDMRP's programs and funded studies, or receive funding opportunity notifications by email, visit <https://cdmrp.health.mil>. Women's health portfolio inquiries can be submitted to dha.detrick.cdmrp.mbx.public-affairs@health.mil.

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Surveillance Snapshot

Mid-Season Vaccine Effectiveness Estimates for Influenza: The Department of Defense Global Respiratory Pathogen Surveillance Program, 2024–2025 Season

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The Department of Defense Global Respiratory Pathogen Surveillance Program (DoDGRPSP) is an active sentinel respiratory surveillance program that resides at the Defense Centers for Public Health–Dayton (DCPH-D), located at Wright-Patterson Air Force Base. The DoDGRPSP assesses influenza vaccine effectiveness (VE) among Military Health System (MHS) beneficiaries at 118 sites worldwide.

This mid-season analysis includes respiratory specimens from MHS beneficiaries who sought outpatient medical care from November 24, 2024 through March 15, 2025 at a military hospital or clinic and met the influenza-like illness (ILI) case definition. DoDGRPSP methods, including ILI case definition, questionnaire submission, vaccination ascertainment, specimen collection, transportation, testing, and sequencing, have been previously described.¹

A test-negative, case-control study design was used to estimate influenza VE against symptomatic laboratory-confirmed influenza. Cases were defined as an ILI patient testing positive for any influenza virus (sub)type with control specimens that had tested negative for influenza. Vaccinated patients were those receiving the 2024–2025 influenza vaccine at least 14 days before symptom onset. Those vaccinated less than 14 days before specimen collection were excluded. VE methodology has previously been described.^{2,3}

Specimens were analyzed at Landstuhl Regional Medical Center, Incirlik AB, and DCPH-D by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) and/or viral culture (at DCPH-D only). VE analyses were conducted for influenza A (any subtype), influenza A(H1N1)pdm09, and A(H3N2) for all beneficiaries, adults as well as children. VE estimates were adjusted for confounding factors such as age group, month of illness, and geographic region. Service members, patients less than 6 months old, and individuals with unknown vaccination status were excluded from VE analysis. The analysis included 295 participants who tested positive for influenza and 965 controls who tested negative for influenza.

Adjusted VE estimates among all beneficiaries for influenza A (any subtypes), influenza A(H1N1)pdm09, and influenza A(H3N2) were 25% (95% confidence interval [CI] -1, 44), 58% (95% CI, 31, 74), and 42% (95% CI, 14, 62), respectively. Adjusted VE for children was 27% (95% CI, -5, 50), 69% (95% CI, 43, 83), and 36% (95% CI, -5, 61), while among adults it was 17% (95% CI, -35, 49), 37% (95% CI, -43, 72), and 52% (95% CI, 2, 76) for influenza A (any subtype), influenza A(H1N1)pdm09, and influenza A(H3N2), respectively. VE for influenza B was not calculated due to a small number of cases.

This study reports low to moderate VE, but not all estimates were significant. There was moderate effectiveness against influenza A(H1N1)pdm09 in all beneficiaries and children ages 6 months to 17 years. In adults (ages 18–64 years) and all beneficiaries there was moderate effectiveness against influenza A(H3N2). VE estimates against influenza A (any subtype) for all beneficiaries, children, and adults were non-significant and not effective among children for influenza A(H3N2) and in adults for influenza A(H1N1)pdm09.

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Disclaimer

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TABLE. Influenza Vaccine Effectiveness Against Symptomatic Laboratory-Confirmed Ambulatory Influenza, Military Health System Beneficiaries, 2024–2025 Season

