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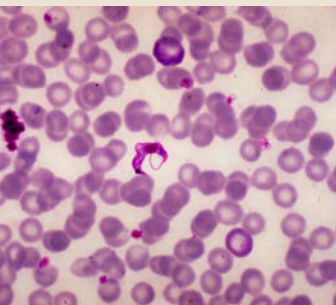
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Malaria infection remains an important health threat to U.S. service members who are located in endemic areas because of long-term duty assignments, participation in shorter-term contingency operations, or personal travel. In 2017, a total of 32 service members were diagnosed with or reported to have malaria, which is the lowest number of cases in any given year during the 10-year surveillance period. The relatively low numbers of cases during 2012–2017 mainly reflect decreases in cases acquired in Afghanistan, a reduction due largely to the progressive withdrawal of U.S. forces from that country. The percentage of cases of malaria caused by unspecified malaria species (53.1%; n=17) in 2017 was the highest during any given year of the surveillance period. The percentages of cases caused by *Plasmodium vivax* (15.6%; n=5), *P. falciparum* (25.0%; n=8), and by *P. malariae* (6.3%, n=2) remained similar to those of the preceding 4 years, although the numbers of cases decreased. Malaria was diagnosed at or reported from 19 different medical facilities in the U.S., Afghanistan, Qatar, Germany, Djibouti, Japan, and Korea. Providers of medical care to military members should be knowledgeable of, and vigilant for, clinical manifestations of malaria outside of endemic areas.

Globally, the annual incidence rate of malaria is estimated to have decreased by 18% between 2010 and 2016, from 76 to 63 cases per 1,000.¹ As a result of international efforts to control malaria during the past decade, many countries have reported substantial reductions in the numbers of malaria cases and deaths.² Despite these global reductions in malaria incidence and mortality rates, the World Health Organization estimated that there were 216 million cases of symptomatic malaria worldwide in 2016, an increase of about 5 million cases from 2015.¹ A total of 91 countries reported indigenous malaria cases in 2016, with countries in Africa accounting for around 90% of worldwide malaria cases and deaths.¹ The majority of these cases and deaths are due to mosquito-transmitted *Plasmodium falciparum* and occur 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} About 4% of estimated cases globally are due to *P. vivax*, but

outside the African continent the proportion of *P. vivax* infections is approximately 36%.¹

Since 1999, the *MSMR* has published periodic updates on the incidence of malaria among U.S. service members.^{3,4} 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).^{5,6} 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.⁷⁻¹⁵ 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.⁸⁻¹¹

MSMR malaria updates from the past 5 years documented that the annual case counts among service members after 2011 were the lowest in more than a decade.^{4,16-19} In particular, these updates showed that the numbers of cases associated with service in Afghanistan had decreased substantially in the past 5 years, presumably due to the dramatic reduction in the numbers of service members serving there. This update for 2017 uses methods similar to those employed in previous analyses to describe the epidemiologic patterns of malaria incidence in active and reserve component service members of the U.S. Armed Forces.

METHODS

The surveillance period was 1 January 2008 through 31 December 2017. The surveillance population included Army, Navy, Air Force, and Marine Corps active and reserve component members of the U.S. Armed Forces. The Defense Medical Surveillance System (DMSS) was searched to identify reportable medical events and hospitalizations (in military and nonmilitary 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 non-primary diagnosis of malaria due to a specific *Plasmodium* species; 4) a hospitalization record with a non-primary diagnosis of malaria plus a diagnosis of anemia, thrombocytopenia and related conditions, or malaria complicating pregnancy in any diagnostic position; or 5) a hospitalization record with a non-primary diagnosis of malaria plus diagnoses of signs or symptoms consistent with malaria (as listed in the *Control of Communicable Diseases Manual, 18th Edition*)²⁰ in each diagnostic position antecedent to malaria. The relevant ICD-9 and ICD-10 codes are shown in **Table 1**. Malaria diagnoses that were recorded only in the records of outpatient encounters (i.e., not hospitalized or reported as a notifiable event) were not considered case-defining for this analysis.

This analysis allowed one 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 was used to classify the *Plasmodium* species.

Presumed locations of malaria acquisition were estimated using a hierarchical algorithm: 1) cases hospitalized 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 to a malarious country were considered acquired in that country; and 5) cases diagnosed among service members who had been deployed to Afghanistan or Korea within 2 years prior to diagnosis were considered acquired in those respective countries. All remaining cases were considered acquired in unknown locations.

For the first time in the *MSMR* annual malaria update, a sensitivity analysis was conducted to determine the number and percentage of confirmed cases during 2017 that had documentation of a positive laboratory test in DMSS for malaria.

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

	ICD-9 codes	ICD-10 codes
Malaria (<i>Plasmodium</i> species)		
<i>P. falciparum</i>	084.0	B50
<i>P. vivax</i>	084.1	B51
<i>P. malariae</i>	084.2	B52
<i>P. ovale</i>	084.3	B53.0
Unspecified	084.4, 084.5, 084.6, 084.8, 084.9	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

In 2017, a total of 32 service members were diagnosed with or reported to have malaria (**Table 2**). That total was the lowest number of cases in any given year during the surveillance period (**Figure 1**). Of the total cases, 22 (68.8%) had records of laboratory tests performed for malaria and 17 (53.1%) had positive test results documented in DMSS. The percentage of cases of malaria caused by unspecified malaria species (53.1%; n=17) in 2017 was the highest during any given year of the surveillance period. The percentages of cases caused by *Plasmodium vivax* (15.6%; n=5), *P. falciparum* (25.0%; n=8), and *P. malariae* (6.3%, n=2) remained similar to those of the preceding 4 years, although the numbers of cases decreased (**Figure 1**).

Similar to 2016, the majority of U.S. military members diagnosed with malaria in 2017 were male (96.9%), active component members (81.3%), in the Army (75.0%), and in their 20s (56.3%) (**Table 2**).

Of the 32 malaria cases in 2017, more than one-third (34.4%) of the infections were considered to have been acquired in Africa (n=11); 28.1% (n=9) in unknown locations; 21.9% (n=7) in Afghanistan; and 15.6% (n=5) in Korea (**Figure 2**). There were no cases identified from South/Central America in 2017. One of the two cases of malaria due to *P. malariae* was reported to have been acquired in Afghanistan, and the other was acquired in an unknown location. Of the 11 malaria infections considered acquired in Africa in 2017, three were linked to Djibouti, two to Nigeria, two to Sierra Leone, and single cases were linked to Cameroon, Ghana, Guinea, and Liberia (**data not shown**).

