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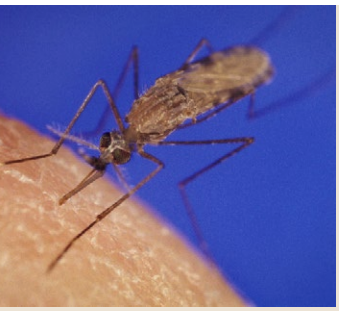

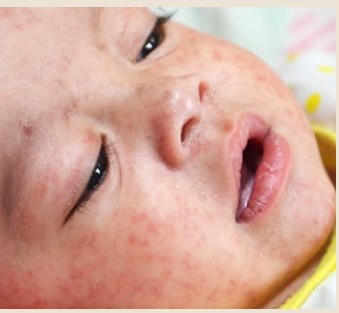

Update: Malaria, U.S. Armed Forces, 2019

Malaria infection remains an important health threat to U.S. service members who are located in endemic areas because of long-term duty assignments, participation in shorter-term contingency operations, or personal travel. In 2019, a total of 35 service members were diagnosed with or reported to have malaria. This represents a 40.7% decrease from the 59 cases identified in 2018. The relatively low numbers of cases during 2012–2019 mainly reflect decreases in cases acquired in Afghanistan, a reduction due largely to the progressive withdrawal of U.S. forces from that country. Although the number of cases of malaria caused by *Plasmodium falciparum* decreased in 2019, the percentage of such cases (54.3%) was the highest during any given year of the 2010–2019 surveillance period. Eleven cases of malaria were attributed to an unspecified/other source (31.4%). The number of malaria cases caused by *P. vivax* (n=5) was one of the lowest observed during the 10-year surveillance period, and the percentage (14.3%) of such cases remained one of the lowest. Malaria was diagnosed at or reported from 17 different medical facilities in the U.S., Germany, Afghanistan, and Korea. Providers of medical care to military members should be knowledgeable of and vigilant for clinical manifestations of malaria outside of endemic areas.

WHAT ARE THE NEW FINDINGS?

The 2019 total of 35 malaria cases among active and reserve component service members was tied with the 2017 total for the lowest annual counts of cases during the past 10 years. The 2019 proportion of cases (54.3%) due to *P. falciparum* was the highest of the 10-year period.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

The decrease in total counts of malaria cases during the last decade and the increased proportion of cases due to *P. falciparum* both reflect the reduced numbers of service members exposed to malaria (especially *P. vivax*) in Afghanistan. The persistent threat from *P. falciparum* associated with duty in Africa underscores the importance of preventive measures effective against this most dangerous strain of malaria.

Globally, the incidence rate of malaria is estimated to have decreased by 19.7% between 2010 and 2018, from 71 to 57 cases per 1,000 population at risk between 2010 and 2018.[1] However, for the third consecutive year, the World Health Organization reported a relative plateauing in the numbers of cases and rates of malaria: in 2018, there were an estimated 228 million cases of malaria compared to 231 million in 2017 and 227 million in 2016; the incidence rate had decreased to 57 per 1,000 population at risk in 2014 but remained steady through 2018.[1] During the 6 years prior, the number of people contracting malaria globally had been steadily decreasing, from 251 million in 2010 to 219 million in 2015.[1]

Countries in Africa accounted for around 93% of worldwide malaria cases and 94% of all malaria-related deaths in 2018.[1] The majority of these cases and deaths were due to mosquito-transmitted *Plasmodium falciparum* and occurred in sub-Saharan Africa among children under 5 years of age, but *P. vivax, P. ovale*, and *P. malariae* can also cause severe disease.[1,2] Globally, 3.3% of estimated malaria cases are due to *P. vivax*; however, 85% of vivax malaria cases occurred in 6 countries including India, Afghanistan, Pakistan, Ethiopia, Papua New Guinea, and Indonesia.[1]

The *MSMR* has published annual updates on the incidence of malaria among U.S. service members since 2001 (the first 6 updates were limited to Army members).[3] The *MSMR*'s focus on malaria reflects both historical lessons learned about this mosquito-borne disease and the continuing threat that it poses to military operations and service members' health. Malaria infected many thousands of service members during World War II (approximately 695,000 cases), the Korean War (approximately 390,000 cases), and the conflict in Vietnam (approximately 50,000 cases).[4,5] More recent military engagements in Africa, Asia, Southwest Asia, the Caribbean, and the Middle East have necessitated heightened vigilance, preventive measures, and treatment of cases.[6–15]

In the planning for overseas military operations, the geography-based presence or absence of the malaria threat is usually known and can be anticipated. However, when preventive countermeasures are needed, their effective implementation is multifaceted and depends on the provision of protective equipment and supplies, individuals' understanding of the threat and attention to personal protective measures, treatment of malaria cases, and medical surveillance. The U.S. Armed Forces have long had policies and prescribed countermeasures effective against vector-borne diseases such as malaria, including chemoprophylactic drugs, permethrin-impregnated uniforms and bed nets, and topical insect repellents containing N,N-diethyl-meta-toluamide (DEET). When cases and outbreaks of malaria have occurred, they generally have been due to poor adherence to chemoprophylaxis and other personal preventive measures.[7–10]

MSMR malaria updates from the past 7 years documented that the annual case counts among service members after 2011 were the lowest in more than a decade.[16] In particular, these updates showed that the numbers of cases associated with service in Afghanistan had decreased substantially in the past 7 years, presumably because of the dramatic reduction in the numbers of service members assigned there.[17] This update for 2019 uses methods similar to those employed in previous analyses to describe the epidemiologic patterns of malaria incidence among service members in the active and reserve components of the U.S. Armed Forces.

METHODS

The surveillance period was 1 January 2010 through 31 December 2019. The surveillance population included Army, Navy, Air Force, and Marine Corps active and reserve component members of the U.S. Armed Forces. The records of the Defense Medical Surveillance System (DMSS) were searched to identify reportable medical events and hospitalizations (in military and non-military facilities) that included diagnoses of malaria. A case of malaria was defined as an individual with 1) a reportable medical event record of confirmed malaria; 2) a hospitalization record with a primary diagnosis of malaria; 3) a hospitalization record with a nonprimary diagnosis of malaria due to a specific *Plasmodium* species; 4) a hospitalization record with a nonprimary diagnosis of malaria plus a diagnosis of anemia, thrombocytopenia and related conditions, or malaria complicating pregnancy in any diagnostic position; 5) a hospitalization record with a nonprimary diagnosis of malaria plus diagnoses of signs or symptoms consistent with malaria (as listed in the *Control of Communicable Diseases Manual*, *18th edition*[18]) in each diagnostic position antecedent to malaria; or 6) a positive malaria antigen test plus an outpatient record with a diagnosis of malaria in any diagnostic position within 30 days of the specimen collection date. The relevant International Classification of Diseases, 9th and 10th Revision (ICD-9 and ICD-10, respectively) codes are shown in **Table 1**. Laboratory data for malaria were provided by the Navy and Marine Corps Public Health Center.

This analysis allowed 1 episode of malaria per service member per 365-day period. When multiple records documented a single episode, the date of the earliest encounter was considered the date of clinical onset and the most specific diagnosis recorded within 30 days of the incident diagnosis was used to classify the *Plasmodium* species.

Presumed locations of malaria acquisition were estimated using a hierarchical algorithm: 1) cases diagnosed in a malarious country were considered acquired in that country, 2) reportable medical events that listed exposures to malaria endemic locations were considered acquired in those locations, 3) reportable medical events that did not list exposures to malaria endemic locations but were reported from installations in malaria endemic locations were considered acquired in those locations, 4) cases diagnosed among service members during or within 30 days of deployment or assignment to a malarious country were considered acquired in that country, and 5) cases diagnosed among service members who had been deployed or assigned to a malarious country within 2 years before diagnosis were considered acquired in those respective countries. All remaining cases were considered acquired in unknown locations.

RESULTS

In 2019, a total of 35 service members were diagnosed with or reported to have malaria **(Table 2)**. That total was one of the lowest number of cases in any given year during the surveillance period and represents a 40.7% decrease from the 59 cases identified in 2018 **(Figure 1)**. The percentage of 2019 cases of malaria caused by *P. falciparum* (54.3%) was the highest during any given year of the surveillance period. The highest previous annual percentage

TABLE 1. ICD-9 and ICD-10 diagnosis codes used in defining cases of malaria from the records for inpatient encounters (hospitalizations)

	ICD-9	ICD-10
Malaria (*Plasmodium* species)		
P. falciparum	84.0	B50
P. vivax	84.1	B51
P. malariae	84.2	B52
P. ovale	84.3	B53.0
Unspecified	84.4, 84.5, 84.6, 84.8, 84.9	B53.1, B53.8, B54
Anemia	280–285	D50–D53, D55–D64
Thrombocytopenia	287	D69
Malaria complicating pregnancy	647.4	O98.6
Signs, symptoms, or other abnormalities consistent with malaria	276.2, 518.82, 584.9, 723.1, 724.2, 780.0, 780.01, 780.02, 780.03, 780.09, 780.1, 780.3, 780.31, 780.32, 780.33, 780.39, 780.6, 780.60, 780.61, 780.64, 780.65, 780.7, 780.71, 780.72, 780.79, 780.97, 782.4, 784.0, 786.05, 786.09, 786.2, 786.52, 786.59, 787.0, 787.01, 787.02, 787.03, 787.04, 789.2, 790.4	E87.2, J80, M54.2, M54.5, N17.9, R05, R06.0, R06.89, R07.1, R07.81, R07.82, R07.89, R11, R11.0, R11.1, R11.2, R16.1, R17, R40, R41.0, R41.82, R44, R50, R51, G44.1, R53, R56, R68.0, R68.83, R74.0

ICD, International Classification of Diseases.

TABLE 2. Malaria cases by *Plasmodium* species and selected demographic characteristics, U.S. Armed Forces, 2019

	P. vivax	*P. falciparum*	Unspecified/ other	Total	
	No.	No.	No.	No.	%
Component					
Active	5	15	10	30	85.7
Reserve/Guard	0	4	1	5	14.3
Service					
Army	5	14	10	29	82.9
Navy	0	1	0	1	2.9
Air Force	0	4	1	5	14.3
Marine Corps	0	0	0	0	0.0
Sex					
Male	5	17	11	33	94.3
Female	0	2	0	2	5.7
Age group (years)					
<20	0	0	0	0	0.0
20–24	1	3	4	8	22.9
25–29	4	3	4	11	31.4
30–34	0	7	1	8	22.9
35–39	0	4	2	6	17.1
40–44	0	1	0	1	2.9
45+	0	1	0	1	2.9
Race/ethnicity group					
Non-Hispanic white	5	6	8	19	54.3
Non-Hispanic black	0	10	1	11	31.4
Other	0	3	2	5	14.3
Total	5	19	11	35	100.0

No., number.

of *P. falciparum* was 46.8% in 2014. Of the 16 cases in 2019 not attributed to *P. falciparum*, 5 (14.3%) were identified as due to *P. vivax* and 11 (31.4%) were labeled as associated with other/unspecified types of malaria. The number of malaria cases caused by *P. vivax* in 2019 was one of the lowest observed during the 10-year surveillance period; the percentage of such cases remained one of the lowest. There was 1 case identified as having been caused by either *P. malariae* or *P. ovale* in 2019 **(Figure 1)**.

Similar to 2018, the majority of U.S. military members diagnosed with malaria in 2019 were male (94.3%), active component members (85.7%), in the Army (82.9%), and in their 20s (54.3%) **(Table 2)**.

Of the 35 malaria cases in 2019, slightly less than two-fifths of the infections were considered to have been acquired in Africa (37.1%; n=13); about one-third (31.4%; n=11) were attributed to Afghanistan; and about one-fourth (25.7%; n=9) could not be associated with a known, specific location. The remaining cases were attributed to Korea (5.7%; n=2); no cases were considered to have been acquired in South/Central America **(Figure 2)**. Of the 13 malaria infections considered acquired in Africa in 2019, 4 were linked to Cameroon; 3 to Togo; 2 to Kenya; and 1 each to Djibouti, Liberia, Niger, and Nigeria **(data not shown)**.

During 2019, malaria cases were diagnosed or reported from 17 different medical facilities in the U.S., Germany, Afghanistan, and Korea **(Table 3)**. Almost one-third (31.4%; 11/35) of the total cases with a known location of diagnosis were reported from or diagnosed outside the U.S., which represents a slight increase from the 25.4% of malaria cases in this category in 2018. The largest number of malaria cases associated with a single medical facility during 2019 was 8 at the Evans Army Community Hospital in Fort Carson, CO.

In 2019, the percentage of malaria cases that were acquired in Africa (37.4%; n=13) increased from 2018 (25.4%) but was similar to the percentages in 2016 and 2017 **(Figure 2)**. The percentage of Afghanistan-acquired cases (31.4%; n=11) in 2019 was similar to the percentage in 2018, which was the highest that it had been since 2013. The percentage of malaria cases acquired in Korea (5.7%; n=2) in 2019 was the lowest it had been since 2013 **(Figure 2)**.

Between 2010 and 2019, the majority of malaria cases were diagnosed or reported during the 6 months from the middle of spring through the middle of autumn in the Northern Hemisphere **(Figure 3)**. In 2019, 77.1% (27/35) of malaria cases among U.S. service members were diagnosed during May–October **(data not shown)**. This proportion is similar to the 72.0% (432/600) of cases diagnosed during the same 6-month intervals over the entire 10-year surveillance period. During 2010–2019, the proportions of malaria cases diagnosed or reported during May–October varied by region of acquisition: Korea (91.9%; 57/62); Afghanistan (81.0%; 201/248); Africa (59.8%; 104/174); and South/Central America (50.0%; 3/6) **(data not shown)**.