| Type of Influenza | Population | Vaccinated | Cases | | Controls | | Crude VE (95% CI) | Adjusted VE ^a (95% CI) |
|-------------------|-------------------|------------|-------|------|----------|------|----------------------|--------------------------------------|
| | | | No. | % | No. | % | | |
| A (any subtype) | Adults | Yes | 56 | 61.5 | 217 | 64.2 | 11 (-44, 45) | 17 (-35, 49) |
| | | No | 35 | 38.5 | 121 | 35.8 | | |
| A (any subtype) | Children | Yes | 136 | 66.7 | 434 | 69.2 | 11 (-25, 36) | 27 (-5, 50) |
| | | No | 68 | 33.3 | 193 | 30.8 | | |
| A (any subtype) | All beneficiaries | Yes | 192 | 65.1 | 651 | 67.5 | 10 (-18, 32) | 25 (-1, 44) |
| | | No | 103 | 34.9 | 314 | 32.5 | | |
| A(H1N1)pdm09 | Adults | Yes | 14 | 53.8 | 217 | 64.2 | 35 (-45, 71) | 37 (-43, 72) |
| | | No | 12 | 46.2 | 121 | 35.8 | | |
| A(H1N1)pdm09 | Children | Yes | 21 | 45.7 | 434 | 69.2 | 63 (32, 80) | 69 (43, 83) |
| | | No | 25 | 54.3 | 193 | 30.8 | | |
| A(H1N1)pdm09 | All beneficiaries | Yes | 35 | 48.6 | 651 | 67.5 | 54 (26, 72) | 58 (31, 74) |
| | | No | 37 | 51.4 | 314 | 32.5 | | |
| A(H3N2) | Adults | Yes | 18 | 46.2 | 217 | 64.2 | 52 (7, 75) | 52 (2, 76) |
| | | No | 21 | 53.8 | 121 | 35.8 | | |
| A(H3N2) | Children | Yes | 51 | 55.4 | 434 | 69.2 | 45 (14, 65) | 36 (-5, 61) |
| | | No | 41 | 44.6 | 193 | 30.8 | | |
| A(H3N2) | All beneficiaries | Yes | 69 | 52.7 | 651 | 67.5 | 46 (22, 63) | 42 (14, 62) |
| | | No | 62 | 47.3 | 314 | 32.5 | | |

Abbreviations: CI, confidence interval; No., number; VE, vaccine effectiveness.

^aAdjusted for age group, geographic region and month of illness.

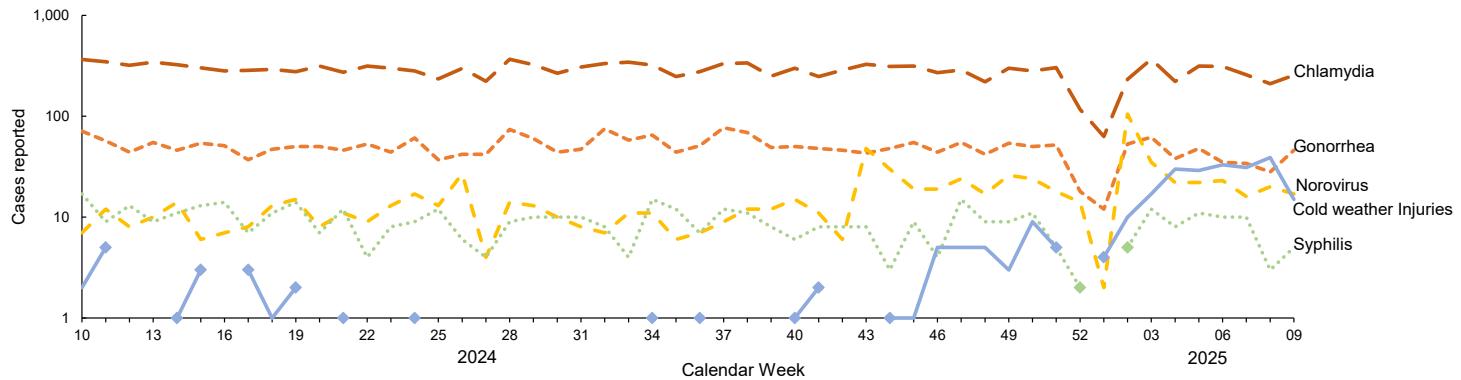
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Reportable Medical Events at Military Health System Facilities Through Week 9, Ending March 1, 2025

Idalia Aguirre, MPH; Matthew W.R. Allman, MPH; Anthony R. Marquez, MPH; Katherine S. Kotas, MPH

TOP 5 REPORTABLE MEDICAL EVENTS^a BY CALENDAR WEEK, ACTIVE COMPONENT (MARCH 9, 2024–MARCH 1, 2025)



Abbreviation: RMEs, reportable medical events.