During 2017, malaria cases were diagnosed or reported from 19 different medical facilities in the U.S., Germany, Korea, Afghanistan, Djibouti, Japan, and Qatar (**Table 3**). Two-fifths (40.0%) of the total cases with known locations of diagnosis were reported from or diagnosed outside the U.S., which is an increase from the almost one-quarter (24.0%) of cases in this category in 2016. The largest number of malaria cases associated with a single medical facility during 2017 was

TABLE 2. Malaria cases, by *Plasmodium* species and selected demographic characteristics, active and reserve components, U.S. Armed Forces, 2017

	<i>P. vivax</i>	<i>P. falciparum</i>	Unspecified or <i>P. malariae</i> ^a	Total	% of total
Component					
Active	5	6	15	26	81.3
Reserve/Guard	0	2	4	6	18.8
Service					
Army	4	7	13	24	75.0
Navy	0	1	4	5	15.6
Air Force	1	0	1	2	6.3
Marine Corps	0	0	1	1	3.1
Sex					
Male	5	7	19	31	96.9
Female	0	1	0	1	3.1
Age group					
<20	0	0	1	1	3.1
20–24	3	1	4	8	25.0
25–29	1	3	6	10	31.3
30–34	1	2	2	5	15.6
35–39	0	1	5	6	18.8
40–44	0	0	1	1	3.1
45+	0	1	0	1	3.1
Race/ethnicity					
Non-Hispanic white	1	2	11	14	43.8
Non-Hispanic black	1	4	5	10	31.3
Other	3	2	3	8	25.0
Total	5	8	19	32	100.0

^aThere were no cases of *P. ovale* identified in 2017.

four at the Naval Medical Center in Portsmouth, VA.

The percentage of Africa-acquired cases (34.4%; n=11) in 2017 was similar to the percentages of Africa-acquired cases observed in 2013 through 2016 (Figure 2). The percentage of Afghanistan-acquired cases (21.9%; n=7) in 2017 was the highest that it has been since 2013, but lower than the percentages observed during 2008–2012. The percentage of malaria cases acquired in Korea (15.6%; n=5) in 2017 was lower than percentages during 2014–2016 but higher than those during 2008–2013 (Figure 2).

During the period from 2008 through 2017, the majority of malaria cases were diagnosed or reported in the 6 months from the middle of spring to the middle of autumn in the Northern Hemisphere (Figure 3). In 2017, 75.0% (24 of 32) of malaria

cases among U.S. service members were diagnosed during May–October. This proportion is similar to the 70.3% (461 of 656) of cases diagnosed during the same 6-month intervals over the entire 10-year surveillance period. During 2008–2017, the proportions of malaria cases diagnosed or reported during May–October varied by region of acquisition: Korea (89.3%); Afghanistan (79.9%); Africa (56.8%); and South/Central America (50.0%) (data not shown).

EDITORIAL COMMENT

MSMR annual reports on malaria incidence among all U.S. services began in 2007. The current report and those of the previous 5 years document that the

lowest annual numbers of cases during the interval 2001–2017 were in the past 6 years, reaching a nadir of 32 in 2017. The next lowest annual number of malaria cases occurred in 2015 (n=35). Most of the marked decline in the past 6 years is attributable to the decrease in 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. 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. The finding that *P. falciparum* malaria was diagnosed in a quarter of the cases in 2017 further underscores the need for continued emphasis on prevention of this disease, given its potential severity and risk of death.

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*)²⁰ 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 incubation period can be remarkably long, ranging from 1 to 18 months.²¹

FIGURE 1. Numbers of malaria cases, by *Plasmodium* species and calendar year of diagnosis/report, active and reserve components, U.S. Armed Forces, 2008–2017

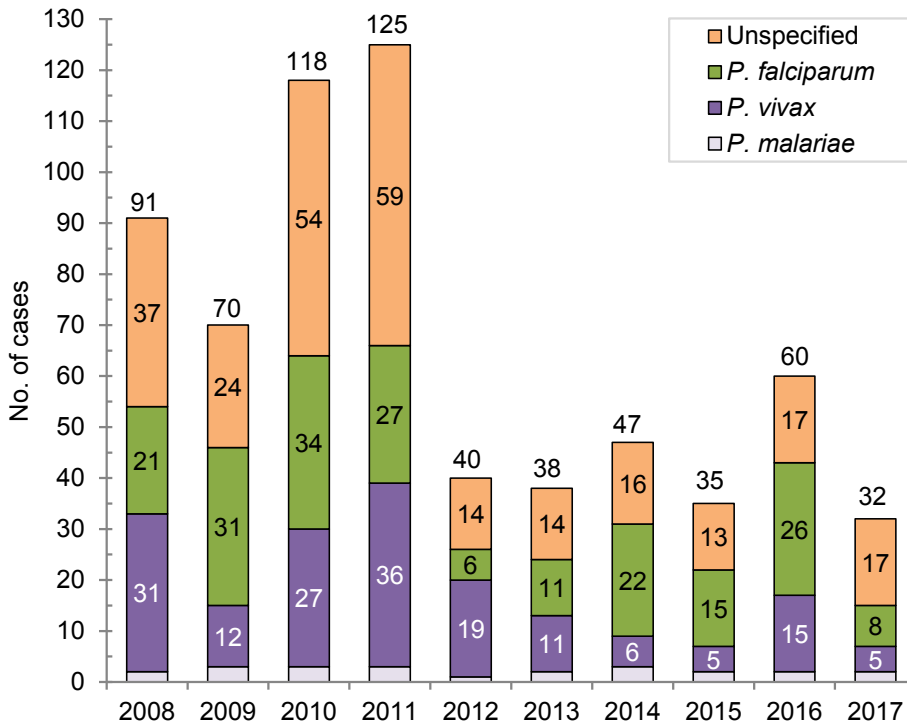
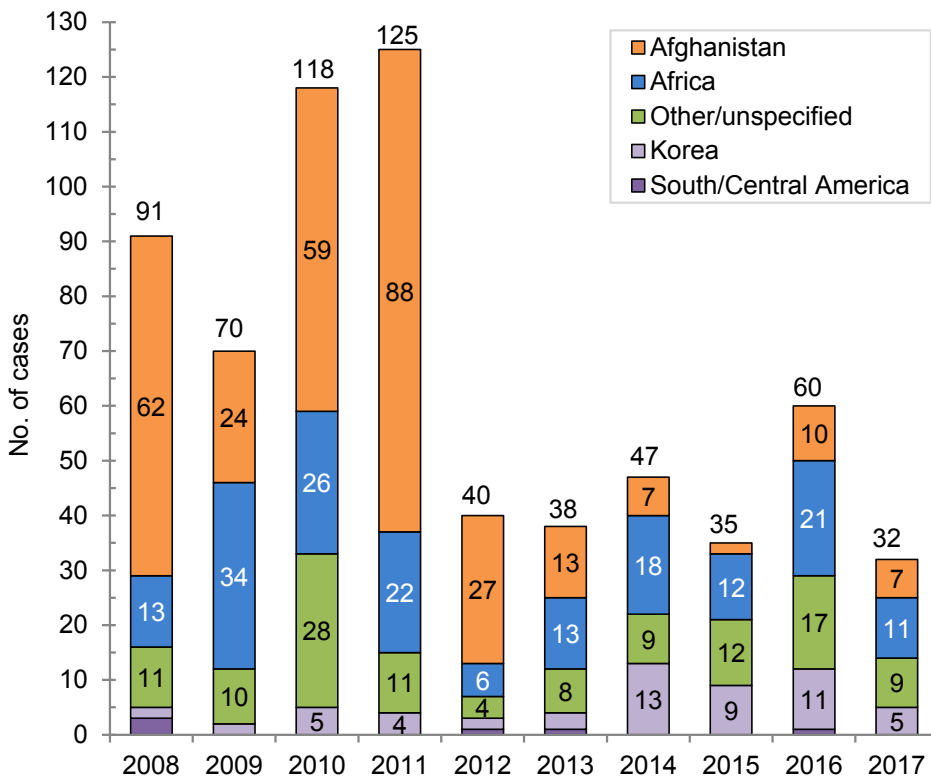