EDITORIAL COMMENT

MSMR annual reports on malaria incidence among all U.S. services began in 2007. The current report documents that the number of cases during 2019 decreased from 2018 and was one of the lowest of any of the previous years in the 2010–2019 surveillance period. The same number of malaria cases (n=35) was reported in 2017. Most of the marked decline in the past 8 years is attributable to the decrease in

FIGURE 1. Numbers of malaria cases, by *Plasmodium* species and calendar year of diagnosis or report, active and reserve components, U.S. Armed Forces, 2010–2019

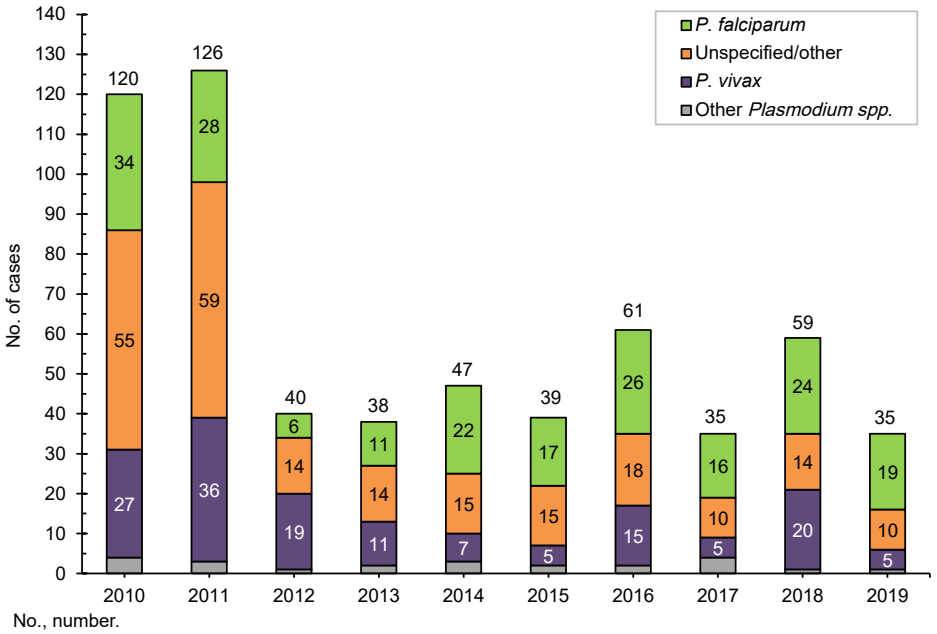

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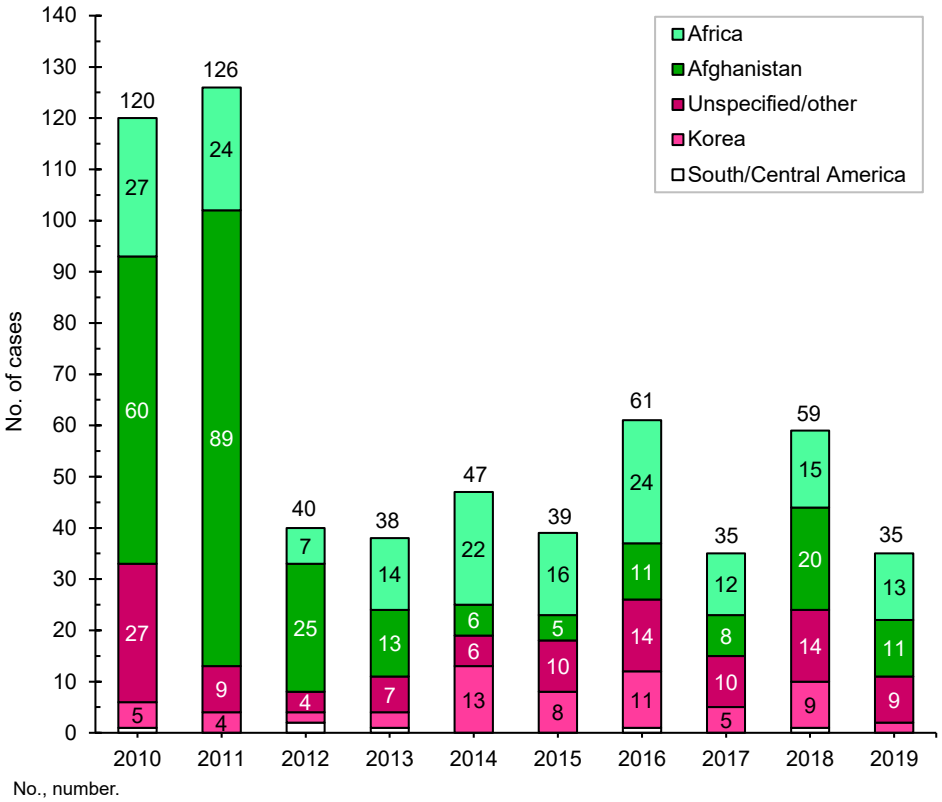
FIGURE 2. Annual numbers of malaria cases, by location of acquisition, U.S. Armed Forces, 2010–2019



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numbers of malaria cases associated with service in Afghanistan. The dominant factor in that trend has undoubtedly been the progressive withdrawal of U.S. forces from that country.

This report also documents the fluctuating incidence of acquisition of malaria in Africa and Korea among U.S. military members during the past decade. Although the predominant species of malaria in Korea and Afghanistan has been *P. vivax*, the more dangerous *P. falciparum* species is of primary concern in Africa. This report documents that the 2019 percentage of cases caused by *P. falciparum* was the highest of any year of the surveillance period. The planning and execution of military operations on that continent must incorporate actions to counter the threat of infection by that potentially deadly parasite wherever it is endemic. The 2014–2015 employment of U.S. service members to aid in the response to the Ebola virus outbreak in West Africa is an example of an operation where the risk of *P. falciparum* malaria was significant.[15,19] The finding that *P. falciparum* malaria was diagnosed in more than one-half of the cases in 2019 further underscores the need for continued emphasis on prevention of this disease, given its potential severity and risk of death. Moreover, a recent article noted the possibility of false negative results for *P. falciparum* on the rapid diagnostic tests favored by units in resource limited or austere locations.[20] Although more research is needed, commanders and unit leaders may need to be especially vigilant with forces that are far forward.

The observations about the seasonality of diagnoses of malaria are compatible with the presumption that the risk of acquiring and developing symptoms of malaria in a temperate climatic zone of the Northern Hemisphere would be greatest during May–October. Given the typical incubation periods of malaria infection (approximately 9–14 days for *P. falciparum*, 12–18 days for *P. vivax* and *P. ovale*, and 18–40 days for *P. malariae*)[18] and the seasonal disappearance of biting mosquitoes during the winter, most malaria acquired in Korea and Afghanistan would be expected to cause symptoms during the warmer months of the year. However, it should be noted that studies of *P. vivax* malaria in Korea have found that the time between primary infection and clinical illness among different *P. vivax* strains ranges between 8 days and 8–13 months and that as many as 40–50% of infected individuals may not manifest the symptoms of their primary illness until 6–11 months after infection.[21,22] Klein and colleagues recently reported a cluster of 11 U.S. soldiers with *P. vivax* malaria

TABLE 3. Number of malaria cases, by geographical locations of diagnosis or report and presumed location of acquisition, active and reserve components, U.S. Armed Forces, 2019

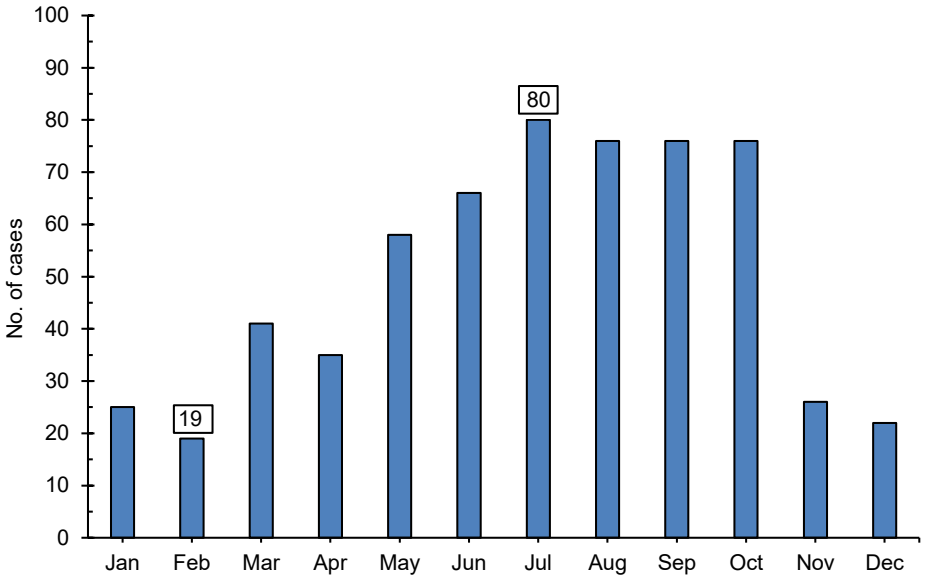
	Location of acquisition					Total	
	Korea	Afghanistan	Africa	South/ Central America	Other/ unknown location		
	No.	No.	No.	No.	No.	No.	%
Location where diagnosed or reported from							
Evans ACH, Fort Carson, CO	0	7	1	0	0	8	22.9
Landstuhl RMC, Germany	0	1	3	0	3	7	20.0
Womack AMC, Fort Bragg, NC	0	1	2	0	0	3	8.6
Tripler AMC, Honolulu, HI	1	0	0	0	1	2	5.7
Walter Reed NMMC, Bethesda, MD	0	0	1	0	1	2	5.7
455th Air Expeditionary Wing, Bagram AFB, Afghanistan	0	2	0	0	0	2	5.7
6th Medical Group, MacDill AFB, Tampa, FL	0	0	1	0	0	1	2.9
Eisenhower AMC, Fort Gordon, GA	0	0	1	0	0	1	2.9
Winn ACH, Fort Stewart, GA	0	0	0	0	1	1	2.9
23rd Medical Group, Moody AFB, GA	0	0	1	0	0	1	2.9
Blanchfield ACH, Fort Campbell, KY	0	0	1	0	0	1	2.9
General Leonard Wood ACH, Fort Leonard Wood, MO	0	0	0	0	1	1	2.9
Moncrief AHC, Fort Jackson, SC	0	0	0	0	1	1	2.9
NMC, Portsmouth, VA	0	0	1	0	0	1	2.9
17th Medical Group, Goodfellow AFB, TX	0	0	0	0	1	1	2.9
Ansbach AHC, Ansbach, Germany	0	0	1	0	0	1	2.9
Camp Casey, Tongduchon, Korea	1	0	0	0	0	1	2.9

No., number; ACH, Army Community Hospital; RMC, Regional Medical Center; AMC, Army Medical Center; NMMC, National Military Medical Center; AFB, Air Force Base; AHC, Army Health Clinic; NMC, Naval Medical Center.

who were likely infected at a training area located near the southern border of the demilitarized zone in 2015.[23] Nine of the malaria cases developed their first symptoms of infection 9 or more months after exposure and after their departure from Korea.[23] Transmission of malaria in tropical regions such as sub-Saharan Africa is less subject to the limitations of the seasons as in temperate climates but depends more on other factors affecting mosquito breeding, such as the timing of the rainy season and altitude (below 2,000 meters).[24]

There are significant limitations to this report that should be considered when interpreting the findings. For example, the ascertainment of malaria cases is likely incomplete; some cases treated in deployed or non-U.S. military medical facilities may not have been reported or otherwise ascertained at the time of this analysis.

FIGURE 3. Cumulative numbers of diagnoses and reported cases of malaria, by month of clinical presentation or diagnosis, U.S. Armed Forces, January 2010–December 2019



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Furthermore, it should be noted that the medical records of the DMSS do not contain medical data from military treatment facilities that are using the new electronic health records of MHS GENESIS, which was implemented at different sites throughout 2017. These sites include Naval Hospital Oak Harbor, Naval Hospital Bremerton, Air Force Medical Services Fairchild, and Madigan Army Medical Center. Therefore, the medical encounter data for individuals seeking care at any of these facilities were not captured in this analysis.

Diagnoses of malaria that were documented only in outpatient settings without records of a positive malaria antigen test and that were not reported as notifiable events were not included as cases. Also, the locations of infection acquisitions were estimated from reported relevant information. Some cases had reported exposures in multiple malarious areas, and others had no relevant exposure information. Personal travel to or military activities in malaria-endemic countries were not accounted for unless specified in notifiable event reports.

As in prior years, in 2019 most malaria cases among U.S. military members were treated at medical facilities remote from malaria endemic areas. Providers of acute medical care to service members (in both garrison and deployed settings) should be knowledgeable of and vigilant for the early clinical manifestations of malaria among service members who are or were recently in malaria-endemic areas. Care providers should also be capable of diagnosing malaria (or have access to a clinical laboratory that is proficient in malaria diagnosis) and initiating treatment (particularly when *P. falciparum* malaria is clinically suspected).

Continued emphasis on adherence to standard malaria prevention protocols is warranted for all military members at risk of malaria. Personal protective measures against malaria include the proper wear of permethrin-treated uniforms and the use of permethrin-treated bed nets; the topical use of military-issued, DEET-containing insect repellent; and compliance with prescribed chemoprophylactic drugs before, during, and after times of exposure in malarious areas. Current Department of Defense guidance about medications for prophylaxis of malaria summarizes the roles of chloroquine, atovaquone-proguanil, doxycycline, mefloquine, primaquine, and tafenoquine.[25,26]

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Diabetes Mellitus and Gestational Diabetes, Active and Reserve Component Service Members and Dependents, 2008–2018

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During 2008–2018, a total of 12,582 active component service members received incident diagnoses of any diabetes mellitus (DM), for a crude overall incidence rate of 84.8 per 100,000 person-years. More than four-fifths of incident cases were type 2 DM. The overall rates of this form of DM among Asian/Pacific Islander and non-Hispanic black active and reserve component service members were 1.5 or more times the rates among their respective counterparts in other race/ethnicity groups. Crude annual rates of type 2 DM diagnoses among active and reserve component members peaked in 2010 and then decreased to their lowest points in 2018. From 2010 through 2018, decreases in rates of incident type 2 DM diagnoses were observed among active and reserve component members in all subgroups examined (sex, age, race/ethnicity, service), with the greatest slopes of decline seen among service members aged 40 years or older, Asian/Pacific Islanders, and Army members. During 2008–2018, total counts of incident diagnoses of type 2 DM among Military Health System (MHS) dependents decreased by 66.0%, from 29,625 to 10,066. The overall crude prevalence of gestational DM ranged from 7.3% among active component service women to 8.4% among female MHS dependents. Comparisons to data from U.S. civilian populations are made when appropriate.

WHAT ARE THE NEW FINDINGS?

During the 11-year surveillance period, annual incidence rates of type 2 DM decreased steadily among service members in the active component (57.7% decline) and reserve component (56.9%) and among MHS dependents (66.0%). Crude annual prevalence rates of gestational DM approximately doubled among women in the active and reserve component and among female MHS dependents.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Although the incidence rates of DM have been decreasing among service members and dependents, DM presents barriers to the ability of service members to fully participate in military operations, especially those involving deployment. Efforts to sustain the health of the force should include continued surveillance of DM incidence, ongoing research and preventive measures to reduce comorbidities and risk factors, and modification of lifestyle choices and habits to reduce the risk of developing DM.