^aCases are shown on a logarithmic scale.

Note: There were 0 reported cold weather injury cases during weeks 12–13, 16, 20, 22–23, 25–33, 35, 37–39, 42–43, 52. There were no syphilis cases reported during week 1 of 2025.

Reportable Medical Events (RMEs) are documented in the Disease Reporting System internet (DRSi) by health care providers and public health officials throughout the Military Health System (MHS) for monitoring, controlling, and preventing the occurrence and spread of diseases of public health interest or readiness importance. These reports are reviewed by each service's public health surveillance hub. The DRSi collects reports on over 70 different RMEs, including infectious and non-infectious conditions, outbreak reports, STI risk surveys, and tuberculosis contact investigation reports. A complete list of RMEs is available in the *2022 Armed Forces Reportable Medical Events Guidelines and Case Definitions*.¹ Data reported in these tables are considered provisional and do not represent conclusive evidence until case reports are fully validated.

Total active component cases reported per week are displayed for the top 5 RMEs for the previous year. Each month, the graph is updated with the top 5 RMEs, and is presented with the current month's (February 2025) top 5 RMEs, which may differ from previous months. COVID-19 is excluded from these graphs due to changes in reporting and case definition updates in 2023.

For questions about this report, please contact the Disease Epidemiology Branch at the Defense Centers for Public Health–Aberdeen. Email: dha.apg.pub-health-a.mbx.disease-epidemiologyprogram13@health.mil

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TABLE. Reportable Medical Events, Military Health System Facilities, February 2025^a