FIGURE 2. Annual numbers of cases of malaria associated with specific locations of acquisition, active and reserve components, U.S. Armed Forces, 2008–2017



On the other hand, compared to temperate climates, transmission of malaria in tropical regions such as sub-Saharan Africa is less subject to changes in temperature and depends more on other factors affecting mosquito breeding such as the timing of the rainy season and altitude (below 2,000 meters).²²

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. It is unclear why 47% of cases were missing positive confirmed laboratory tests. Possible reasons include false positives that were reported as confirmed reportable events, or laboratory tests that were performed by outsourced testing facilities. Furthermore, it should be noted that medical data from military treatment facilities that are using MHS GENESIS, which was implemented at different sites throughout 2017, are not available in DMSS. 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 one of these facilities are not captured in this report.

A review of the series of *MSMR* reports on malaria reveals that the annual counts of cases for the most recent year have often been revised upward when the data analyses are repeated for subsequent updates. For example, this update reports 35 cases for 2015, but the original count in the update for that year reported 30 cases. Similarly, the original count of 38 cases for 2012 was revised upward to 40 cases the following year. It is possible that future analyses will find more than the 32 cases associated with 2017 reported in this update. Additionally, only malaria infections that resulted in hospitalizations in fixed facilities or were reported as notifiable medical events were considered cases for this report. Infections that were treated only in outpatient settings and not reported as notifiable events were not included as cases. Also, the locations of infection acquisitions were estimated

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, 2017

Location where diagnosed or reported from	Presumed location of infection acquisition						% of total 2017 cases
	Korea	Afghanistan	Africa	South/Central America	Other or unknown location	Total for location of diagnosis or report	
Naval Medical Center Portsmouth, VA	0	0	1	0	3	4	12.5
Army Community Hospital, Fort Campbell, KY	0	0	0	0	3	3	9.4
Carl R. Darnall Army Medical Center, Fort Hood, TX	0	1	2	0	0	3	9.4
Brian Allgood Army Community Hospital, Seoul, Korea	3	0	0	0	0	3	9.4
Location not reported	0	1	1	0	0	2	6.3
455th Air Expeditionary Wing, Bagram Air Force Base, Afghanistan	0	2	0	0	0	2	6.3
Expeditionary Medical Facility, Djibouti	0	0	2	0	0	2	6.3
Bassett Army Community Hospital, Fort Wainwright, AK	1	0	0	0	0	1	3.1
Naval Medical Center, San Diego, CA	0	0	1	0	0	1	3.1
Kimbrough Ambulatory Care Center, Fort Meade, MD	0	0	1	0	0	1	3.1
99th Medical Group, Nellis Air Force Base, NV	0	1	0	0	0	1	3.1
Moncrief Army Health Clinic, Fort Jackson, SC	0	0	1	0	0	1	3.1
Dilorenzo Health Clinic, DC	0	0	0	0	1	1	3.1
87th Medical Group, Joint Base McGuire-Dix-Lakehurst, NJ	0	0	0	0	1	1	3.1
Guthrie Ambulatory Health Care Clinic, Fort Drum, NY	0	0	1	0	0	1	3.1
Landstuhl Regional Medical Center, Germany	0	1	0	0	0	1	3.1
Naval Hospital Yokosuka, Japan	0	0	0	0	1	1	3.1
Grafenwoehr Army Health Clinic, Germany	0	0	1	0	0	1	3.1
Camp Casey, Tongduchon, Korea	1	0	0	0	0	1	3.1
379th Air Expeditionary Wing, Al Udeid Air Base, Qatar	0	1	0	0	0	1	3.1
Total	5	7	11	0	9	32	

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 2017 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

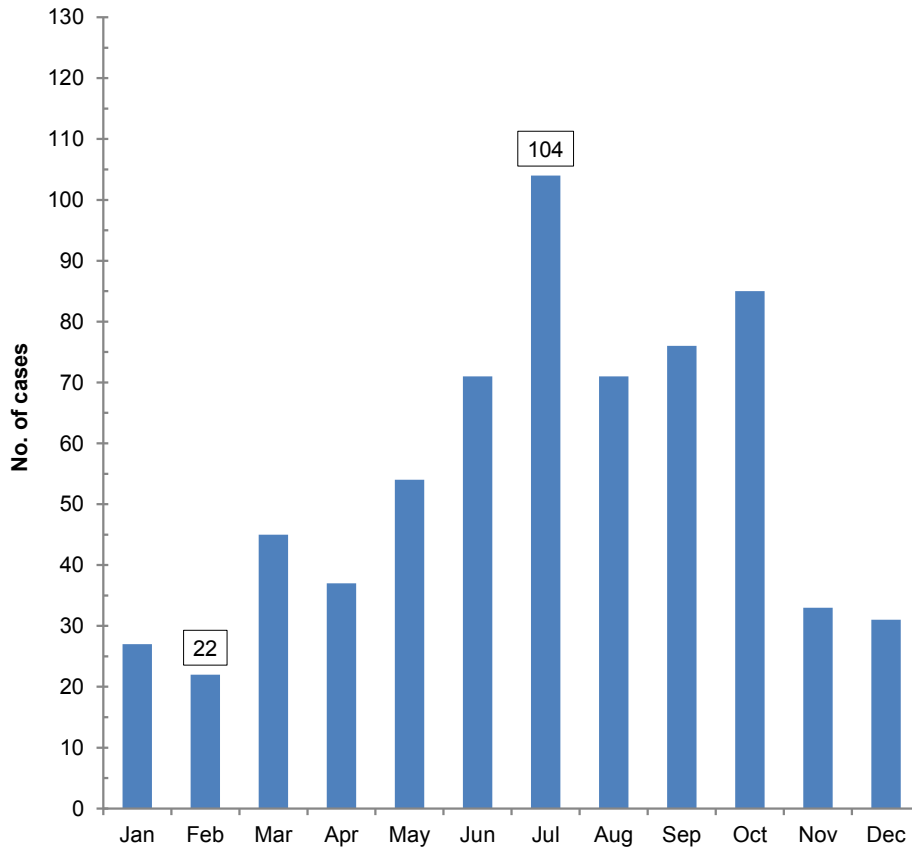
diagnosis) and initiating treatment (particularly when *P. falciparum* malaria is clinically suspected).