Diabetes mellitus (DM) is a group of chronic metabolic conditions characterized by high blood glucose levels (hyperglycemia) resulting from a decreased ability to produce and/or use insulin. Over the long term, high blood glucose levels and other DM-related metabolic abnormalities are associated with complications including heart disease, vision loss, and kidney damage.[1] The total cost of diagnosed diabetes (types 1 and 2) in the U.S. in 2017 was estimated at $327 billion, including $237 billion in direct costs and $90 billion in reduced productivity.[2] Comorbidities accounted for a large portion of the medical costs associated with diabetes.[2]

Type 1 DM is generally first diagnosed in children and young adults and is characterized by a severe impairment of insulin production due to autoimmune destruction of pancreatic ß-cells, leading to absolute insulin deficiency.[1] Usually diagnosed later in life, type 2 DM is the more common form, accounting for over 90% of all diagnosed adult cases.[1] Type 2 DM develops when there is a diminished response to the action of insulin (insulin resistance) in muscle, liver, and fat cells; as a result, the pancreas produces more insulin to help glucose enter cells.[1] Over time, ß-cell insulin secretion is insufficient to compensate for insulin resistance and blood glucose levels rise.[3] Obesity; older age; family history of type 2 DM (first-degree relative); being of Asian or Pacific Islander, non-Hispanic black, Hispanic, or American Indian descent; hypertension or dyslipidemia; and a sedentary lifestyle are key risk factors for type 2 DM.[1,3,4] Recent analyses of data from the National Health Interview Survey (NHIS) indicated that annual age-adjusted incidence rates of diagnosed DM among adults aged 18 years or older in the U.S. civilian population decreased significantly, from 7.8 per 1,000 persons in 2009 to 6.0 per 1,000 persons in 2017.[5] This decline in the rate of incident cases of diagnosed DM came after decades of increases and appears to be driven primarily by a decrease among non-Hispanic whites.[5]

Gestational diabetes mellitus (GDM) is generally defined as glucose intolerance with onset or first recognition during pregnancy.[6] GDM develops during pregnancy in women whose pancreatic function is insufficient to overcome the insulin resistance secondary to increased release of placental lactogen and other hormones

(e.g., growth hormone, estrogen, progesterone, prolactin).[7] Women with GDM are at considerably increased risk for pregnancy and delivery complications, including fetal macrosomia, preeclampsia, neonatal hypoglycemia, and cesarean delivery.[6,8] Major risk factors for GDM include history of GDM, older maternal age, overweight and obesity, family history of DM (first-degree relative), polycystic ovary syndrome, non-white race, hypertension, and hyperlipidemia.[1,6,9,10]

GDM is estimated to affect 1–14% of pregnancies each year in the U.S., depending on the characteristics of the population studied, diagnostic criteria used, and the method of case ascertainment employed.[11–14] In the U.S., the prevalence of GDM varies among race/ethnicity groups, generally corresponding to the prevalence of type 2 DM, with higher rates among non-Hispanic black, Hispanic, American Indian, Pacific Islander, and Asian (South or East Asian) women compared to non-Hispanic white women.[15] Prevalence of GDM in the U.S. has been increasing over time, possibly because of increasing maternal overweight and obesity during pregnancy and older age at child bearing.[13,15–17] Women who are affected by GDM have more than a 7-fold increased risk of developing type 2 DM later in life compared to those who have a pregnancy without GDM.[18] Up to half of all women with GDM progress to develop type 2 DM, with the highest occurrence rate in the first 5 years after pregnancy.[18–22]

DM of any type is a disqualifying condition for entry into U.S. military service, and the U.S. Armed Forces require service members to meet physical fitness and anthropometric standards.[23,24] However, despite adherence to physical fitness standards, service members remain at risk of developing DM. A 2017 *MSMR* analysis of administrative data from the Military Health System (MHS) estimated that during 2008–2015, an annual average of 1,135 active component service members received incident clinical diagnoses of DM.[25] The current analysis updates and expands on this earlier work by describing the incidence of DM diagnoses and the prevalence of GDM diagnoses among active and reserve component service members and MHS dependents (i.e., family members) during 2008–2018. In addition, estimates of the percentage of women who progressed from GDM to type 2 DM and the percentage of women who progressed from type 2 DM to GDM are reported.

METHODS

The surveillance period was 1 January 2008 to 31 December 2018. The surveillance population included all active and reserve component service members in the U.S. Army, Navy, Air Force, and Marine Corps, as well as family member dependents. Diagnoses of DM and GDM were ascertained from records maintained in the Defense Medical Surveillance System (DMSS) that document inpatient and outpatient encounters of service members and non-service member beneficiaries. Such records reflect care in fixed military treatment facilities of the MHS and in civilian sources of health care underwritten by the Department of Defense (DoD).

A case of DM was defined by having a record of 2 or more inpatient or outpatient medical encounters occurring within 90 days of each other, with any of the defining diagnoses of type 1 or type 2 DM in the first diagnostic position **(Table 1)**. Individuals were classified as type 1 or 2 cases based on the diagnoses reported in the 2 case-defining encounters. If both type 1 and type 2 DM diagnoses were reported during an individual's 2 case-defining medical encounters, the individual was classified as having an "unspecified" type of DM. For women, inpatient medical encounters with a DM diagnosis were excluded if there was also a diagnosis for labor and delivery (International Classification of Diseases [ICD]-9: 650.*–669.*, V27.*; ICD-10: O60.*–O77.*, O80.*–O82.*, Z37.*) in any diagnostic position within 6 months after the encounter. DM encounters with an additional diagnosis of "diabetes mellitus complicating pregnancy childbirth or the puerperium" (ICD-9: 648.0*; ICD-10: O24.4*, O24.91*, O24.92, O24.93) in any diagnostic position were also excluded. These encounters were excluded because of the assumption that the diagnosis was truly for GDM.

The incidence date for DM was the date of the first inpatient or outpatient encounter that included a diagnosis of DM. For the incidence analysis, an individual was considered an incident case only once per lifetime. Prevalent cases (i.e., cases occurring before the start of the surveillance period) were excluded, and active component person-time was censored at the time of the incident case diagnosis. For the reserve component, service members were counted in the denominator for each year that they did not have an incident DM diagnosis in any previous year.

For active component service members, incidence rates of DM were calculated per 100,000 person-years (p-yrs). For reserve component service members, incidence rates of DM were calculated per 100,000 persons because p-yrs for activated service time were not available. For dependents, only counts of incident cases of DM were described since the DMSS does not contain denominator data for non-service member beneficiaries.

For the prevalence analysis, prevalent cases were defined as individuals who 1) met criteria for becoming an incident case of DM, including cases before 2008, and 2) had a DM diagnosis in the first diagnostic position for any type of DM in an inpatient or outpatient encounter during the given calendar year. For service members, prevalence was calculated as the number of prevalent cases divided by the total number of service members who served during the specified calendar year. Because the DMSS does not contain denominator data for non-service members, only the number of prevalent cases among dependents was ascertained.

A woman was considered a case of GDM if she had an inpatient encounter with a live birth diagnosis (ICD-9: V27.* [excluding V27.1, V27.4, V27.7]; ICD-10: Z37.* [excluding Z37.1, Z37.4, Z37.7]) in any diagnostic position plus at least 1 of the following between 280 days before and 7 days after the delivery event: 1) an inpatient or outpatient encounter with a GDM diagnosis (ICD-9: 648.0*; ICD-10: O24.4*, O24.91*, O24.92, O24.93) in any diagnostic position, 2) an inpatient encounter with a diagnosis for abnormal glucose tolerance (ICD-9: 648.8*; ICD-10: O99.81*) in any

TABLE 1. ICD-9 and ICD-10 diagnostic codes used for identification of DM cases

ICD-9[a]	ICD-10[a]
250.00–250.03 Diabetes mellitus without mention of complication	E10* Type 1 diabetes mellitus
250.10–250.13 Diabetes with ketoacidosis	E11* Type 2 diabetes mellitus
250.20–250.23 Diabetes with hyperosmolarity	
250.30–250.33 Diabetes with other coma	
250.40–250.43 Diabetes with renal manifestations	
250.50–250.53 Diabetes with ophthalmic manifestations	
250.60–250.63 Diabetes with neurological manifestations	
250.70–250.73 Diabetes with peripheral circulatory disorders	
250.80–250.83 Diabetes with other specified manifestations	
250.90–250.93 Diabetes with unspecified complication	
Exclusions	
Labor and delivery:	
650.*–669.*, V27.*	O60.*–O77.*, O80.*–O82.*, Z37.*
Diabetes mellitus complicating pregnancy, childbirth or the puerperium:	
648.0*	O24.4*, O24.91*, O24.92, O24.93

[a]An asterisk (*) indicates that any subsequent digit/character is included.
ICD, International Classification of Diseases; DM, diabetes mellitus.

diagnostic position, or 3) 2 or more outpatient encounters at least 7 days apart with a diagnosis of abnormal glucose tolerance (ICD-9: 648.8*; ICD-10: O99.81*) in any diagnostic position. Women with a prior diagnosis of DM (ICD-9: 250.*; ICD-10: E10.*, E11.*) in any diagnostic position of an inpatient or outpatient encounter were excluded from the analysis.

The denominator for calculating the prevalence rate of GDM was the number of live births in each calendar year. A new live birth was eligible to be counted once every 280 days.[26] Of these births, the proportion of those with an associated GDM diagnosis was calculated. The reference date for assigning the year of the birth and the GDM diagnosis was the date of the inpatient admission for the live birth. Prevalence rates were calculated per 100 live births.

The number of women who were diagnosed as an incident case of GDM who later met criteria for becoming a case of DM was also described. For this calculation, incident cases of DM were reascertained so that some of the previously described exclusion criteria could be relaxed. In particular, in counting incident cases of DM, encounters for DM were not excluded if there was a diagnosis for labor and delivery within 6 months after the encounter. Additionally, the number of women with incident type 2 DM who were later diagnosed as a case of GDM was determined. For this analysis, incident cases of GDM were reascertained again to relax the exclusion criteria. Specifically, GDM cases with a prior diagnosis of DM were not excluded. Finally, for active component service women, follow-up period was calculated as the time from incident diagnosis (GDM or type 2 DM) to the time of their departure from service or the end of the study period, whichever came first. Follow-up period was not calculated for reserve component service women because information on the start and end dates of their active duty service periods was not available.

RESULTS

Diabetes mellitus

Active component: During 2008–2018, a total of 12,582 active component service members received incident diagnoses of any DM, for a crude overall incidence rate of 84.8 per 100,000 p-yrs **(Table 2)**. More than four-fifths (n=10,633; 84.5%) of incident cases were type 2 DM. The crude overall incidence rate of type 2 DM was 71.6 per 100,000 p-yrs.

Among active component service members, overall incidence rates of type 2 DM diagnoses increased exponentially with increasing age **(Table 2)**. Male service members had an overall rate 1.5 times that among females (75.4 per 100,000 p-yrs and 50.2 per 100,000 p-yrs, respectively). The overall rates of type 2 DM diagnoses were highest among Asian/Pacific Islanders (169.5 per 100,000 p-yrs) and non-Hispanic blacks (154.9 per 100,000 p-yrs) and lowest among non-Hispanic whites (44.5 per 100,000 p-yrs). Across the services, crude overall incidence rates of type 2 DM diagnoses were highest among Army and Navy members (91.2 per 100,000 p-yrs and 86.5 per 100,000 p-yrs, respectively) and lowest among Marine Corps members (19.1 per 100,000 p-yrs).

Crude annual incidence rates of type 2 DM diagnoses among active component service members peaked in 2010 at 96.4 per 100,000 p-yrs and then decreased by almost three-fifths to 40.7 per 100,000 p-yrs in 2018 **(Figure 1)**. During this 9-year period, decreases in rates of incident type 2 DM diagnoses occurred in both sexes, in all age groups, among all race/ethnicity groups, and across all services **(Figures 1–4)**. Between 2010 and 2018, the slope of decline in annual rates was greatest for service members aged 40 years or older, with slopes decreasing with decreasing age **(Figure 2)**. The slope of decline during this period was greatest among Asian/Pacific Islander service members and smallest among non-Hispanic white service members **(Figure 3)**. Across the services, the slope of decline during 2010–2018 was greatest among Army and Navy members and smallest among Marine Corps members **(Figure 4)**.

TABLE 2. Incident diagnoses and incidence rates of DM, active and reserve components, U.S. Armed Forces, 2008–2018

	Active component				Reserve component			
	Type 2 DM		Any DM[a]		Type 2 DM		Any DM[a]	
	No.	Rate[b]	No.	Rate[b]	No.	Rate[c]	No.	Rate[c]
Total	10,633	71.6	12,582	84.8	6,503	63.8	7,106	69.8
Sex								
Male	9,512	75.4	11,272	89.4	5,725	69.2	6,246	75.5
Female	1,121	50.2	1,310	58.7	778	40.6	860	44.9
Age group (years)								
<20	67	6.9	167	17.1	15	1.5	38	3.8
20–24	440	9.2	1,050	22.0	88	3.7	204	8.5
25–29	741	20.9	1,219	34.4	246	12.3	364	18.2
30–34	1,182	51.1	1,452	62.8	392	27.8	478	33.9
35–39	2,466	144.7	2,733	160.5	826	72.8	890	78.5
40+	5,737	374.4	5,961	389.6	4,936	220.6	5,132	229.6
Race/ethnicity group								
Non-Hispanic white	3,960	44.5	5,139	57.7	3,298	49.1	3,698	55.0
Non-Hispanic black	3,693	154.9	4,142	173.8	1,832	117.9	1,960	126.2
Hispanic	1,315	67.2	1,494	76.4	781	69.0	836	73.8
Asian/Pacific Islander	949	169.5	983	175.6	326	103.2	333	105.4
American Indian/Alaska Native	93	59.1	108	68.6	53	64.3	57	69.2
Other/unknown	623	70.8	716	81.4	213	55.8	222	58.2
Service								
Army	5,166	91.2	5,973	105.5	4,923	72.3	5,346	78.5
Navy	3,052	86.5	3,506	99.5	485	62.6	536	69.2
Air Force	2,010	56.8	2,453	69.4	1,053	50.5	1,159	55.6
Marine Corps	405	19.1	650	30.7	42	8.1	65	12.6

[a]Type 1, type 2, or unspecified DM.
[b]per 100,000 person-years.
[c]per 100,000 persons.
DM, diabetes mellitus; No., number.

Reserve component: During the 11-year surveillance period, a total of 7,106 reserve component service members received incident diagnoses of any DM, for a crude overall incidence rate of 69.8 per 100,000 persons **(Table 2)**. The vast majority (n=6,503; 91.5%) of incident cases were type 2 DM. The crude overall incidence rate of type 2 DM was 63.8 per 100,000 persons. With the exception of race/ethnicity group, patterns of subgroup-specific overall rates of type 2 DM among reserve component service members were similar to those noted among active component members, with the highest rates observed in males, those aged 40 years or older, and Army members. Among reserve component service members, non-Hispanic blacks had the highest rate of type 2 DM **(Table 2)**.

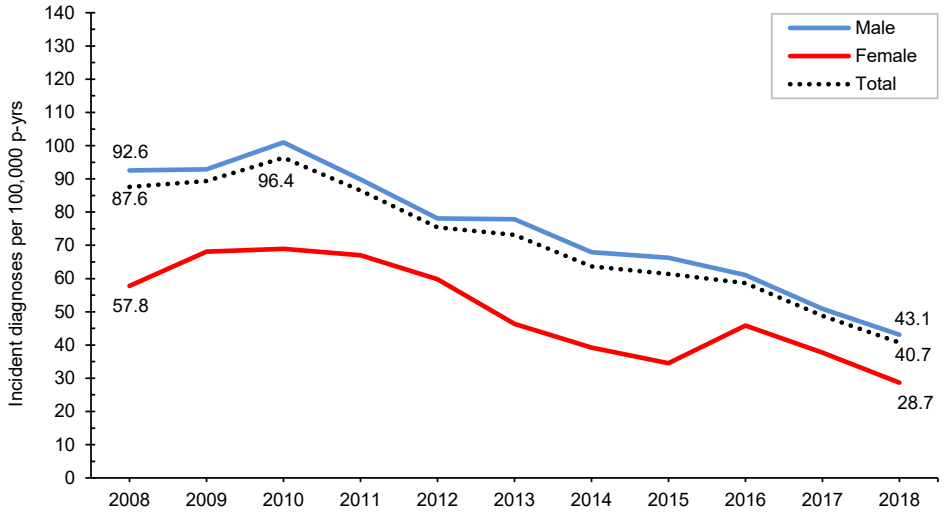
Crude annual incidence rates of type 2 DM diagnoses among reserve component service members peaked in 2010 at 92.7 per 100,000 persons and then decreased by more than half to 40.0 per 100,000 persons in 2018 **(data not shown)**. As was observed among active component members during the period from 2010 through 2018, decreases in rates of incident type 2 DM diagnoses occurred in both sexes, in all age groups, among all race/ethnicity groups, and across all services, with the greatest slopes of decline among service members aged 40 years or older, Asian/Pacific Islander service members, and Army members **(data not shown)**.

MHS dependents: From 2008 through 2018, a total of 249,394 MHS dependents received any incident DM diagnoses, 90.5% of whom were affected by type 2 DM **(data not shown)**. The vast majority of dependents diagnosed with type 2 DM were female (94.2%) and 45 years or older (86.9%) **(data not shown)**. Over the course of the 11-year period, total counts of incident diagnoses of type 2 DM in this population decreased by 66.0%, from 29,625 to 10,066 **(Figure 5)**.