| Reportable Medical Event ^b | Active Component | | | | | MHS Beneficiaries ^d |
|---|------------------|--------------|----------|----------|------------|--------------------------------|
| | February 2025 | January 2025 | YTD 2025 | YTD 2024 | Total 2024 | February 2025 |
| | No. | No. | No. | No. | No. | No. |
| Amebiasis | 2 | 4 | 6 | 1 | 15 | 0 |
| Arboviral diseases, neuroinvasive and non-neuroinvasive | 0 | 0 | 0 | 0 | 3 | 0 |
| Brucellosis | 0 | 0 | 0 | 0 | 1 | 0 |
| COVID-19-associated hospitalization or death | 2 | 3 | 5 | 15 | 41 | 13 |
| Campylobacteriosis | 10 | 23 | 33 | 25 | 326 | 11 |
| Chikungunya virus disease | 0 | 0 | 0 | 0 | 1 | 0 |
| <i>Chlamydia trachomatis</i> | 1,042 | 1,185 | 2,227 | 2,842 | 15,637 | 127 |
| Cholera | 0 | 0 | 0 | 0 | 3 | 0 |
| Coccidioidomycosis | 2 | 0 | 2 | 17 | 53 | 2 |
| Cold weather injury ^e | 121 | 87 | 208 | 113 | 172 | N/A |
| Cryptosporidiosis | 3 | 8 | 11 | 19 | 82 | 0 |
| Cyclosporiasis | 0 | 0 | 0 | 0 | 11 | 0 |
| Dengue virus infection | 0 | 1 | 1 | 1 | 12 | 0 |
| <i>E. coli</i> , Shiga toxin-producing | 2 | 4 | 6 | 5 | 93 | 1 |
| Ehrlichiosis/anaplasmosis | 0 | 0 | 0 | 0 | 1 | 0 |
| Giardiasis | 5 | 9 | 14 | 17 | 98 | 4 |
| Gonorrhea | 142 | 211 | 353 | 535 | 2,768 | 21 |
| <i>Haemophilus influenzae</i> , invasive | 1 | 0 | 1 | 1 | 3 | 3 |
| Heat illness ^e | 13 | 6 | 19 | 24 | 1,277 | N/A |
| Hepatitis A | 0 | 0 | 0 | 1 | 7 | 0 |
| Hepatitis B, acute and chronic | 7 | 6 | 13 | 26 | 106 | 3 |
| Hepatitis C, acute and chronic | 3 | 0 | 3 | 9 | 29 | 6 |
| Influenza-associated hospitalization ^f | 14 | 19 | 33 | 27 | 54 | 73 |
| Lead poisoning, pediatric ^g | N/A | N/A | N/A | N/A | N/A | 5 |
| Legionellosis | 0 | 0 | 0 | 3 | 5 | 0 |
| Leprosy | 0 | 0 | 0 | 0 | 1 | 0 |
| Listeriosis | 0 | 1 | 1 | 0 | 0 | 0 |
| Lyme disease | 2 | 1 | 3 | 9 | 101 | 1 |
| Malaria | 0 | 0 | 0 | 2 | 21 | 0 |
| Meningococcal disease | 0 | 0 | 0 | 0 | 2 | 0 |
| Mpox | 0 | 1 | 1 | 2 | 14 | 0 |
| Mumps | 0 | 0 | 0 | 0 | 0 | 1 |
| Norovirus | 74 | 185 | 259 | 48 | 653 | 68 |
| Pertussis | 2 | 6 | 8 | 3 | 39 | 6 |
| Post-exposure prophylaxis against Rabies | 37 | 33 | 70 | 95 | 623 | 28 |
| Q fever | 0 | 0 | 0 | 0 | 3 | 0 |
| Rubella | 0 | 0 | 0 | 0 | 0 | 1 |
| Salmonellosis | 4 | 4 | 8 | 14 | 160 | 3 |
| Schistosomiasis | 0 | 0 | 0 | 0 | 1 | 0 |
| Shigellosis | 2 | 2 | 4 | 7 | 53 | 1 |
| Spotted fever rickettsiosis | 2 | 1 | 3 | 0 | 22 | 0 |
| Syphilis (all) ^h | 28 | 36 | 64 | 122 | 518 | 9 |
| Toxic shock syndrome | 0 | 0 | 0 | 1 | 2 | 0 |
| Trypanosomiasis | 0 | 1 | 1 | 1 | 5 | 0 |
| Tuberculosis | 0 | 0 | 0 | 1 | 7 | 0 |
| Tularemia | 0 | 0 | 0 | 1 | 1 | 0 |
| Typhoid fever | 0 | 0 | 0 | 0 | 1 | 0 |
| Typhus fever | 0 | 1 | 1 | 1 | 2 | 1 |
| Varicella | 1 | 1 | 2 | 4 | 18 | 6 |
| Zika virus infection | 0 | 0 | 0 | 1 | 1 | 0 |
| Total case counts | 1,521 | 1,839 | 3,360 | 3,993 | 23,046 | 394 |

Abbreviations: MHS, Military Health System; YTD, year-to-date; no., number; *E.*, *Escherichia*; N/A, not applicable.

^aRMEs submitted to DRSI as of Mar. 24, 2025. RMEs were classified by date of diagnosis or, where unavailable, date of onset. Monthly comparisons are displayed for the period of Jan. 1, 2025–Jan. 31, 2025 and Feb. 1, 2025–Feb. 28, 2025. YTD comparison is displayed for the period of Jan. 1, 2025–Feb. 28, 2025 for MHS facilities. Previous year counts are provided as the following: previous YTD, Jan. 1, 2024–Feb. 29, 2024; total 2024, Jan. 1, 2024–Dec. 31, 2024.

^bRME categories with 0 reported cases among active component service members and MHS beneficiaries for the time periods covered were not included in this report.

^cServices included in this report include the Army, Navy, Air Force, Marine Corps, Coast Guard, and Space Force, including personnel classified as Active Duty, Cadet, Midshipman, or Recruit in DRSI.

^dBeneficiaries include: individuals classified as Retired and Family Members (including Spouse, Child, Other, Unknown). National Guard, Reservists, civilians, contractors, and foreign nationals were excluded from these counts.

^eOnly reportable for service members.

^fInfluenza-associated hospitalization is reportable only for individuals under age 65 years.

^gPediatric lead poisoning is reportable only for children aged 6 years or younger.

^hThe observed drop in syphilis cases from 2024 to 2025 may be due, in part, to an updated case validation process that began Jan. 2024.





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