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, and primaquine.²³

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FIGURE 3. Cumulative numbers of diagnoses and reported cases of malaria, by month of clinical presentation or diagnosis, active and reserve components, U.S. Armed Forces, January 2008–December 2017



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Surveillance for Vector-borne Diseases Among Active and Reserve Component Service Members, U.S. Armed Forces, 2010–2016

Francis L. O'Donnell, MD, MPH (COL, Ret., USA); Shauna Stahlman, PhD, MPH; Michael Fan, PhD

This report summarizes available health record information about the occurrence of vector-borne infectious diseases among members of the U.S. Armed Forces during a recent 7-year surveillance period. Information about confirmed, possible, and suspected cases was obtained from electronic reports of reportable medical events (RMEs) and records of diagnoses documented during hospitalizations and outpatient healthcare encounters. Lyme disease and malaria were the most common diagnoses among confirmed and possible cases. Diagnoses of chikungunya and Zika were elevated in the years following their respective entries into the Western Hemisphere. Large numbers of diagnoses of arboviral diseases were recorded in the category of suspected cases, but the overwhelming majority were associated with coding errors and tentative diagnoses not subsequently confirmed. For many confirmed cases, documentation could not be found in healthcare databases for positive laboratory tests that would be the basis for confirmation. Discussion covers the limitations of the available data and the importance to surveillance of RMEs, confirmatory laboratory tests, and accurate recording of diagnoses and their codes.

Although infectious diseases pose a threat to the health of all human beings, the levels of risk can, at times, be increased for military service members. Factors that may increase the risks of infectious diseases for service members include exposure to climatic extremes; conduct of military operations in field settings where food, water, and sanitary conditions are less than optimal; and exposure to reservoirs and vectors of infectious disease in locations where military training and operations are conducted. Once the role of microorganisms in causing human disease was discovered and methodically studied, it became apparent that one pathway through which humans acquire infectious diseases is transmission of pathogens by arthropod vectors. The organized response to the threat of such illnesses included generations

of study by medical scientists who helped elucidate the role of such vectors and who developed preventive strategies.

Within the U.S. Armed Forces, considerable effort has been applied to the prevention and treatment of vector-borne diseases. A key component of that effort has been the surveillance of vector-borne diseases to inform the steps needed to identify where and when threats exist and to evaluate the impact of preventive measures. Although such surveillance can be focused on the study of the arthropods themselves, this report summarizes the findings of an analysis of available health record information about the occurrence of vector-borne infectious diseases among members of the U.S. Armed Forces during a recent 7-year surveillance period.

METHODS

The surveillance period was 1 January 2010 through 31 December 2016. The surveillance population included all active and reserve component service members in the Army, Navy, Air Force, or Marine Corps who served at any time during the period and who accessed care through either a military medical facility/provider or a civilian facility/provider (if paid for by the Military Health System). All data used to ascertain cases for this analysis were derived from the electronic records of the Defense Medical Surveillance System (DMSS). It is Department of Defense (DoD) policy that cases of certain specified medical conditions and events of public health importance shall be reported electronically through military health channels for surveillance purposes.¹ Conditions covered by this policy are referred to as reportable medical events (RMEs). The content of such electronic reports is stored in the databases of the DMSS. The vector-borne diseases that are the focus of this report are listed in **Table 1**. Almost all vector-borne diseases of concern for military service members are designated as RMEs. Cases of babesiosis, bartonellosis, and sandfly fever are not required to be reported.

For this analysis, a “confirmed” case was defined as an individual identified through an RME report of a vector-borne disease that was described as “confirmed” by having met specified laboratory or epidemiologic criteria.¹ A “possible” case was defined by a record of hospitalization with a diagnosis for a vector-borne disease (**Table 1**) in any diagnostic position. A “suspected” case was defined by either: 1) an RME of a vector-borne disease without laboratory or epidemiologic confirmation; or 2) a record of an outpatient medical

TABLE 1. ICD-9 and ICD-10 diagnostic codes used for classification of possible and suspected vector-borne diseases

Vector-borne disease	ICD-9	ICD-10
Arboviral diseases, neuroinvasive and non-neuroinvasive	062.*, 063.*, 064.*, 066.1–066.2, 066.4–066.9	A83.*–A84.*, A85.2, A93.0, A93.2–A93.8, A94
Eastern equine encephalitis	062.2	A83.2
Australian (Murray Valley) encephalitis, Oropouche virus	062.4, 062.8–062.9	A83.4, A93.0
California virus encephalitis	062.5	A83.5
Japanese encephalitis	062.0	A83.0
Tick-borne encephalitis	063.*	A84.0–A84.1, A84.9
Western equine encephalitis	062.1	A83.1
St. Louis encephalitis	062.3	A83.3
West Nile virus	066.4*	A92.3*
Other mosquito-borne viral fever	066.3	A92.1–A92.2, A92.8–A92.9
Chikungunya	-	A92.0
Rift Valley fever	-	A92.4
Zika virus infection	-	A92.5
Hemorrhagic fevers	065.*	A98.0–A98.2
Crimean-Congo HF	-	A98.0
Omsk HF	-	A98.1
Kyasanur Forest disease	-	A98.2
Dengue	061	A90, A91
Ehrlichiosis/anaplasmosis	082.4*	A77.4*
Filariasis	125.*	B72, B73.*, B74.*
Leishmaniasis	085.*	B55.*
Lyme disease	088.81	A69.2*
Malaria	084.0–084.6, 084.8–084.9	B50.*–B54.*
Plague	020.*	A20.*
Relapsing fever	087.*	A68.*
Rocky Mountain spotted fever	082.0–082.3, 082.8–082.9	A77.0–A77.3, A77.8–A77.9
Trypanosomiasis	086.*	B56.*–B57.**
Tularemia	021.*	A21.*
Typhus	080, 081.0, 081.1, 081.2, 081.9	A75.*
Yellow fever	060.*	A95.*
Babesiosis - Not an RME	088.82	B60.0
Bartonellosis - Not an RME	088.0	A44.*
Sandfly fever - Not an RME	066.0	A93.1

RME, reportable medical event

encounter with a diagnosis of a vector-borne disease in the first or second diagnostic position.

An individual could be counted once per lifetime for each type of vector-borne disease. For example, an individual could be counted once for malaria and once for leishmaniasis during the surveillance period. Individuals diagnosed as a case prior to the start of the surveillance period were excluded. Confirmed cases were prioritized over possible and suspected cases, respectively. A sensitivity analysis was conducted to determine the number and percentage of confirmed cases that had documentation of a positive laboratory test in DMSS for the given vector-borne disease.

Laboratory records for all confirmed cases of vector-borne diseases except for Lyme disease and malaria were reviewed. Because of the large number of confirmed cases of Lyme disease and malaria, a 10% random sample of Lyme cases (n=68) and a 20% random sample of malaria cases (n=70) were reviewed for documented laboratory tests.

RESULTS

For the 7-year surveillance period, DMSS records had documentation of 1,436 confirmed cases of vector-borne diseases, 536 possible cases, and 8,667 suspected cases among service members of the active and reserve components (**Table 2**). Active component service members comprised 84% of confirmed cases, 67% of possible cases, and 72% of suspected cases. Of all 22 types of vector-borne diseases that were sought in DMSS records, 14 different diseases were reported among the confirmed cases. Seventeen different diagnoses were named among possible cases, and 21 diagnoses were identified among the suspected cases (**Table 2**).

Confirmed cases

Lyme disease (n=721) contributed by far the largest proportion (50%) of confirmed vector-borne disease cases. Malaria (n=346), dengue (n=86), chikungunya

(n=78), and Rocky Mountain spotted fever (n=64) were the next most common incident confirmed cases occurring during the surveillance period (Table 2). These five most common types of confirmed cases together comprised 90% of all confirmed cases. There were no confirmed incident cases of other mosquito-borne viral fever, hemorrhagic fevers, filariasis, plague, yellow fever, babesiosis, bartonellosis, or sandfly fever (Table 2).