Gestational diabetes mellitus

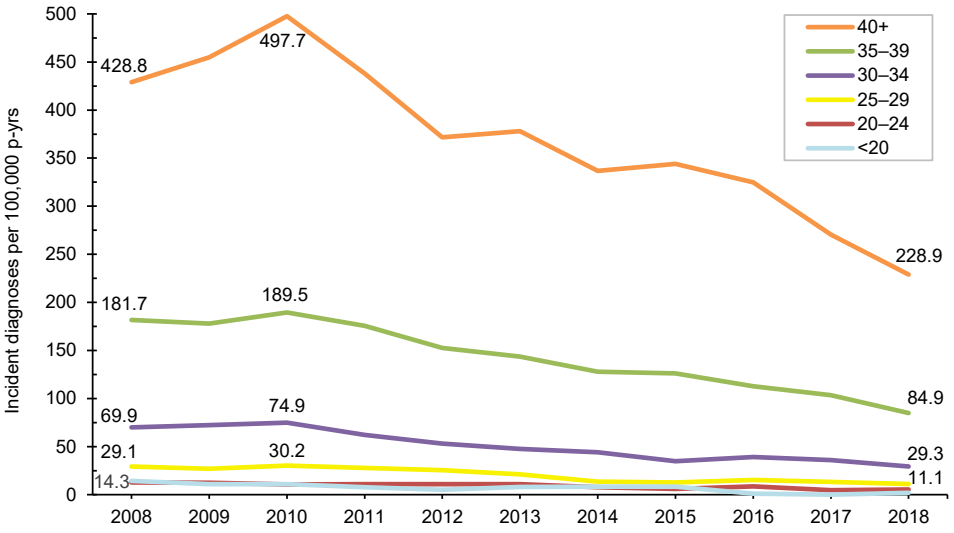
Active component: Between 2008 and 2018, 7.3% (n=10,603) of the total live births to active component service women were associated with a diagnosis of GDM **(Table 3)**. Overall prevalence of GDM increased with increasing age and was highest among Asian/Pacific Islander service women (12.4% of total live births).

FIGURE 1. Annual incidence rates of type 2 DM diagnoses, by sex, active component, U.S. Armed Forces, 2008–2018



DM, diabetes mellitus; p-yrs, person-years.

FIGURE 2. Annual incidence rates of type 2 DM diagnoses, by age group, active component, U.S. Armed Forces, 2008–2018



DM, diabetes mellitus; p-yrs, person-years.

Across the services, overall prevalence of GDM ranged from 5.2% among female Marine Corps members to 7.6% among female Navy members.

Overall, crude annual prevalence rates of GDM among active component service women more than doubled from 4.9 per 100 live births in 2008 to 10.6 per 100 live births in 2018 **(Figure 6)**. This increase in prevalence rates over time was observed in all subgroups examined (sex, age, race/ethnicity, service). Among active component service women, 1.5% of women with incident GDM diagnoses were later diagnosed with type 2 DM **(Table 4)**; more than three-quarters (76.4%) of these women were diagnosed with type 2 DM within 5 years of their incident GDM diagnoses **(data not shown)**. The average follow-up period for service women after their incident GDM diagnosis was 3.1 years **(data not shown)**. Conversely, 3.5% of women with incident type 2 DM diagnoses were later diagnosed with GDM; the majority (76.9%) of these service women developed GDM within 5 years of their incident type 2 DM diagnoses **(data not shown)**. The average follow-up period for women after their incident type 2 DM diagnosis was 2.5 years **(data not shown)**.

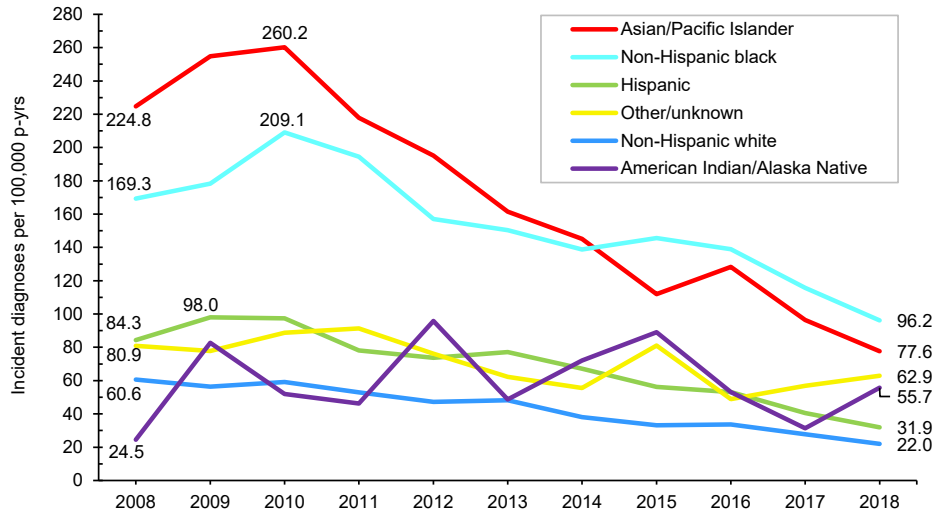
Reserve component: During the 11-year surveillance period, 8.2% (n=2,329) of the total live births to reserve component service women were associated with a diagnosis of GDM **(Table 3)**. Overall prevalence of GDM generally increased with increasing age and was highest among Asian/Pacific Islander service women (15.2% of total live births). Across the services, overall prevalence of GDM ranged between 6.0% among female Marine Corps members and 8.8% among female Navy and Air Force members.

Overall, crude annual prevalence rates of GDM among reserve component service women nearly doubled from 6.8 per 100 live births in 2008 to 13.0 per 100 live births in 2018 **(data not shown)**. This increase in prevalence rates over time was observed in all subgroups examined (age, race, service). Among reserve component service women, 0.9% of women with incident GDM were later diagnosed with type 2 DM **(Table 4)**; nearly two-thirds (65.0%) were diagnosed with type 2 DM within 5 years of their incident GDM diagnoses **(data not shown)**. Of the women with incident type 2 DM diagnoses, 1.7% were later diagnosed with GDM **(Table 4)**; the vast majority (92.3%) of these women were diagnosed with GDM within 5 years of their incident type 2 DM diagnoses **(data not shown)**.

MHS dependents: Of the total live births to female MHS dependents during 2008–2018, 8.4% (n=87,813) were associated with a diagnosis of GDM **(data not shown)**. As was observed among active and reserve component service women, overall prevalence of GDM among female dependents increased with increasing age **(data not shown)**.

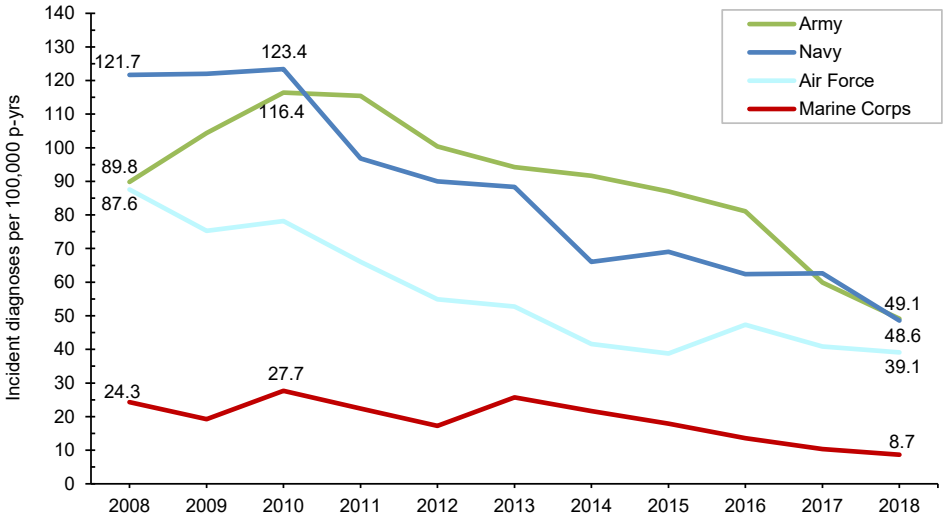
Crude annual prevalence rates of GDM among female MHS dependents more than doubled from 6.1 per 100 live births in 2008 to 13.2 per 100 live births in 2018 **(data not shown)**. This increase in prevalence rates over time was observed in

FIGURE 3. Annual incidence rates of type 2 DM diagnoses, by race/ethnicity group, active component, U.S. Armed Forces, 2008–2018



DM, diabetes mellitus; p-yrs, person-years.

FIGURE 4. Annual incidence rates of type 2 DM diagnoses, by service, active component, U.S. Armed Forces, 2008–2018



DM, diabetes mellitus; p-yrs, person-years.

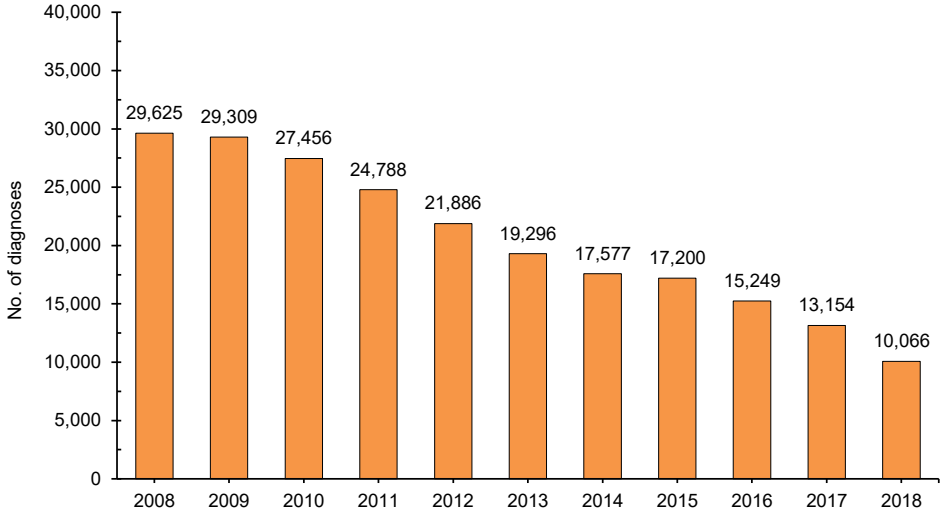
all age groups (0–17, 18–44, and 45–64). Among female MHS dependents, 2.0% of women with incident GDM were later diagnosed with type 2 DM **(Table 4)**. Conversely, 0.5% of women with incident type 2 DM were later diagnosed with GDM. As was observed among active and reserve component service women, the majority of female non-service member beneficiaries who developed type 2 DM after having been diagnosed with GDM or who developed GDM after having been diagnosed with type 2 DM did so within 5 years of their initial DM diagnoses (70.1% and 90.9%, respectively) **(data not shown)**.

EDITORIAL COMMENT

The current analysis found that from 2008 through 2018, the crude annual incidence of type 2 DM diagnoses decreased among active component service members overall and among all subgroups examined; the greatest decrease in crude annual rates of type 2 DM was seen between 2010 and 2018. Although incidence rates of diagnosed DM among adults aged 18 years or older in the U.S. civilian population during this period were considerably higher than among comparably aged active component and reserve component members, the approximate timing of the peaks in rates was somewhat similar; a peak in annual age-adjusted incidence of diagnosed DM was observed in 2009 in the former and 2010 in the latter.[5] Potential explanations for the prolonged decrease in type 2 DM incidence observed in both the U.S. military and civilian populations include increased awareness,[27] education,[27] risk factor modification,[28–31] and/or a reduction in the pool of undiagnosed type 2 DM through the intensification of diagnostic and screening activities.[32–34] However, recent published reviews have argued that DM risks have not decreased in the U.S. general population sufficiently to explain this trend.[33,34]

As expected, the majority of incident diagnoses of DM among service members were reported as type 2 cases. The demographic differences in type 2 DM incidence observed in the current analysis are consistent with those documented in civilian populations in the U.S. and elsewhere.[1,4–6,34] Males have a higher risk of developing type 2 DM compared to females; incidence increases with age in both sexes.[1,4–6] The overall incidence rates of diagnoses of this form of DM among Asian/Pacific Islander and non-Hispanic black active and reserve component service members were 1.5 or more times the rates among their respective counterparts in other race/ethnicity groups. Comparable differences between the incidence of type 2 DM among non-Hispanic blacks and those in other race/ethnicity groups (non-Hispanic whites and Asians) have been reported in the adult civilian U.S. population using 2013–2015 NHIS data.[35] Epidemiologic studies and U.S. national surveillance have demonstrated that Asians have a higher prevalence of type 2 DM compared to non-Hispanic whites but a lower prevalence than that

FIGURE 5. Annual counts of incident type 2 DM diagnoses, MHS dependents, 2008–2018



DM, diabetes mellitus; MHS, Military Health System; No., number.

TABLE 3. Prevalence of GDM, active and reserve component service women, 2008–2018

	Active component		Reserve component	
	No.	%	No.	%
Total	10,603	7.3	2,329	8.2
Age group (years)				
<20	119	3.3	10	3.0
20–24	3,061	5.3	354	5.3
25–29	3,308	7.3	694	7.0
30–34	2,520	9.4	787	10.4
35–39	1,308	12.4	399	12.2
40+	287	16.2	85	12.0
Race/ethnicity group				
Non-Hispanic white	4,567	6.9	1,312	7.8
Non-Hispanic black	2,286	6.2	439	7.9
Hispanic	1,831	7.9	282	8.2
Asian/Pacific Islander	732	12.4	98	15.2
American Indian/Alaska Native	180	9.2	42	5.9
Other/unknown	1007	8.8	68	9.8
Service				
Army	4,049	7.5	1,361	7.9
Navy	2,857	7.6	290	8.8
Marine Corps	620	5.2	29	6.0
Air Force	3,077	7.2	649	8.8

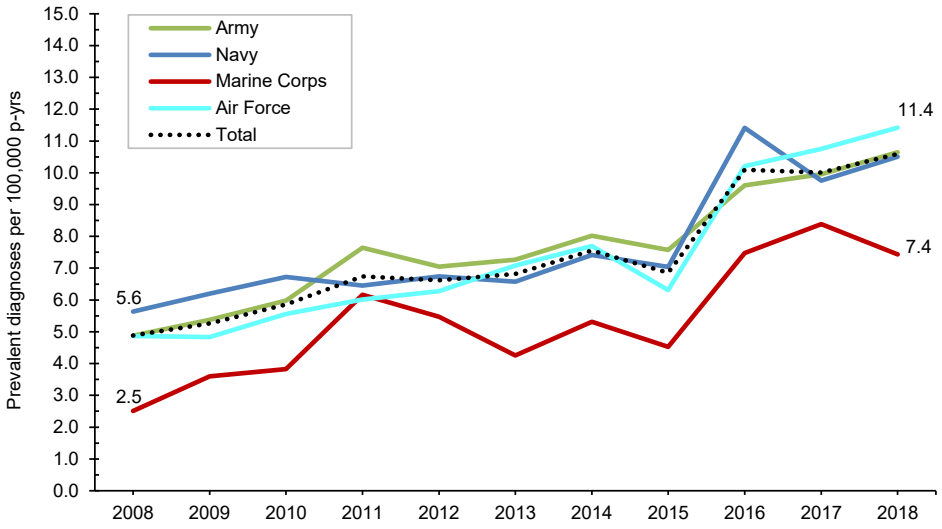
GDM, gestational diabetes mellitus; No., number.

of non-Hispanic blacks and Hispanics.[36,37] However, disaggregation of Asian/Pacific Islander subgroups has shown that there is considerable variation in incidence within this group, with Pacific Islanders, South Asians, and Filipinos having the highest incidence of diabetes among all race/ethnicity groups.[38]

Over the 11-year surveillance period, 12,582 active component and 7,106 reserve component service members received clinical diagnoses of DM. Using 2015–2016 National Health and Nutrition Examination Survey (NHANES) data, the Centers for Disease Control and Prevention (CDC) estimated that among the 5.6% of U.S. adults aged 20–44 years with DM, 2.4% were undiagnosed.[39] Prevalences of both diagnosed and undiagnosed DM would be expected to be much lower among U.S. service members than similarly aged U.S. civilians because of disqualifying standards for enlistment (i.e., having a history of DM, unresolved pre-DM[1] within the last 2 years, or GDM), height and weight requirements that discourage obesity,[24] and mandatory medical examinations in addition to free access to health care.