On average, 44.5% of confirmed cases (excluding Lyme disease and malaria) had the performance of a laboratory test documented for the vector-borne disease of interest and 35.9% had a documented positive laboratory result (Table 3). Positive laboratory results were more commonly available for service members diagnosed with Rocky Mountain spotted fever (79.7%) and arboviral diseases (57.9%). For the random sample of 68 confirmed cases of Lyme disease, 79.4% had documentation of a laboratory test having been performed and 69.1% had documentation of a positive laboratory test. For the random sample of 70 malaria cases, 64.3% had documentation of a laboratory test having been performed and 51.4% had documentation of a positive laboratory test.

Possible cases

Lyme disease (n=129), malaria (n=122), dengue (n=79), neuroinvasive and non-neuroinvasive arboviral diseases (n=67), and Rocky Mountain spotted fever (n=54) were the most common possible cases (diagnoses during hospitalizations) identified during the surveillance period (Table 2). These five diseases accounted for 84.1% of all possible cases. There were no possible cases of chikungunya, Rift Valley fever, Zika virus infection, yellow fever, or sandfly fever.

Suspected cases

The diagnosis with the largest number of suspected cases (RME reports of diagnoses not described as “confirmed” and diagnoses recorded during outpatient encounters) was Lyme disease (n=3,268) (Table 2). There were 3,100 suspected cases of “arboviral disease, neuroinvasive and non-neuroinvasive” during the surveillance period.

TABLE 2. Numbers of confirmed, possible, and suspected cases of vector-borne diseases, active and reserve components, U.S. Armed Forces, 2010–2016

	Confirmed cases			Possible cases			Suspected cases		
	AC	RC	AC+RC	AC	RC	AC+RC	AC	RC	AC+RC
Lyme disease	629	92	721	76	53	129	1,904	1,364	3,268
Malaria	306	40	346	96	26	122	339	136	475
Dengue	68	18	86	52	27	79	110	65	175
Chikungunya	32	46	78	–	–	–	8	10	18
Rocky mountain spotted fever	55	9	64	42	12	54	282	167	449
Zika virus infection	37	15	52	–	–	–	22	4	26
Arboviral diseases, neuroinvasive and non-neuroinvasive	18	1	19	42	25	67	2,778	322	3,100
Ehrlichiosis/anaplasmosis	13	1	14	22	11	33	70	58	128
Leishmaniasis	32	1	33	8	1	9	104	37	141
Trypanosomiasis	9	1	10	1	–	1	62	15	77
Tularemia	5	–	5	2	1	3	10	6	16
Relapsing fever	3	–	3	4	7	11	111	50	161
Typhus	2	2	4	4	–	4	19	8	27
Rift Valley fever	1	–	1	–	–	–	–	–	–
Babesiosis	–	–	–	5	3	8	27	49	76
Hemorrhagic fevers	–	–	–	3	4	7	30	8	38
Other mosquito-borne viral fever	–	–	–	2	3	5	204	84	288
Bartonellosis	–	–	–	2	–	2	16	15	31
Filariasis	–	–	–	–	1	1	22	25	47
Plague	–	–	–	–	1	1	17	9	26
Yellow fever	–	–	–	–	–	–	81	16	97
Sandfly fever	–	–	–	–	–	–	2	1	3
Total	1,210	226	1,436	361	175	536	6,218	2,449	8,667

AC, active component; RC, reserve component

Other relatively frequent suspected cases were malaria (n=475), Rocky Mountain spotted fever (n=449), and “other mosquito-borne viral fever” (n=288). The five most common suspected cases accounted for 87.5% of all suspected cases of vector-borne diseases. The only vector-borne disease of interest for which there was no suspected case was Rift Valley fever (Table 2).

Lyme disease

Lyme disease was the most common diagnosis recorded in the categories of confirmed, possible, and suspected cases. The annual numbers of confirmed cases were highest in 2011 and 2012 and the fewest

cases were reported in 2015 (Figure 1). The trends over time were similar for confirmed and suspected cases, but no such trend was evident for possible (hospitalized) cases (data not shown).

Chikungunya

Of the 78 confirmed cases of chikungunya, 64 were reported during the peak year 2014. There were no confirmed, possible, or suspected cases of chikungunya before 2014 (data not shown). Fifty of the confirmed cases were reported from Puerto Rico and 43 of those cases affected members of the National Guard (n=35) and Reserves (n=8). Only four of the cases in

TABLE 3. Proportions of confirmed cases of vector-borne diseases that had records of laboratory results in the Defense Medical Surveillance System (DMSS), active and reserve components, U.S. Armed Forces, January 2010–December 2016

	No. of confirmed cases	% with laboratory test performed	% with positive laboratory result
Lyme disease ^a	68	79.4	69.1
Dengue	86	44.2	30.2
Chikungunya	78	65.4	50.0
Rocky Mountain spotted fever	64	79.7	79.7
Zika virus infection	52	69.2	55.8
Arboviral diseases, neuroinvasive and non-neuroinvasive	19	73.7	57.9
Ehrlichiosis/anaplasmosis	14	71.4	50.0
Leishmaniasis	33	12.1	9.1
Malaria ^a	70	64.3	51.4
Trypanosomiasis	10	60.0	40.0
Tularemia	5	0.0	0.0
Relapsing fever	3	33.3	33.3
Typhus	4	25.0	25.0
Rift Valley fever	1	0.0	0.0

^aRandom samples of 68 (10%) Lyme disease cases and 70 (20%) malaria cases were checked for laboratory tests.

Puerto Rico occurred in members of the Air Force; all other cases were among Army personnel (**data not shown**).

Zika virus infection

All 52 confirmed cases of Zika virus infection were reported in 2016. All but one of the 26 suspected cases were documented in 2016. Medical facilities in Puerto Rico and Florida diagnosed nine of the confirmed cases and 10 of the suspected cases (**data not shown**). Of the 26 suspected cases of Zika virus infection identified, only three were based on outpatient diagnoses following the introduction of the ICD-10 diagnostic code specific to Zika in October 2015. The other 23 suspected cases were based on reports of RMEs that did not specify sufficient information to conclude that the diagnosis was confirmed (**data not shown**).

Rocky Mountain spotted fever

Among those vector-borne diseases considered to have been endemic in the U.S. for many years, Rocky Mountain spotted fever was the second most common (after Lyme disease) among confirmed

(n=64), possible (n=54), and suspected (n=449) cases (**Table 2**). The current RME guidelines include Rocky Mountain spotted fever in the broader category of Spotted Fever Rickettsiosis.¹

Dengue

Of the 86 confirmed cases of dengue, 30 were reported from facilities outside the continental U.S. (OCONUS), with the largest numbers reported from Honduras (n=12), Puerto Rico (n=8), and Japan (n=5). Of the 79 possible cases of dengue, 23 were hospitalized OCONUS and the largest numbers were associated with Japan (n=7), Puerto Rico (n=5), and South Korea (n=3) (**data not shown**).

Malaria

About one-third (32.1%; n=111) of the 346 confirmed cases of malaria were reported from OCONUS (**data not shown**). Of these 111 OCONUS cases, 48 cases (43.2%) were reported from Afghanistan, 28 from Germany (25.2%), and 20 were reported from South Korea (18.0%). Of the 122 possible (hospitalized) cases, 11 were

diagnosed in Germany and five in South Korea. The overwhelming majority (n=85) were diagnosed in CONUS (**data not shown**). Among the 122 possible cases, the hospital records of 100 of them contained a specific ICD-9 or ICD-10 code for malaria in the first diagnostic position (**data not shown**). The highest numbers of possible cases of malaria were documented in 2010 (n=25) and 2011 (n=36), but the counts in subsequent years were much lower (**Figure 2**).

Leishmaniasis

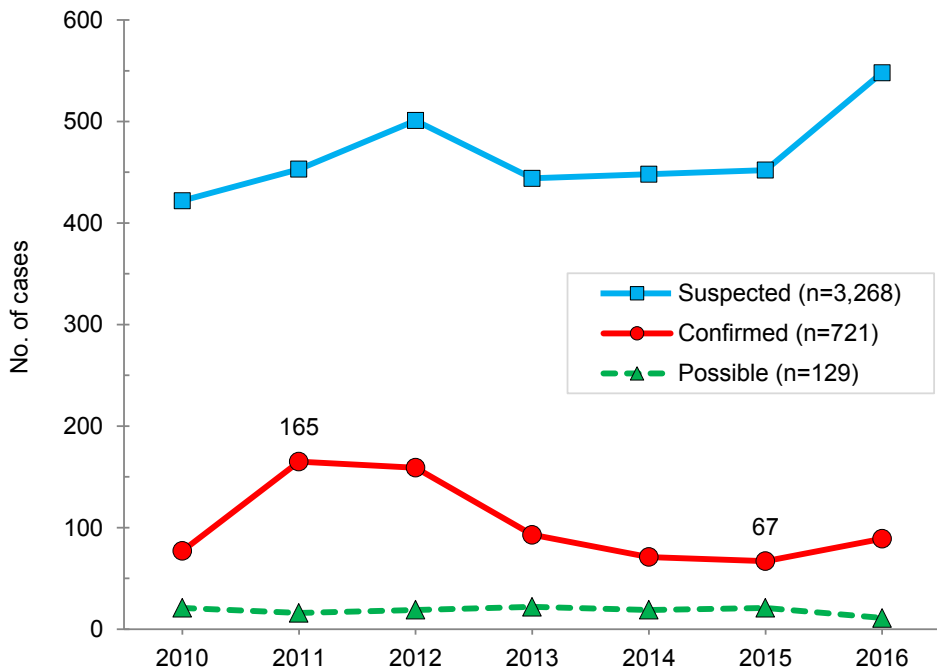
During 2010–2016, 29 of the 33 confirmed cases of leishmaniasis were reported before 2013 and eight of the nine possible cases were documented before 2013. Of the 141 suspected cases, 94 were recorded before 2013 (**data not shown**).

Arboviral diseases, neuroinvasive and non-neuroinvasive

The category of arboviral diseases, neuroinvasive and non-neuroinvasive, used in this analysis consisted of those diseases grouped together in the DoD Guidelines for RMEs and specified in the ICD-9 and ICD-10 coding systems (**Table 1**).¹ The only specific diagnoses in this grouping for which there were confirmed cases were West Nile virus (n=16) and St. Louis encephalitis (n=1). Two other confirmed cases were not identified specifically (**data not shown**).

Approximately 83% (n=2,577) of the 3,100 suspected cases of arboviral disease were specified to be diagnoses of Japanese encephalitis (JE) (**data not shown**). Of the suspected cases of JE, 759 were documented in outpatient records in which the code in the first diagnostic position was 062.0 (Japanese encephalitis). Among these 759 records, 539 had no code in the second diagnostic position. For the rest of the 759 records, the second position contained either a code for anthrax disease (n=11) or a V-code for “need for prophylactic immunization” (n=209). For another 1,778 suspected cases, the code for JE was in the second diagnostic position and the codes in the first diagnostic position were for either anthrax (n=75), tuberculin skin test (n=18), “need for prophylactic immunization”

FIGURE 1. Numbers of confirmed, possible, and suspected cases of Lyme disease, by calendar year of diagnosis/report, active and reserve components, U.S. Armed Forces, 2010–2016



(n=301), or general medical examination (n=1,384). A total of 1,321 of these suspected cases were recorded at one military installation during 2012–2014, including 1,122 in 2014 alone. Given the nature of the accompanying recorded codes, the code for JE disease was likely erroneously used to denote administration of JE vaccine (data not shown).

Other mosquito-borne viral fever

This ICD category includes a variety of specific diagnoses. The only confirmed cases from this category during 2010–2016 were chikungunya, Zika virus infection, and Rift Valley fever. None of those conditions had a specific ICD code until the implementation of the ICD-10 coding system in October 2015. Before that time, DoD had distributed guidance to report, via the RME system, cases of chikungunya (guidance effective July 2014) and Zika virus infection (guidance effective May 2016).^{2,3} Both conditions were added to the formal RME list of reportable conditions in July 2017.¹

Review of the single RME report of a case of Rift Valley fever suggested that the individual had a travel history limited to

Puerto Rico and the eastern U.S. Because there was also no laboratory confirmation of the diagnosis in DMSS records, the accuracy of this diagnosis of Rift Valley fever is uncertain (data not shown).

EDITORIAL COMMENT

The finding that Lyme disease was, by far, the most common confirmed vector-borne disease among members of the U.S. Armed Forces is consistent with Centers for Disease Control and Prevention surveillance reports that the disease is also the most common vector-borne disease in the U.S., with an estimated 300,000 cases per year.⁴ Previous *MSMR* reports have indicated that the incidence of Lyme disease among service members rose between 2001 and 2010 but was relatively stable among other Military Health System beneficiaries during that period. Other *MSMR* reports describe Lyme disease incidence, its geographic distribution, clinical presentation, and tick vectors.⁵⁻⁹

Chikungunya first became established in the Western Hemisphere in December

2013.¹⁰ In 2014 and 2015, the infection spread throughout most of the hemisphere, with more than 2 million suspected cases to date in 47 countries and territories, including at least 13 autochthonous cases in Florida and Texas.¹¹ The numbers of cases in the hemisphere have declined since 2014, and the incidence in service members has declined in parallel with that trend.¹¹