Military medical retention standards require that service members diagnosed with DM while in service and who have a hemoglobin A1c (HbA1c) level "greater than 7.0% despite lifestyle modification for 6 months, intolerance, or declination of medical therapy" be referred to a medical evaluation board, which assesses their medical fitness and makes recommendations about follow-up care.[23] Having a chronic condition such as DM does not necessarily preclude continued military service; factors such as occupation and severity of disease affect the decision regarding continuation of military service. As described in the Department of Defense Instruction (DoDI) 6490.07,[40] medical evaluators must consider rations, duty assignment, and medical services available in theater when deciding whether an individual with DM is deployable. A waiver allowing deployment is permissible by which certain service members with DM can take part in "contingency deployments." A contingency is defined as "a situation requiring military operations in response to natural disasters, terrorists, subversives, or as directed

FIGURE 6. Annual rates of prevalent diagnoses of GDM, by service, active component, U.S. Armed Forces, 2008–2018



GDM, gestational diabetes mellitus; p-yrs, person-years.

by appropriate authority to protect U.S. interests."[40] A contingency deployment is defined as "a deployment that is limited to outside the continental U.S., over 30 days in duration, and in a location with medical support from only nonfixed (temporary) military medical treatment facilities."[40] A minimum of a medical record review by a trained DoD healthcare provider is required to determine whether a service member with a chronic medical condition can deploy; this determination is based on the severity and stability of the condition, as well as the environment and other requirements that may be anticipated during deployment.[39] DM type 1 or 2 treated with insulin or oral hypoglycemic agents is specifically identified in DoDI 6490.07 as a high-risk condition, as the disease and certain medications for its treatment could cause sudden incapacitation.[40] A recent study of U.S. Army, Navy, Air Force, and Marine Corps members with DM who had at least 1 deployment during 2005–2017 and for whom paired pre- and post-deployment HbA1c data were available (n=474) demonstrated that Hb1Ac levels remained stable for those who met adequate glycemic targets (less than 7.0%).[41]

As described in DoDI 6025.19,[42] individual medical readiness requires an annual periodic health assessment that provides an opportunity to assess the overall health and medical readiness status of each service member. Consequently, the military departments may initiate preventive services as warranted, refer service members to the primary healthcare provider for further evaluation as indicated, and document any further plan that may be needed. Service members may therefore be more educated and informed regarding DM risk factors and disease symptoms. As a result, higher proportions of detectable cases may be identified among them. The higher crude overall rates of DM diagnoses in the Army and the Navy likely reflect, at least in part, different demographic makeups (e.g., Marine Corps members are, on average, younger than other services' personnel[43]), varying frequencies and intensities of physical activity (military and/or leisure), and/or more complete and timely case identification in these services than in the other services. Any further investigation of these differences should examine adjusted (e.g., by age, sex, race/ethnicity) incidence rates among members within the services. It is important to note that the prevalence of obesity in the identified DM cases was not examined in this analysis but would be relevant to potential studies of adjusted rates of this condition across the services.

In the current analysis, the overall crude prevalence of GDM ranged from 7.3% among active component service women to 8.4% among female MHS dependents. This range of prevalence estimates aligns with previous studies in U.S. subpopulations.[11–17,22,44,45] Analysis of 2007–2010 data from the CDC's Pregnancy Risk Assessment Monitoring System found that GDM prevalence ranged from 4.6% to 9.2% depending on the method of report (4.6% based on birth certificates, 8.7% as reported by questionnaire, and 9.2% based on either method).[11] An analysis of 2012–2016 MHS administrative data from active component service women yielded GDM prevalence estimates that ranged from 5.8% to 6.8%, with the highest rates among those in the oldest age group.[46] In the current analysis, increases in annual prevalence rates over time were observed in all subgroups examined (age, race/ethnicity, service). The U.S. civilian population has experienced similar increases in the prevalence of GDM.[11,13,15,16]

Among female service members and MHS dependents with GDM, between 0.9%

TABLE 4. Progressions from GDM to type 2 DM and from type 2 DM to GDM, active and reserve component service women and female dependents, 2008–2018

	Progression from GDM to type 2 DM			Progression from type 2 DM to GDM		
	No. of initial cases of GDM	No. of later cases of type 2 DM	% progression	No. of initial cases of type 2 DM	No. of later cases of GDM	% progression
Active component service women	9,561	144	1.5	1,121	39	3.5
Reserve component service women	2,136	20	0.9	778	13	1.7
Female dependents	77,828	1,583	2.0	212,522	1,115	0.5

GDM, gestational diabetes mellitus; DM, diabetes mellitus; No., number.

(reserve component) and 2.0% (dependents) had subsequent diagnoses of type 2 DM. Estimates of progression from GDM to type 2 DM among women in the U.S. civilian population are considerably higher and range from 15% to 50% depending on the characteristics of the population studied, diagnostic criteria employed, method of report, and follow-up period.[18–22,42,47] It is important to note that the lack of comparability of these studies precludes direct comparison to the current results. Regardless of the relatively low estimates of conversion, the current findings highlight the public health importance of diabetes education, testing, and ongoing clinical follow-up for diabetes well beyond the traditional 6-month postpartum time period.

Several limitations should be considered when interpreting the results of the current analysis. First, incident cases of DM were ascertained from diagnosis codes recorded on administrative records of medical encounters. The reliability of diagnoses of DM on such records may be variable (e.g., some encounters that raise clinical suspicion of or "rule out" DM may be incorrectly documented with diagnostic codes specific for DM). To increase the likelihood that individuals with DM diagnosis codes were true cases, the surveillance case definition required at least 2 medical encounters with primary diagnoses of DM within a 90-day period. In addition, this report summarized diagnoses of DM that were reported from medical encounters in fixed U.S. military and civilian (i.e., purchased care) medical facilities if reimbursed through the MHS. Because records of civilian health care not reimbursed by the MHS were not available for this analysis, the numbers and rates of incident diagnoses of DM reported here are likely an underestimate of the actual numbers and rates of incident diagnoses of this condition.

It is predicted that approximately 1 in 3 people with diabetes are undiagnosed.[48] The changing demographics of the obstetric population, including advanced maternal age and obesity, have led to an increasing number of women entering pregnancy with unrecognized diabetes.[49] Thus, in the current study, some of the women with GDM who later developed type 2 DM likely represent previously undiagnosed type 2 DM that was first recognized during screening in pregnancy. However, unlike the civilian population, where testing for diabetes in women at high risk may not occur before an unplanned conception, active and reserve component service women of reproductive age are routinely screened before conception.

DM is one of the costliest diseases in the U.S. During 1996–2013, healthcare spending on DM increased twice as fast as all other conditions combined, with the highest annual growth rates seen among those aged 20–44 years.[50] Despite declines in incidence of type 2 DM diagnoses among active and reserve component service members over the course of the last 8 years of the surveillance period, sustained surveillance of DM along with continued research on comorbidities, risk factors, and lifestyle choices on DM incidence are warranted.

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Increased Risk for Stress Fractures and Delayed Healing with NSAID Receipt, U.S. Armed Forces, 2014–2018

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Previous studies have suggested that the use of nonsteroidal antiinflammatory drugs (NSAIDs) is associated with an increased risk of stress fractures due to their inhibitory effect on bone formation. The current study evaluated the relative risk of stress fractures in active duty service members with and without previous receipt of NSAIDs. A total of 7,036 cases of stress fracture and 28,141 matched controls were identified between June 2014 and December 2018 and included in the analysis. A subset of cases were evaluated for delayed healing diagnoses within 90 days following incident case diagnosis using International Classification of Diseases, 10th Revision (ICD-10) diagnosis codes. Prior receipt of NSAIDs was associated with an increased incidence of stress fractures (adjusted incidence rate ratio=1.70; 95% confidence interval [CI]:1.58–1.82; p<.0001). Among stress fracture cases, prior receipt of NSAIDs was associated with increased diagnosis of delayed healing (adjusted odds ratio=1.41; 95% CI: 1.12–1.77; p=.004). These findings may have significant implications for military readiness because NSAIDs are used extensively and stress fractures are already a major contributor to the burden of healthcare encounters and lost duty time.

WHAT ARE THE NEW FINDINGS?

This is the first *MSMR* report on the association between prior NSAID receipt and incident stress fracture diagnosis in service members. Prior NSAID receipt was associated with a 70% increased incidence of stress fracture. Among cases, the odds of a delayed healing diagnosis among NSAID recipients were 1.4 times that of nonrecipients.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

This study suggests that receiving NSAIDs may increase the risk for stress fracture among active component service members. These stress fracture injuries may contribute to lost duty days and reduce deployment readiness because of physical limitation.

Service members in the U.S. Armed Forces participate in intense physical activity when training and performing their job responsibilities. The physical activity can potentially result in overuse injuries because the repetitive force exerted by the musculoskeletal system may cause cumulative microtraumatic damage leading to strains, sprains, and stress fractures.[1–3] Injuries, including stress fractures, are a major public health concern among the military because of their high prevalence, the associated lost working time, and the cost of treatment. A previous *MSMR* article estimated that there were 31,349 incident stress fractures diagnosed (a rate of 3.2 per 1,000 person-years) among active component service members from 2004 through 2010.[3] A recent study among the Royal Marines during commando training found that, on average, the rehabilitation time for stress fractures ranged from 12 to 21 weeks depending on the site of fracture.[4] The burden associated with stress fractures is high when taking into consideration the incidence rate, slow recovery time, and medical cost of treatment.

Hughes and colleagues examined the association between stress fractures and nonsteroidal antiinflammatory drugs (NSAIDs) in a U.S. Army population and found that both NSAIDs and acetaminophen potentially increase the risk for stress fractures.[2] If NSAID use is associated with an increase in stress fracture risk, this finding could have a sizable impact on military readiness given the widespread use of these drugs. In 2014, approximately 82% (n=418,579) of active duty U.S. Army service members filled at least 1 NSAID prescription.[5] Many service members could be unknowingly increasing their risk for stress fractures by taking medications to decrease the pain and swelling associated with other physical complaints.

The use of NSAIDs to treat swelling and pain from fractures has been widely debated. Studies have claimed that NSAIDs could increase the risk of a fracture or delay the healing of a fracture because of the drug's inhibitory effect on bone metabolism.[2,6–10] In theory, this claim is plausible when considering the impact of the mechanism of action for NSAIDs on the physiological process of bone metabolism. Bone metabolism involves osteoclasts and osteoblasts, which are responsible for the removal of bone and the growth of bone, respectively.[9–12] Bone metabolism can be grouped into 2 processes: bone modeling and bone remodeling.[10,11] During bone modeling, there is bone formation on the surface of bones in response to mechanical loading.[10,11] The loading initiates osteoclast-mediated biochemical signaling and Wnt/β-catenin pathway activation, which are crucial for osteoblast differentiation, proliferation, and bone formation.[10] During bone remodeling, there is bone resorption and then bone formation to replace old or damaged bone.[10,11] During remodeling, osteoclasts remove the area of damaged bone and osteoblasts then replace it with

new bone. However, the new bone is temporarily more porous, and in turn, more fragile and injury prone.[10]

Bone metabolism can be both stimulated and inhibited by a group of physiologically active lipid compounds called prostaglandins, which are responsible for the differentiation of osteoclasts and osteoblasts as well as resorbing activity of mature osteoclasts.[9,10,12,13] There are 2 initiators to the production of prostaglandins: cyclooxygenase-1 (COX-1) enzyme and cyclooxygenase-2 (COX-2) enzyme. COX-1 produces prostaglandins in response to physiological conditions such as tissue homeostasis and cell-to-cell signaling, while COX-2 produces them in response to inflammation.[9,10,12,14] NSAIDs inhibit the activity of COX by competing with arachidonic acid for binding to the enzyme.[9,12] Therefore, NSAIDs reduce the production of prostaglandins, limiting the differentiation of osteoclasts and osteoblasts and the resorbing activity of osteoclasts, which then inhibits bone resorption and formation. In theory, this inhibition could interfere with bone modeling and remodeling and increase the risk of fracture or delayed healing. Studies have shown that the timing of NSAID use is key to the inhibition of bone modeling.[10,15–17] Bone formation is suppressed if NSAIDs are taken before bone loading, but not if NSAIDs are taken afterwards.[10,15–17]

NSAIDs can be categorized by their inhibiting effect on the COX enzymes. Each class of NSAID is selective to binding to COX enzymes with varying degrees. The nonselective COX inhibitors impede the activity of both COX-1 and COX-2 enzymes with no discrimination.[14] Preferentially selective COX-2 inhibitors impede COX-2 activity at lower drug concentrations, but there is some COX-1 inhibition at label dose. Selective COX-2 inhibitors (coxibs) impede COX-2 activity but not COX-1 at label dose.[14] Studies have indicated a negative effect of NSAIDs on the bone healing process because NSAIDs limit osteogenesis and angiogenesis through blocking COX-2.[14,18–20] However, NSAIDs have other mechanisms that can impair healing from a bone injury. Besides limiting osteogenesis and angiogenesis, NSAIDs can initiate apoptosis, alter collagen content and fiber size, and modify genes produced from a signaling pathway that plays a role in differentiation and proliferation of osteoblast precursor cells.[14,21]

Some animal studies have provided evidence that bone repair is either delayed or impaired by NSAID treatment and that the degree of delay in bone healing depends on the type of fracture and type of NSAID prescribed.[7,11,22] Human studies examining the effect of NSAIDs on fracture healing have observed inconsistent results. A retrospective study of patients with tibia fractures found that patients taking any NSAIDs were more likely to have delayed healing compared to those patients not taking any NSAIDs.[7,23] In addition, a retrospective analysis examining healing from a fracture of the femur diaphysis found that there was an association between nonunion and use of NSAIDs after injury.[7,24] This study also identified patients who, although their fractures had united, showed a delay in healing after taking NSAIDs.[7,24] In contrast, a double-blind randomized study examined healing from Colles fractures after treating postmenopausal women with either piroxicam or placebo and found no statistically significant delay in healing with the NSAID treatment.[7,25]

Although it has been suggested that NSAIDs may increase risk for fractures and delay bone repair, the findings from studies on such topics have been mixed. The objective of this study was to estimate the risk of stress fracture following receipt of NSAIDs among active component military service members between June 2014 and December 2018. In addition, the current study evaluated the association between NSAID receipt and International Classification of Diseases, 10th Revision (ICD-10) coded diagnosis of delayed healing among incident stress fracture cases.

METHODS

The eligible study population consisted of active component service members in the Army, Air Force, Navy, or Marine Corps who served for any length of time between 1 June 2014 and 31 December 2018. This study period was selected based on the availability of pharmacy data in the Defense Medical Surveillance System (DMSS). All study data were derived from the DMSS, a relational database maintained by the Armed Forces Health Surveillance Branch. Multiple data sources feed information into the DMSS, forming tables related to demographic characteristics, prescriptions dispensed, and administrative health records. Pharmacy data in the DMSS are derived from the Pharmacy Data Transaction Service (PDTS), which has information on outpatient prescriptions dispensed by mail order, at military treatment facilities (MTFs), by Veterans Affairs for dual eligible beneficiaries, and at civilian facilities if billed through TRICARE. The medical encounters in the DMSS contain records of both hospitalizations and ambulatory visits in fixed MTFs and civilian treatment facilities billed through TRICARE.

To qualify as an incident case of stress fracture, an individual had to have either 1) an outpatient medical encounter with a qualifying ICD-9 or ICD-10 diagnosis code for stress fracture **(Table 1)** in any diagnostic position followed by another outpatient medical encounter for a diagnosed stress fracture within 14 to 90 days later or 2) a hospitalization with a diagnosis code for stress fracture in any diagnostic position. The incidence date, also referred to as reference date for controls, was the date of the first qualifying encounter. If there was a hospitalization and an outpatient encounter on the same day, then inpatient records were prioritized over outpatient encounters. If the first encounter occurred before the surveillance period, the service member was considered a prevalent case and was excluded from the analysis. An individual could be counted as an incident case only once per lifetime. Those who had any outpatient diagnoses of stress fracture during their military service before the first qualifying encounter were excluded.

The first part of the study employed a case-control design with risk-set matching to assess the association between prescribed NSAID and incident stress fracture diagnosis among active component service members from June 2014 through December 2018. Up to 4 controls were matched to each case based on sex, race/ethnicity, service branch, age (within 1 year), and

TABLE 1. Stress fracture and vitamin D deficiency case defining ICD-9 and ICD-10 codes

ICD-9 diagnostic codes		ICD-10 diagnostic codes[a]	
Stress fracture			
Stress fracture of the foot and toes			
733.94	Stress fracture of the metatarsals	M84.374*–M84.379*	Stress fracture, foot and toes
Stress fracture of leg			
733.93	Stress fracture of tibia or fibula	M84.36*	Stress fracture, tibia or fibula
733.97	Stress fracture of shaft of femur	M84.351*, M84.352*, M84.353*	Stress fracture, femur
Stress fracture of pelvic region			
733.96	Stress fracture of femoral neck	M84.359*	Stress fracture, hip
733.98	Stress fracture of pelvis	M84.350*	Stress fracture, pelvis
Stress fracture of unspecified/other region			
733.95	Stress fracture of other bone	M84.30*, M84.38*	Stress fracture, unspecified/other site
		M84.31*	Stress fracture, shoulder
		M84.32*	Stress fracture, humerus
		M84.33*	Stress fracture, ulna and radius
		M84.344*, M84.345*, M84.346*	Stress fracture, fingers
		M84.341*, M84.342*, M84.343*	Stress fracture, hand
		M84.371*–M84.373*	Stress fracture, ankle
Vitamin D deficiency			
268.9	Unspecified vitamin D deficiency	E55.9	Vitamin D deficiency, unspecified

[a]An asterisk (*) indicates that any subsequent digit/character, excluding those ending in S, is included.
ICD, International Classification of Diseases.

time in service category. Random selection was performed if more than 4 controls were matched to a case. Race/ethnicity was coded as non-Hispanic white, non-Hispanic black, Hispanic, Asian/Pacific Islander, American Indian/Alaska Native, and other/unknown. Time in service was categorized as less than 4 months, 4 months to less than 1 year, 1 year to less than 2 years, 2 years to less than 5 years, and 5 years or more. Controls were allowed to be matched to multiple cases if they fit the matching criteria and were able to become a case later in the study. Controls with any diagnosis of a stress fracture in an inpatient or outpatient encounter on or before the reference date were excluded from being a control for that match.

To measure exposure, prescription records were included in the analysis if the records contained an American Hospital Formulary Service (AHFS) therapeutic class code for NSAID (280804) and the drug (brand or generic) name (**Table 2**). An individual was considered exposed to an NSAID if the prescription date was 30 to 180 days before the reference date. NSAID use within 30 days before the reference date was not considered a qualifying exposure in order to avoid the potential effects of reverse causation from the use of prescribed NSAIDs to treat the pain of a pre-clinical stress fracture.[2] Service members could be exposed to multiple NSAIDs during the 30- to 180-day exposure period, and indicator variables were created to identify the different NSAID classes.

Vitamin D deficiency was included in the analysis as a potential confounding factor since several studies have suggested that this deficiency is related to both NSAID use and stress fractures.[26–29] For this study, a case of vitamin D deficiency was defined as having a hospitalization or ambulatory encounter with an ICD-9 or ICD-10 diagnosis code for vitamin D deficiency in any diagnostic position within 1 year before to 6 months following the reference date **(Table 2)**.

The study secondarily assessed the association between NSAID receipt and diagnosis of delayed healing among the subset of incident stress fracture cases identified during the period between October 2015 and December 2018. A case was considered delayed healing if there was an ICD-10 diagnosis code beginning with "M843" (stress fracture) and ending in "G" (subsequent encounter for fracture with delayed healing) recorded during an inpatient or outpatient encounter within 90 days of the incident stress fracture diagnosis.

For the first part of the study, adjusted incidence rate ratios and associated 95% confidence intervals (CIs) were calculated using a multivariable logistic regression model to estimate the effect of NSAID receipt on incident stress fracture diagnosis. The model adjusted for sex, race/ethnicity, service, age, time in service, recruit status, occupation, and diagnosis of vitamin D deficiency. The same adjusted incidence rate ratio was calculated for just the Army population. For the second part of the study, adjusted odds ratios and associated 95% CIs were calculated using

TABLE 2. NSAID classes and drug names included in the analysis

NSAID class	Drug name	Brand and generic names
Propionic acid derivatives	Ibuprofen	Aches-N-Pain, Advil, Caldolor, Duexis, Children's Advil, Children's Ibuprofen, Children's Motrin, IBU, IBU-200, Ibuprofen, Ibuprofen IB, Ibuprofen M, Infants' Ibuprofen, Motrin, Motrin IB, Wal-profen, Motrin Suspension
	Naproxen	Aleve, Anaprox, Anaprox DS, EC-Naprosyn, EC-Naproxen, Naprelan, Naprosyn, Naproxen, Naproxen Sodium, Naproxen Sodium CR, Naproxen Sodium DS, Naproxen Sodium ER, Vi-movo, All Day Pain Relief
	Fenoprofen	Fenoprofen Calcium, Fenortho, Nalfon
	Ketoprofen	Ketoprofen, Ketoprofen Micronized
	Oxaprozin	Oxaprozin, Daypro
Salicylates	Aspirin	Adult Aspirin Regimen, Anacin, Ascriptin, Aspir-81, Aspir-Low, Aspirin, Aspirin EC, Bayer Chewable Aspirin, Butalbital-Aspirin-Caffeine, Butalbital Compound, Children's Aspirin, Ecotrin, Empirin, Excedrin Migraine, Extraprin, Farbital, Fiorinal, Headache Relief, Low-dose Aspirin, Low Dose Aspirin EC, Migraine Formula, Migraine Relief, Pain Reliever Plus, St. Joseph Aspirin, Yosprala, YSP Aspirin
	Salsalate	Diflunisal, Choline Mag Trisalicylate, Disalcid, Salflex, Salsalate
Preferential COX-2 inhibitors	Meloxicam	Meloxicam, Mobic, Vivlodex
	Etodolac	Etodolac, Etodolac ER, Lodine, Lodine XL
	Nabumetone	Nabumetone, Relafen
Selective COX-2 inhibitors	Celecoxib	Celebrex, Celecoxib
Indole derivatives	Sulindac	Clinoril, Sulindac
	Indomethacin	Indocin, Indocin SR, Indomethacin, Indomethacin ER, Tivorbex
Aryl acetic acid derivatives	Diclofenac	Arthrotec 50, Arthrotec 75, Cambia, Cataflam, Diclofenac Sodium, Diclofenac Sodium ER, Diclofenac Sodium-Misoprost, Diclofenac Potassium, Diclofenac Epolamine, Flector, Klofensaid II, Pennsaid, Zipsor, Zorvolex, Voltaren-XR
	Tolmetin	Tolmetin Sodium
	Ketorolac	Ketorolac Tromethamine, Sprix, Toradol
Anthranilic acid derivatives	Mefenamic acid	Mefenamic Acid, Meclofenamate Sodium, Ponstel
Oxicams	Piroxicam	Piroxicam, Feldene
Alkanone	Flurbiprofen	Flurbiprofen

NSAID, nonsteroidal antiinflammatory drug; COX, cyclooxygenase.

multivariable logistic regression to estimate the effect of NSAID receipt on delayed healing diagnosis among stress fracture cases. Covariates adjusted for in the model were age, sex, race/ethnicity, vitamin D deficiency, time in service, service branch, military occupation, and recruit status.

RESULTS

A total of 7,039 incident stress fracture cases were identified among active component service members from June 2014 through December 2018; however, 3 cases were excluded from the analysis because matched controls could not be identified. The cases excluded were an Asian female Marine and two additional females who were older than 45 years old. A total of 28,141 controls were selected, resulting in a total sample size of 35,177 **(Table 3)**. Among the cases, stress fractures occurred predominantly within the leg (54.0%). As a result of the matching process, the distribution of sex, race/ethnicity, age, service, and time in service was similar between cases and controls. Compared to controls, cases consisted of higher percentages of recruits (21.1% vs. 31.5%, respectively), enlisted personnel (89.1% vs. 94.4%, respectively), individuals with diagnosed vitamin D deficiency (0.6% vs. 6.5%, respectively), and NSAID receipt (17.5% vs. 22.9%, respectively). Propionic acid derivatives were the most common NSAIDs dispensed within the 30 to 180 days before the stress fracture diagnosis (for cases) or reference date (for controls) in the study population (16.7%), followed by preferential COX-2 inhibitors (1.6%) **(Table 3)**. Of the propionic acid derivatives, the most commonly dispensed drugs were ibuprofen (56.4%) and naproxen (27%) **(data not shown)**. In the final adjusted model, service members who received NSAIDs had an incidence of stress fracture diagnoses that was 1.70 times (95% CI: 1.58–1.82; p<.0001) that of those who had not received NSAIDs **(data not shown)**. When this model was restricted to the Army population, soldiers who

TABLE 3. Characteristics of stress fracture cases and matched controls at the time of matching, active component, U.S. Armed Forces, 30 June 2014–31 December 2018

	Case		Control		Total	
	No.	%	No.	%	No.	%
Total	7,036	20.0	28,141	80.0	35,177	100.0
Site						
Foot/toes	1,396	19.8	--	--	--	--
Leg	3,801	54.0	--	--	--	--
Pelvic region	1,305	18.6	--	--	--	--
Other/unspecified	534	7.6	--	--	--	--
Sex						
Male	4,490	63.8	17,960	63.8	22,450	63.8
Female	2,546	36.2	10,181	36.2	12,727	36.2
Age group (years)						
<20	2,359	33.5	9,503	33.8	11,862	33.7
20–24	2,710	38.5	10,883	38.7	13,593	38.6
25–29	1,096	15.6	4,290	15.2	5,386	15.3
30–34	439	6.2	1,720	6.1	2,159	6.1
35–39	245	3.5	1,005	3.6	1,250	3.6
40–44	118	1.7	468	1.7	586	1.7
45+	69	1.0	272	1.0	341	1.0
Race/ethnicity group						
Non-Hispanic white	4,056	57.7	16,224	57.7	20,280	57.7
Non-Hispanic black	1,201	17.1	4,802	17.1	6,003	17.1
Hispanic	1,191	16.9	4,764	16.9	5,955	16.9
Asian/Pacific Islander	332	4.7	1,328	4.7	1,660	4.7
American Indian/Alaska Native	59	0.8	235	0.8	294	0.8
Other/unknown	197	2.8	788	2.8	985	2.8
Service						
Army	4,196	59.6	16,783	59.6	20,979	59.6
Navy	684	9.7	2,736	9.7	3,420	9.7
Marine Corps	1,290	18.3	5,158	18.3	6,448	18.3
Air Force	866	12.3	3,464	12.3	4,330	12.3
Rank/grade						
Enlisted	6,645	94.4	25,075	89.1	31,720	90.2
Officer	391	5.6	3,066	10.9	3,457	9.8
Recruit status						
Yes	2,215	31.5	5,949	21.1	8,164	23.2
No	4,821	68.5	22,192	78.9	27,013	76.8
Military occupation						
Combat-specific[a]	1,085	15.4	4,091	14.5	5,176	14.7
Motor transport	260	3.7	884	3.1	1,144	3.3
Pilot/air crew	31	0.4	347	1.2	378	1.1
Repair/engineering	1,107	15.7	5,466	19.4	6,573	18.7
Communications/intelligence	1,223	17.4	5,786	20.6	7,009	19.9
Healthcare	625	8.9	2,785	9.9	3,410	9.7
Other/unknown	2,705	38.5	8,782	31.2	11,487	32.7
Time in service						
<4 months	4,785	68.0	19,137	68.0	23,922	68.0
4 months to <1 year	879	12.5	3,516	12.5	4,395	12.5
1 year to <3 years	1,037	14.7	4,148	14.7	5,185	14.7
3 to <5 years	321	4.6	1,284	4.6	1,605	4.6
≥5 years	14	0.2	56	0.2	70	0.2
Vitamin D deficiency						
Yes	459	6.5	176	0.6	635	1.8
No	6,577	93.5	27,965	99.4	34,542	98.2
NSAID receipt						
Yes	1,614	22.9	4,924	17.5	6,538	18.6
No	5,422	77.1	23,217	82.5	28,639	81.4
NSAID class						
Selective COX-2 inhibitors	56	0.8	183	0.7	239	0.7
Preferential COX-2 inhibitors	166	2.4	383	1.4	549	1.6
Fenamates	1	0.0	0	0.0	1	0.0
Oxicam derivatives	2	0.0	15	0.1	17	0.1
Propionic acid derivatives	1,439	20.5	4,433	15.8	5,872	16.7
Salicylates	14	0.2	53	0.2	67	0.2
Alkanones	0	0.0	1	0.0	1	0.0
Aryl acetic acid derivatives	80	1.1	240	0.9	320	0.9
Indole derivatives	25	0.4	63	0.2	88	0.3

[a]Infantry/artillery/combat engineering/armor.
No., number; NSAID, nonsteroidal antiinflammatory drug.

received NSAIDs had 1.64 times (95% CI: 1.49–1.80; p<0.0001) the incidence of stress fracture diagnosis compared to nonrecipients **(data not shown)**.

Of the 7,036 incident stress fracture cases identified in the first part of the study, 5,295 were diagnosed on or after 1 October 2015, after the transition to the ICD-10 coding system, and were included in the second part of the analysis **(Table 4)**. A total of 496 (9.4%) of these cases had a diagnosis for delayed healing within 90 days after the incident stress fracture diagnosis. Distribution of demographic and selected military characteristics among cases with and without delayed healing diagnoses were broadly similar, with the exception that a smaller percentage of delayed healing cases were among recruits (21.0% vs. 32.5%, respectively) and there was a greater percentage of diagnosed vitamin D deficiency among those with delayed healing diagnoses compared to those without (13.1% vs. 6.4%, respectively). In addition, a greater percentage of delayed healing fracture cases occurred among service members in the Air Force (16.7% vs 12.2%, respectively), among service members in communications/intelligence occupations (20.8% vs. 15.9%, respectively), and among service members with 1–3 years of time in service (25.4% vs 16.1%, respectively) compared to controls. In the final adjusted model, those stress fracture cases who received any NSAIDs had odds of a delayed healing diagnosis that were 1.41 times (95% CI: 1.12–1.77; p=.004) those of cases who did not receive any NSAIDs **(data not shown)**.