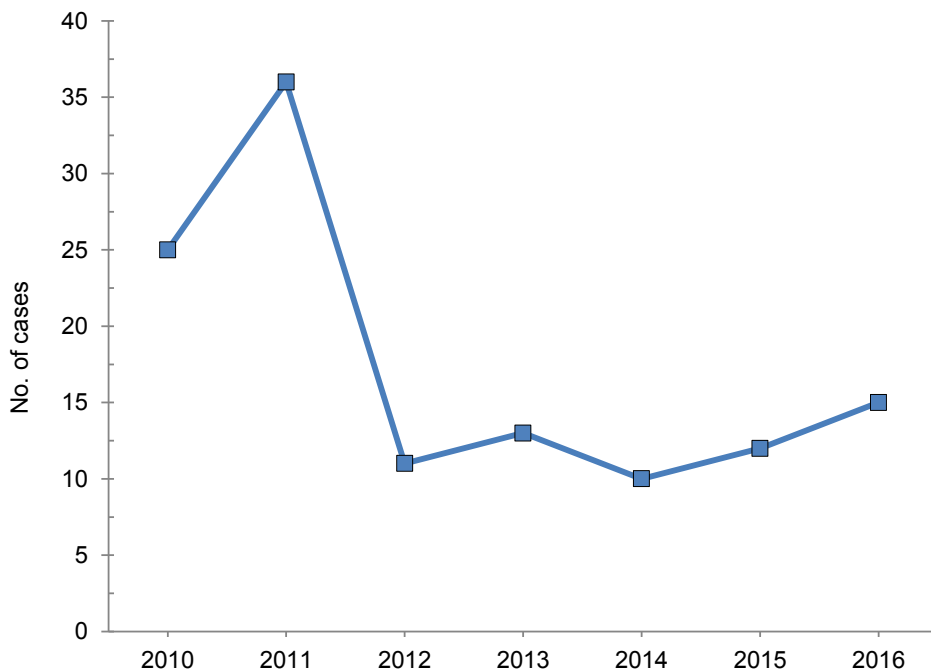
The introduction of Zika virus into the Western Hemisphere in early 2015 resulted in peak incidence in 2016 in both the U.S. overall and among military beneficiaries.¹² Local acquisition of Zika virus infection in U.S. territory was most notable in Puerto Rico (more than 34,000 cases), the Virgin Islands (more than 800 cases), and Florida (at least 244 cases).¹² A *MSMR* report of December 2016 identified 110 confirmed cases among service members, among whom 68 were found to have most likely been exposed to the virus in Puerto Rico.¹²

Confirmed cases of arboviral diseases, neuroinvasive and non-neuroinvasive, were primarily cases of infection by West Nile virus, a virus introduced into the U.S. in 1999.¹³ Of the 19 confirmed cases, 16 were cases of West Nile virus. Nine of those 16 cases were reported in 2012, a year during which the U.S. experienced the largest number of cases (5,674) since 2003.¹³ Note that this category does not include the viruses for chikungunya, Zika virus, dengue, or yellow fever, which were recorded separately.

The 33 confirmed cases (and 150 possible and suspected cases) of leishmaniasis during 2010–2016 contrast sharply with the 1,594 cases reported for the 4 years of 2003–2006.¹⁴ The marked decline after 2006 has been attributed to improved living conditions for service members deployed to Iraq, Kuwait, and Afghanistan (endemic regions for leishmaniasis) as those operational areas matured, and then to the dramatic decline in the numbers of U.S. service members assigned to those areas after the end of Operation Iraqi Freedom, Operation New Dawn, and Operation Joint Endeavor.¹⁴

The 10 confirmed cases of trypanosomiasis were likely all cases of seropositivity for *Trypanosoma cruzi* infection, the agent of American trypanosomiasis (Chagas disease). Comments for all of the RME reports specified either *T. cruzi* infection or seropositivity for that organism either

FIGURE 2. Annual numbers of possible cases of malaria diagnosed during hospitalizations, active and reserve components, U.S. Armed Forces, 2010–2016



without symptoms or in association with blood donation. For none of the confirmed cases did the comments suggest that the diagnosis was African trypanosomiasis (**data not shown**).

Among the five confirmed cases of tularemia, there were no comments in the RME reports that implicated a specific arthropod vector. One report commented that the patient did have contact with a deceased rabbit. It is important to recognize that the cause of tularemia, *Francisella tularensis*, is transmissible through a variety of possible vehicles, including contaminated food, water, blood, animal tissues, and inhalation of contaminated dust.¹⁵ The known arthropod vectors (ticks, deerflies, and mosquitoes) are not necessary for contracting this infection.

This analysis found 346 cases of confirmed and 122 cases of possible malaria based on the receipt of RME reports and hospitalizations, respectively. This result is consistent with findings from the annual *MSMR* reports of malaria incidence, which have traditionally used RME reports and hospitalization records (but not outpatient records) to identify cases of malaria. (See the annual report for malaria in 2017 on pages 2–7 in this issue of the *MSMR*.¹⁶) This

approach has been based on two considerations. First, there has long been recognition that diseases (or injuries) that merit the sending of an RME report often fail to be reflected in such a report.¹⁷ With respect to malaria, there is much uncertainty about what proportion of genuine cases of malaria fail to be reported via the RME system. Second, there has been a presumption that diagnoses recorded at the time of discharge from hospital are based on a careful documentation of diagnoses made during the hospitalization. The sending of RME reports depends on separate, additional actions by local public health officials who have implemented a system for finding, or being notified of, diagnoses of reportable events documented by healthcare providers. The rigor and completeness of such systems varies by location of the military treatment facilities. Furthermore, diagnoses of malaria in service members hospitalized in civilian healthcare facilities are not expected to be reflected in RME reports, as civilian facilities are not required by DoD policy to generate such reports.

Diagnoses recorded at the time of discharge following hospitalization were regarded as “possible” cases. The uncertainty about the accuracy of such diagnoses

is another limitation to this report and to the use of such data for surveillance purposes. Admission to hospital presumes a severity of illness or injury that warrants a greater level of evaluation or treatment than is readily accomplished through outpatient care. It is plausible that many of the possible cases of vector-borne disease in this analysis were diagnosed on the basis of confirmatory laboratory test results. However, no attempt was made to identify laboratory results compatible with the diagnoses of vector-borne disease for those individuals. If cases with positive confirmatory laboratory results were not reported as RMEs by public health officials at the treatment facilities, then such cases would not have been included in this analysis. The result would be underestimates of the incidence of confirmed vector-borne diseases. Future surveillance inquiries would benefit from the incorporation of laboratory test results for the diagnoses in question whenever feasible. DMSS does not contain laboratory results from hospitalizations in civilian facilities. Furthermore, some laboratory tests for unusual diseases are performed in commercial, state, federal, and foreign laboratories whose records are not electronically incorporated into the files of laboratory tests accessible through DoD laboratory databases.

The overwhelming majority of suspected cases were recorded in outpatient care. The data in this report pertaining to counts of suspected cases of JE emphasize the impact of coding errors in outpatient records. These data suggest that ICD-9 and ICD-10 codes for JE disease were used as incorrect surrogates during encounters that included administration of JE vaccine. Because the ICD coding systems did not contain codes specific for that vaccine, a common error was apparently to record the codes for JE infection itself. The correct codes for encounters for JE vaccination were either V04.89 or V05.0 (codes not specific for JE in ICD-9) or the CPT codes 90735 and 90738 (specific for JE). The contrast during a 7-year period between a count of more than 2,500 suspected cases of JE and no confirmed cases of JE is striking. This example highlights the importance to disease surveillance of accurate recording of diagnoses at the time and place of patient care.