EDITORIAL COMMENT

This study found that active component service members who had previously received any NSAIDs experienced a 70% increased incidence in stress fracture diagnoses compared to those who had not received any NSAIDs. Studies of the risk of stress fracture after NSAID use have produced contradictory results. However, several studies suggest that NSAIDs increase risk of stress fractures, especially during times of intense physical training. One study conducted among U.S. Army

TABLE 4. Characteristics of stress fracture cases with and without delayed healing, active component, U.S. Armed Forces, 1 October 2015–31 December 2018

	Fracture cases with delayed healing		Fracture cases without delayed healing		Total	
	No.	%	No.	%	No.	%
Total	496	9.4	4,799	90.6	5,295	100.0
Site						
Foot/toes	106	21.4	1,068	22.3	1,174	22.2
Leg	291	58.7	2,615	54.5	2,906	54.9
Pelvic region	75	15.1	856	17.8	931	17.6
Other/unspecified	24	4.8	260	5.4	284	5.4
Sex						
Male	296	59.7	3,043	63.4	3,339	63.1
Female	200	40.3	1,756	36.6	1,956	36.9
Age group (years)						
<20	150	30.2	1,698	35.4	1,848	34.9
20–24	188	37.9	1,847	38.5	2,035	38.4
25–29	91	18.4	711	14.8	802	15.2
30–34	33	6.7	277	5.8	310	5.9
35–39	19	3.8	153	3.2	172	3.3
40–44	13	2.6	67	1.4	80	1.5
45+	2	0.4	46	1.0	48	0.9
Race/ethnicity group						
Non-Hispanic white	270	54.4	2,751	57.3	3,021	57.1
Non-Hispanic black	89	17.9	813	16.9	902	17.0
Hispanic	94	19.0	837	17.4	931	17.6
Asian/Pacific Islander	18	3.6	226	4.7	244	4.6
American Indian/Alaska Native	3	0.6	43	0.9	46	0.9
Other/unknown	22	4.4	129	2.7	151	2.9
Service						
Army	300	60.5	2,826	58.9	3,126	59.0
Navy	45	9.1	443	9.2	488	9.2
Marine Corps	68	13.7	946	19.7	1,014	19.2
Air Force	83	16.7	584	12.2	667	12.6
Rank/grade						
Enlisted	472	95.2	4,548	94.8	5,020	94.8
Officer	24	4.8	251	5.2	275	5.2
Recruit Status						
Yes	104	21.0	1,688	35.2	1,792	33.8
No	392	79.0	3,111	64.8	3,503	66.2
Vitamin D deficiency						
Yes	65	13.1	307	6.4	372	7.0
No	431	86.9	4,492	93.6	4,923	93.0
Military occupation						
Combat-specific[a]	71	14.3	707	14.7	778	14.7
Motor transport	22	4.4	184	3.8	206	3.9
Pilot/air crew	2	0.4	20	0.4	22	0.4
Repair/engineering	80	16.1	720	15.0	800	15.1
Communications/intelligence	103	20.8	762	15.9	865	16.3
Healthcare	46	9.3	431	9.0	477	9.0
Other/unknown	172	34.7	1,975	41.2	2,147	40.6
Time in service						
<4 months	258	52.0	3,206	66.8	3,464	65.4
4 months to <1 year	74	14.9	525	10.9	599	11.3
1 year to <3 years	126	25.4	771	16.1	897	16.9
3 to <5 years	36	7.3	285	5.9	321	6.1
≥5 years	2	0.4	12	0.3	14	0.3
NSAID receipt						
Yes	173	34.9	1,029	21.4	1,202	22.7
No	323	65.1	3,770	78.6	4,093	77.3
NSAID type						
Selective COX-2 inhibitors	6	1.2	36	0.8	42	0.8
Preferential COX-2 inhibitors	24	4.8	101	2.1	125	2.4
Fenamates	0	0.0	0	0.0	0	0.0
Oxicam derivatives	0	0.0	2	0.0	2	0.0
Propionic acid derivatives	145	29.2	930	19.4	1,075	20.3
Salicylates	2	0.4	10	0.2	12	0.2
Alkanones	0	0.0	0	0.0	0	0.0
Aryl acetic acid derivatives	8	1.6	52	1.1	60	1.1
Indole derivatives	6	1.2	12	0.3	18	0.3

[a]Infantry/artillery/combat engineering/armor.
No., number; NSAID, nonsteroidal antiinflammatory drug.

personnel found that risk of stress fractures was significantly higher in NSAID users, and that this risk increased among the recruits in basic combat training,[2] suggesting that NSAIDs do increase the risk for fractures, especially during times of intense physical training. In a previous retrospective cohort study of regular and incidental NSAID users and control patients, the relative rate for nonvertebral fractures was higher among regular NSAID users in comparison to the control patients.[6,7] However, there was no difference in rates of nonvertebral fractures between the regular and incidental users, which suggests that use of NSAIDs, not the duration of use, increases the risk for fractures.[6,7]

As a secondary objective, the current study examined whether dispensed NSAIDs were associated with diagnoses of delayed healing and found that stress fracture cases with previous NSAID receipt experienced 1.41 times the odds of a delayed healing diagnosis compared to nonrecipients. Previous animal and human studies have provided inconclusive evidence on the effect of NSAIDs on fracture healing.[7,9,10,13–25] Results of several studies suggest the effect of NSAIDs on healing may be different depending on the type of fractures and the timing of NSAID use.[7,10,11,15–17,22] Previous in vitro studies have found that NSAIDs inhibit the proliferation potential of osteogenic cells, deterring the differentiation of osteoblasts, which then prevents the formation of new bone.[9,30–35] This finding lends support to the hypothesis that NSAID use may delay bone healing since the inhibition of these osteogenic cells would result in reduced bone resorption and formation.

The current study was designed to replicate a case-control study by Hughes and colleagues that examined NSAID use and risk of stress fracture among Army members.[2] However, there were some key differences in the designs of this study and the current study. The current study used the same NSAID exposure definition; however, more classes of NSAIDs were included in the current analysis because literature has suggested that these drugs have an effect on osteoblast and osteoclast proliferation.[9,10,15,16,32–34] The current study used a case definition similar to that used by Hughes and colleagues with the exception

that pathological fractures were excluded to avoid any misclassification of fractures from illness.[10] The current study also randomly sampled controls by a 4:1 ratio, with risk-set matching on several demographic variables, while the Hughes and colleagues' study only matched on time in service. The stricter matching rules and shorter study period employed in the current study identified a smaller number of cases than in the reference study. Both studies had a potential for reverse causation because service members could have had prior NSAID use to treat the pain of a pre-clinical stress fracture. In an effort to minimize potential reverse causation, the current study did not consider NSAID use within 30 days before the reference date as exposure to NSAIDs. The reference study used the same rule after conducting a lagged analysis comparing 15-, 30-, and 45-day gaps between NSAID use and stress fracture-related encounter.[2] Based on their analysis, the reference study used a 30-day gap in the exposure definition.[2] The reference study found that NSAID receipt was associated with a 2.9 times increase in stress fracture risk for the Army population, while the current study found a 1.64 times increase in incidence of stress fracture when restricted to Army service members only **(data not shown).**[2] Although both studies demonstrated a statistically significant positive association between prior NSAID receipt and incident stress fracture, the reference study found a more pronounced association.

There are several limitations to the current study. Service members were included as exposed if they had received prescribed NSAIDs; however, medication adherence could not be measured. In addition, severity of stress fracture cannot be determined from administrative healthcare records. Furthermore, individuals may be misclassified as nonexposed if they took over-the-counter NSAIDs. In particular, it is likely the study did not capture instances of ibuprofen or aspirin self-medication for service members who used only over-the-counter drugs, which would not be reflected in Military Health System prescription records. Service members were considered exposed if they received NSAIDs 30 to 180 days before the reference date; however, for recruits, prescription data before basic training were not available, so this data gap may also have resulted in exposure misclassification.

Prospective studies are recommended to confirm the associations between prior receipt of NSAIDs and increased incidence of stress fractures and delayed bone healing and to reduce the possibilities of misclassification bias and reverse causation. If confirmed, these findings may have significant implications for military readiness because NSAIDs are used extensively and stress fractures are already a major contributor to the burden of healthcare encounters and lost duty time.[36,37] Treatment recommendations for stress fractures may need to be adapted to focus more heavily on preventive measures and ensuring adequate healing time with reduced emphasis on NSAID use for relieving pain and swelling symptoms.

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Brief Report

Diagnoses of Scarlet Fever in Military Health System (MHS) Beneficiaries Under 17 Years of Age Across the MHS and in England, 2013–2018

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Scarlet fever is an illness caused by infection with *Streptococcus pyogenes* that most commonly occurs in childhood (peak age = 7–8 years old). It is characterized by an erythematous, sandpaper-like rash due to one of several erythrogenic exotoxins produced by group A streptococci. Scarlet fever typically occurs with streptococcal pharyngitis but may rarely develop with skin or wound infections. Aside from the widespread rash, scarlet fever has the same sequelae and treatment as streptococcal pharyngitis without a rash. Cases typically follow a seasonal pattern, more commonly arising in late fall, winter, and spring. *S. pyogenes* has over 240 distinct serotypes based on M-protein serotype and the more discriminating M-protein gene sequencing (known as *emm* types).[1]

Because scarlet fever is a reportable disease in England, a large increase in incident cases was identified in 2014. This increase has continued to persist throughout the country. Public health surveillance identified a 3- to 4-fold increase in incidence of scarlet fever, which has significantly impacted schools and nurseries in the country.[2] Strains of *S. pyogenes* that were *emm* typed during this time period demonstrated a wide variety of M-protein gene sequences, but a new *emm1* strain ($M1_{UK}$) that is genotypically distinct from other pandemic *emm1* isolates has increased in prevalence in England as invasive streptococcal disease has also risen.[3,4] Although increased incidence of scarlet fever had been described in parts of Asia since 2008, England was the first European country to detect a sudden large-scale increase in cases, and this discovery has led to concern about similar widespread outbreaks occurring in other areas of the world.[2]

Scarlet fever is not a reportable disease in the U.S.,[5] and military surveillance currently does not routinely perform M-protein gene sequencing on group A streptococcus isolates. However, diagnoses of scarlet fever can be identified throughout the Military Health System (MHS) using International Classification of Diseases, 9th and 10th Revision (ICD-9 and ICD-10, respectively) codes. The objectives of this brief report were to review scarlet fever incidence in the MHS among patients under 17 years of age and to identify any large spikes in annual cases at military treatment facilities, particularly at the bases located in England.

METHODS

The surveillance period was 1 January 2013 through 31 December 2018. The surveillance population consisted of beneficiaries of the MHS who were under 17 years of age at the time of the incident diagnosis. Diagnoses of scarlet fever were ascertained from the Defense Medical Surveillance System, which includes administrative records of all medical encounters of individuals who received care in fixed (i.e., not deployed or at sea) medical facilities in the MHS or in civilian facilities when care was reimbursed by the MHS (i.e., purchased care). For surveillance purposes, an incident case of scarlet fever was defined by a qualifying ICD-9 or ICD-10 diagnosis code **(Table 1)** in any diagnostic position of a record of a hospitalization or an outpatient medical encounter. The incidence date was considered the date of the first hospitalization or outpatient medical encounter that included a case-defining diagnosis. An individual could be counted as an incident case of scarlet fever only once during the surveillance period; any beneficiary with a diagnosis of scarlet fever before the surveillance period was excluded from the analysis. Counts of scarlet fever diagnoses and incidence rates were calculated for each year of the surveillance period. Incidence rates were calculated as incident scarlet fever diagnoses per 10,000 person-years (p-yrs) and were stratified by selected demographic characteristics. Denominators for incidence rate calculations were calculated by identifying the number of beneficiaries who had at least 1 medical encounter during each year of the surveillance period. Diagnoses and incidence rates were calculated for the entire MHS in the primary analysis.

A secondary analysis was designed to identify a possible increasing trend in scarlet fever diagnoses in MHS beneficiaries receiving care in England during the surveillance period. For this analysis, cases were restricted to those who received a scarlet fever diagnosis at a facility located in England as identified through the Defense Medical Information System Identifier.

RESULTS

During the 6-year surveillance period, a total of 7,080 MHS beneficiaries under age 17 received an incident diagnosis of scarlet fever; 85 incident cases of scarlet fever were identified in MHS beneficiaries receiving care in England. A slightly greater proportion of cases was diagnosed among male beneficiaries, while the vast majority of cases occurred in beneficiaries under age 10 **(Table 2)**. Across all MHS beneficiaries, the greatest number of scarlet fever cases occurred in 2013 (n=1,366) and the lowest

TABLE 1. ICD-9 and ICD-10 codes used to identify scarlet fever cases

ICD-9 codes		ICD-10 codes	
034.1	Scarlet fever	A38.0	Scarlet fever with otitis media
		A38.1	Scarlet fever with myocarditis
		A38.8	Scarlet fever with other complications
		A38.9	Scarlet fever, uncomplicated

ICD, International Classification of Diseases.

TABLE 2. Counts and percentages of scarlet fever cases, by age and sex, all MHS beneficiaries and beneficiaries within England, 2013–2018

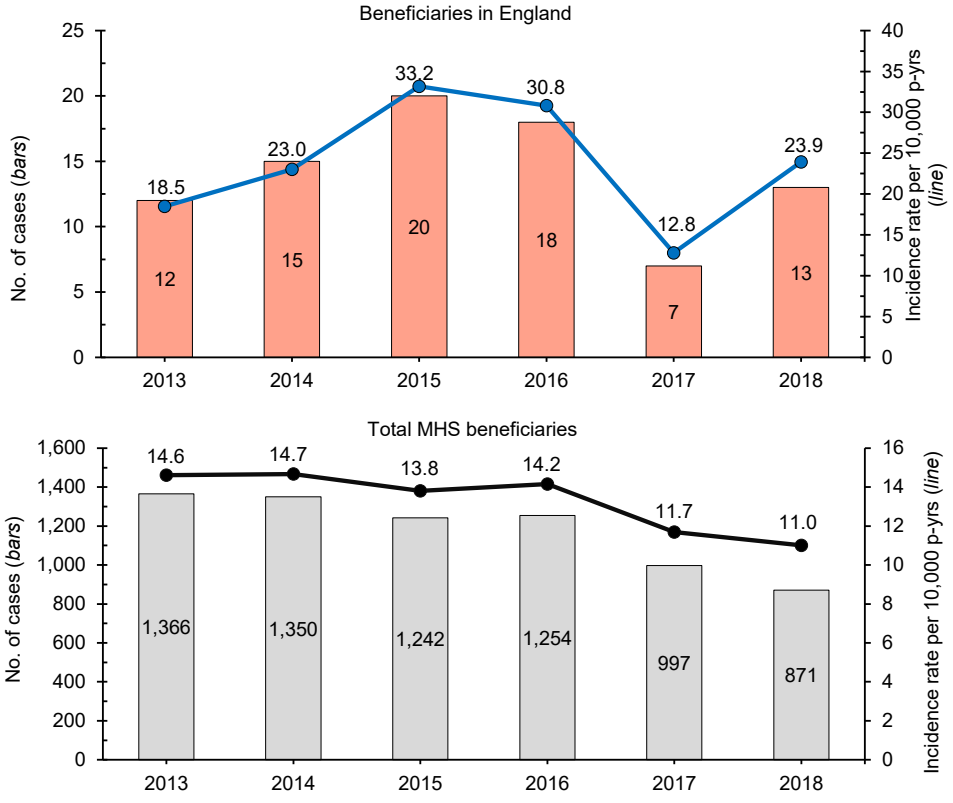
	All MHS		Within England	
	No.	%	No.	%
Total	7,080	100.0	85	100.0
Sex				
Female	3,035	42.9	39	45.9
Male	4,045	57.1	46	54.1
Age group (years)				
<5	3,170	44.8	51	60.0
5–9	3,429	48.4	33	38.8
10–14	430	6.1	1	1.2
15+	51	0.7	0	0.0

MHS, Military Health System; No., number.

number of cases occurred in 2018 (n=871). In contrast, in MHS beneficiaries receiving care in England, the greatest number of scarlet fever cases occurred in 2015 (n=20) and the lowest number of cases in 2017 (n=7) **(Figure).**

Across the MHS as a whole, crude annual incidence rates of scarlet fever diagnoses were relatively stable from 2013 through 2016 and then declined throughout the remainder of the surveillance period. In contrast, crude annual incidence rates among MHS beneficiaries in England increased almost 80% from 2013 through 2015. Subsequently, crude incidence rates declined slightly in 2016 to 30.8 cases per 10,000 p-yrs before declining to their lowest rates during the period in 2017. Rates increased again in 2018 to 23.9 cases per 10,000 p-yrs **(Figure).**

FIGURE. Numbers of incident cases and crude incidence rates of scarlet fever, by location, MHS beneficiaries under 17 years of age, 2013–2018



MHS, Military Health System; p-yrs, person-years.

EDITORIAL COMMENT

In 2014, England experienced a large and unexpected increase in cases of scarlet fever over the previous year, and the increase in cases continued unabated through 2018. Results of the current analysis suggest that a similar increase in cases was seen in MHS beneficiaries in England between 2013 and 2015 and again in 2018, although scarlet fever incidence rates across the entire MHS were relatively stable during the same period.

While this brief report demonstrates that MHS beneficiaries in England did have increased incidence of scarlet fever during a period while England was experiencing an outbreak, it is more difficult to interpret scarlet fever rates across the MHS. A comparison between rates in the entire MHS cohort and the MHS England cohort could be impacted by differential coding practices in England versus other locations in the MHS. Because scarlet fever is not a reportable illness in the U.S., physicians may be more likely to code a streptococcal illness (e.g., strep pharyngitis) and rash separately, rather than using a specific scarlet fever code. Future analyses of all streptococcal infection diagnoses could provide some clarification of this issue. In addition, it is likely that medical providers in England were aware of the ongoing outbreak there and thus more likely to detect and diagnose scarlet fever cases when they presented in American beneficiaries (i.e., detection bias).

Although the increase in incidence rates of scarlet fever in England is striking, it is important to recognize that the increase in the number of cases from year to year was relatively small. Only 85 cases were ascertained over 6 years among MHS beneficiaries in England, and the largest

increase in the absolute number of cases was 6 cases from 2017–2018. When the numbers of cases used to compute rates are small, those rates can have poor reliability. This significant limitation should be considered when interpreting these data. Another limitation is that denominators used in the calculation of incidence rates were based on the number of beneficiaries who sought care at least once during the year rather than the number of beneficiaries eligible for care. Therefore, the denominator used for these calculations is likely an underestimate of the true denominator.

Fluctuations in crude annual rates of scarlet fever are likely due to a number of factors that include the number and emergence of new strep A strains, how widely those strains may be circulating, and the degree of immunity to those strains in a susceptible population. One possible reason for the increase in England has been attributed to a new *emm1* strain of *S. pyogenes*,[3] but it is unclear whether, and to what extent, this may have impacted rates of scarlet fever in MHS beneficiaries. Laboratory surveillance of this and other emerging strains in military populations may be warranted.

Wherever DoD personnel and their families are stationed, they are at risk from infectious outbreaks in the local community and/or country. This brief report provides an example of the importance of monitoring local public health reports to provide optimal medical care to active duty members and MHS beneficiaries.

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MSMR's Invitation to Readers

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

In addition, the *MSMR* encourages the submission for publication of reports on evidence-based estimates of the incidence, distribution, impact, or trends of illness and injuries among members of the U.S. Armed Forces and other beneficiaries of the MHS. Information about manuscript submissions is available at www.health.mil/MSMRInstructions.

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

CORONAVIRUS: INFORMATION FOR DOD HEALTHCARE PROVIDERS AND PUBLIC HEALTH PROFESSIONALS

In response to the 2019 novel coronavirus outbreak, the Department of Defense (DoD) is following the guidance of, and disseminating authoritative information from, the U.S. Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). WHO has named the disease COVID-19 ("coronavirus disease 2019") and declared the outbreak to be a Public Health Emergency of International Concern. The outbreak virus has been named SARS-CoV-2.

DoD healthcare providers and public health professionals should use the wealth of information about the outbreak that can be found through the numerous URL links on the Military Health System (MHS) website at https://www.health.mil/News/In-the-Spotlight/Coronavirus.

SURVEILLANCE AND DISEASE REPORTING

Public health professionals are encouraged to refer to the DoD memorandum "Force Health Protection Guidance for the Novel Coronavirus Outbreak," dated 30 January 2020, particularly for the guidance on reportable medical events. To view the guidance, on the web page listed above, click on the link for "DoD guidelines."

Reports should be submitted through the Disease Reporting System internet (DRSi) for individuals considered to be persons under investigation (PUI) for the outbreak as well as for confirmed cases. CDC criteria for a PUI refer to a person with clinical signs of fever and/or lower respiratory illness and a history of risk of acquiring COVID-19 infection due to contact with a known case of the disease or travel from China. For the full definition of a PUI, see https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html#criteria-evaluation-pui.

All PUIs are to be reported by the installation public health officer via the DRSi in coordination with the service-specific public health chain of command, per the DoD force health protection guidance listed previously. Cases must also be reported to the supporting local or state health department. All DoD medical reporting entities should report COVID-19 PUIs in the DRSi as "COVID-19" and enter all available relevant information into the medical event report. COVID-19 PUIs reported to the DRSi should be classified as "suspect" until the laboratory results are available, at which point they should be classified as either "not a case" or "confirmed."

U.S. ARMY PUBLIC HEALTH CENTER (APHC) REPORTING GUIDANCE IS AVAILABLE AT
https://info.health.mil/hco/phealth/HealthS/Com%20Documents/Instruction%20for%20Reporting%202019-nCoV%20to%20DRSi_5FEB2020.pdf.

NAVY AND MARINE CORPS PUBLIC HEALTH CENTER (NMCPHC) GUIDANCE IS AVAILABLE AT
https://www.med.navy.mil/sites/nmcphc/program-and-policy-support/Pages/Novel-Coronavirus.aspx.

Skin Rashes in Children due to Infectious Causes

David R. Sayers, MD (Maj, USAF, MC); Leslie L. Clark, PhD, MS

In this issue of the *MSMR*, an overview of the incidence of scarlet fever in Military Health System beneficiaries under 17 years of age is presented.[1] The following provides a brief comparison of the characteristics of scarlet fever to other erythematous rashes associated with infectious diseases.

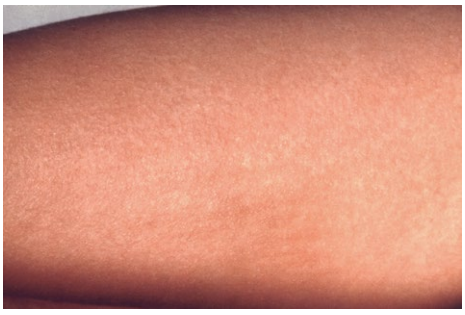
Scarlet fever

Scarlet fever **(Figure 1)** is caused by group A beta-hemolytic streptococcus bacteria.[2] The incubation period is generally 2–5 days with prodromal symptoms of fever, sore throat, abdominal pain, and vomiting for 12–48 hours. The rash typically starts on the face or neck and rapidly spreads to the whole body, including the hands and feet, and is characterized as red, maculopapular, rough lesions commonly referred to as a sandpaper rash. Areas of skin folding—such as the groin, armpits, elbows, and knees—will typically develop a darker redness than other areas with the rash. The duration of the rash is variable from a few days to about 1 week and may be followed by desquamation or peeling of the skin for 1–3 weeks. Associated clinical findings include tonsillitis with cervical lymphadenopathy and a strawberry tongue.[2,3]

Measles

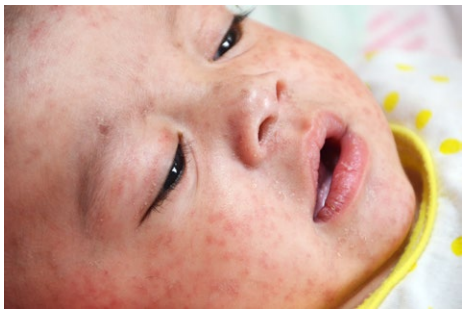
The rubeola virus is the etiologic agent for this infection **(Figure 2)**. After an incubation period of 8–12 days, prodromal symptoms of fever, cough, coryza, and conjunctivitis begin.[4] The rash appears 3–4 days after prodromal symptoms and begins around the ears and hairline on the face and spreads downward, covering the face, trunk, and arms by the second day. Initially the rash is red and maculopapular and becomes confluent by day 3. The rash typically lasts about 5 days and then fades in the same sequence as it appeared. Desquamation or peeling of the skin can follow the rash but does not occur on the palms or soles. The rash is not pruritic. Associated clinical findings include prodromal signs and Koplik spots **(Figure 3)** in the oral mucosa (white pinpoint-sized lesions with a reddened base).[2,4,5]

FIGURE 1. Scarlet fever



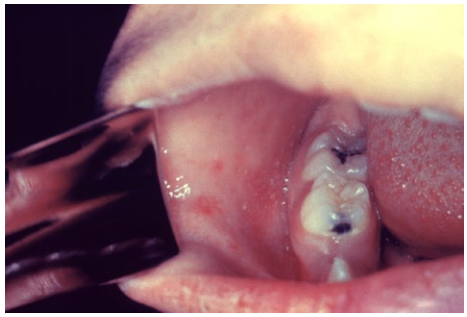
CDC

FIGURE 2. Measles



CDC/Jim Goodson, MPH

FIGURE 3. Measles (Koplik spots)

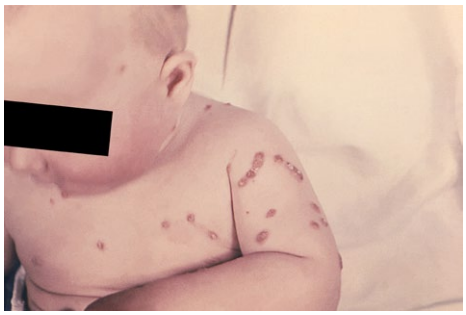


CDC/Jim Goodson, MPH

Varicella (chickenpox)

This disease **(Figure 4)** is caused by the initial infection with varicella-zoster virus. The incubation period is 14–16 days with a prodromal period of 0–2 days including fever, headache, malaise, abdominal pain, and decreased appetite. The rash may start on the chest, back, and face and then spreads over the whole body and is characterized by progression from vesicles in a teardrop shape that then crust and scab over. Patients typically have different stages of the rash on the body when examined. Usually within 24–48 hours, the vesicles progress to the crusting stage. All lesions progress to crusting by 5–10 days. The rash is very itchy. Associated clinical findings include high fever and lymphadenopathy.

FIGURE 4. Varicella (chickenpox)

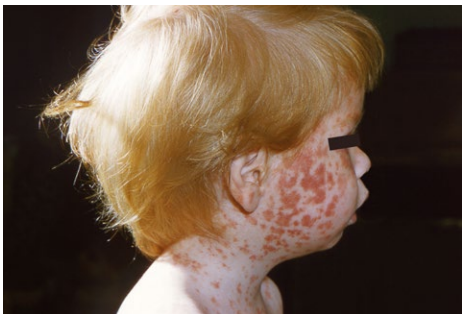


CDC/Susan Lindsley

Rubella (German measles)

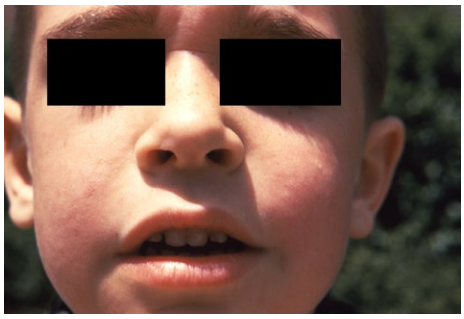
Rubella **(Figure 5)** is caused by the rubella virus and has an incubation period of 16–18 days with a prodromal period of 1–5 days before rash development, which consists of low-grade fever (less than 101°F), headache, conjunctivitis, malaise, lymphadenopathy, cough, and rhinorrhea.[6] The rash typically starts on the face and spreads to the extremities over the next 48 hours and appears as small, fine, maculopapular, pink lesions that tend not to coalesce as the measles rash does. Associated clinical findings include distinctive lymphadenopathy including posterior cervical, suboccipital, and posterior auricular nodes.[2,5]

FIGURE 5. Rubella (German measles)



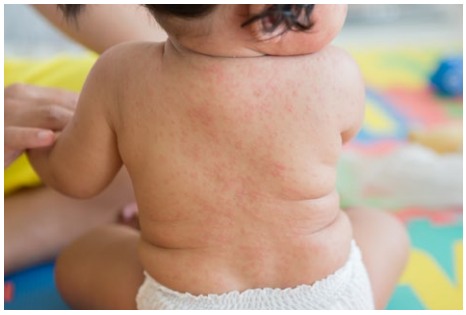
CDC

FIGURE 6. Erythema infectiosum



CDC

FIGURE 7. Roseola (exanthema subitum)



Erythema infectiosum

This illness **(Figure 6)** is caused by human parvovirus B19. The incubation period is 1–2 weeks, and a prodromal period lasts 2–5 days before the rash appears and consists of low-grade fever, coryza, headache, malaise, nausea, and diarrhea.[7] The first stage of the rash usually begins on the cheeks as a solid bright-red eruption with circumoral pallor, giving it a "slapped cheek" appearance. Over the next 1–4 days, the second stage of the rash develops, which is characterized by a maculopapular rash spreading to the trunk and extremities. If central clearing of the rash occurs, it will have a lacelike, reticular pattern. The rash is pruritic and typically fades over 1–3 weeks. Associated clinical conditions include arthropathy; transient aplastic crisis; chronic red cell aplasia; hydrops fetalis; and papular, pruritic eruptions on the hands and feet ("gloves and socks" syndrome).[2,5]

Roseola (exanthema subitum)

Human herpesvirus 6 (HHV-6) is the most common cause of this illness **(Figure 7)**, but other viral causes include HHV-7, enteroviruses, adenoviruses, and parainfluenza type 1. The incubation period is 5–15 days, and a prodromal period consists of high fevers (104–105°F) for 3–4 days.[8] Febrile convulsions may occur in young children. The rash appears as the fever resolves and begins on the chest and abdomen and spreads to the face and extremities and appears as small, separate, rose-pink, blanching, macular or maculopapular lesions. The rash typically resolves after 1–2 days without desquamation. The rash is not itchy. In addition to high fever, occipital adenopathy is a clinical finding along with the rash.[2,5]

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