TABLE 4. Vector-borne diseases, causative pathogen types, vectors, and geographic distribution

Vector-borne disease	Agent	Vector(s)	Geographic distribution
Arboviral diseases, neuroinvasive and non-neuroinvasive			
Eastern equine encephalitis	Virus	Mosquito	Americas
Australian (Murray Valley) encephalitis, Oropouche virus	Virus	Mosquito; midge	Australia, New Guinea; South America, Panama
California virus encephalitis	Virus	Mosquito	United States
Japanese encephalitis	Virus	Mosquito	Asia, Pacific Islands, Australia
Tick-borne encephalitis	Virus	Tick	Europe
Western equine encephalitis	Virus	Mosquito	Americas
St. Louis encephalitis	Virus	Mosquito	Americas
West Nile virus	Virus	Mosquito	Global except Southeast Asia, South America, Australia
Other mosquito-borne viral fever			
Chikungunya	Virus	Mosquito	Africa, Southeast Asia, Philippines, Americas, Pacific Islands
Rift Valley fever	Virus	Mosquito	Africa, Arabia
Zika virus infection	Virus	Mosquito	Africa, Southeast Asia, Americas, Pacific Islands
Hemorrhagic fevers			
Crimean-Congo HF	Virus	Tick	Africa, Central Asia, Europe, Middle East
Omsk HF	Virus	Tick	Russian Federation
Kyasanur Forest disease	Virus	Tick	India
Dengue	Virus	Mosquito	Throughout tropical regions of world
Ehrlichiosis/anaplasmosis	Rickettsia	Tick	North America, Asia, Europe
Filariasis	Helminth	Mosquito	South America, Central America, Africa, Asia, Pacific Islands
Leishmaniasis	Protozoan	Sandfly	Asia, Africa, Middle East, South America, Central America, Mediterranean
Lyme disease	Bacterium	Tick	North America, Europe, China, Japan
Malaria	Protozoan	Mosquito	Tropical regions of Americas, Africa, Asia, Pacific Islands
Plague	Bacterium	Flea	Almost worldwide
Relapsing fever	Bacterium	Tick, louse	Americas, Asia, Europe, Africa
Rocky Mountain spotted fever	Rickettsia	Tick	United States, South America, Central America
Trypanosomiasis	Protozoan	Tsetse fly, reduvid bug	Africa, Central America, South America
Tularemia	Bacterium	Tick, deerfly, mosquito	North America, Europe, Russia, China, Japan
Typhus	Rickettsia	Louse, flea, mite	Central America, South America, Africa, Asia
Yellow fever	Virus	Mosquito	Africa, South America, Central America
Babesiosis - Not an RME	Protozoan	Tick	Almost worldwide
Bartonellosis - Not an RME	Bacterium	Sandfly	Colombia, Ecuador, Peru
Sandfly fever - Not an RME	Virus	Sandfly	Africa, Asia, Europe, South America, Central America

RME, reportable medical event

Another potential limitation to the use of outpatient diagnostic codes by themselves for surveillance purposes is the recording of tentative or “rule-out” diagnoses prior to confirmation of diagnoses. This limitation is particularly important for many infectious disease diagnoses for which confirmation depends on the results of laboratory testing that usually are not available at the time of the initial encounters for care. The surveillance value of tentative outpatient diagnoses can be enhanced if the records of such diagnoses are reconciled with the results of contemporaneous laboratory results to identify those instances in which the diagnoses were eventually substantiated by confirmatory tests. This analysis did not perform such cross-matching of outpatient diagnoses and laboratory results, so the utility of the numbers for suspected cases is severely limited. However, examination of the suspected cases of JE did reveal that coding errors were common, at least during 1 year. On the other hand, the variety of diagnoses recorded for suspected cases suggests that, fortunately, many healthcare providers are considering a broad range of possible conditions in their evaluations of service members whose duties and travel have the potential for exposing them to a variety of otherwise uncommon vector-borne diseases.

A major proportion of the confirmed cases based on RME reports did not have documented laboratory results to confirm the diagnoses. These discrepancies may be attributable to a number of factors. Laboratory test results from civilian treatment facilities and contract, state, or foreign laboratories may not be formally transferred into DoD electronic healthcare records. Also, epidemiologic confirmation is possible for cases that are part of a cluster of a vector-borne disease in which some, but not all, cases are laboratory confirmed. Lastly, some cases of Lyme disease may be considered clinically confirmed on the basis of a history of tick bite and the development of a compatible illness that includes the appearance of the classic erythema migrans rash.

In summary, this report documents the occurrence among service members of cases of vector-borne diseases that are regarded as predictable threats to the health of the force. The estimates of the magnitude of those

threats are constrained by the limitations of the surveillance tools available. Enhancement of those tools could be achieved through more complete reporting of RMEs at the local level. In the meantime, the available data reinforce the need for continued emphasis on the multidisciplinary preventive measures necessary to counter the ever-present threat of vector-borne disease.

For each of the vector-borne diseases that were the subject of this report, **Table 4** contains supplementary information about the nature of the pathogens (virus, bacterium, rickettsia, protozoan, or helminth), the known arthropod vectors, and the reported geographic distribution of the diseases at this time.

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

In addition, 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.

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Diagnostic Evaluation of Military Blood Donors Screening Positive for *Trypanosoma cruzi* Infection

Joseph E. Marcus, MD (Capt, USAF); Bryant J. Webber, MD, MPH (Maj, USAF); Thomas L. Cropper, DVM, MPVM; Matthew C. Wilson, DO (Maj, USAF); Heather C. Yun, MD (Lt Col, USAF)

Routine blood donor screening for *Trypanosoma cruzi*, the causative parasitic agent of Chagas disease, began in the U.S. in 2007. Results of follow-up testing and evaluation after a positive screen have not been studied in the armed forces. Among first-time donors at the Joint Base San Antonio–Lackland Blood Donor Center between January 2014 and December 2016 (N=43,402), a total of 23 (0.05%) screened positive for *T. cruzi*. This descriptive study highlights demographic and follow-up information for all 22 active duty service members who screened positive; a non-active duty member was excluded due to unavailability of clinical records. Members who screened positive received 13 different combinations of confirmatory testing (mean: 2.7 tests per person). In select cases, clinical evaluation included electrocardiogram (n=15) and 30-second rhythm strip (n=5). Two patients met criteria for Chagas disease; 11 patients were considered negative; and nine patients were indeterminate. Among a small cohort of active duty service members who screened positive for *T. cruzi* infection on blood donation, diagnostic evaluation varied considerably. Opportunities exist to decrease heterogeneity of clinical workup and improve evaluation of persons who screen positive.

T*rypanosoma cruzi* is a protozoan parasite transmitted primarily by the kissing bug (triatomine) vector, which feeds on a variety of vertebrate hosts. Human infection occurs when the infective feces of a kissing bug are rubbed into a bite wound or across a mucous membrane. In addition to the vector-borne route, *T. cruzi* can be transmitted congenitally, in contaminated food, or via blood or tissue donation.¹ Infection with *T. cruzi* may cause serious cardiovascular and gastroenterologic pathology.¹⁻³ The prevalence of human Chagas disease is estimated at 5.7 million globally⁴ and 240,000 in the U.S.,⁵ mostly among immigrants from rural areas of Latin America, where vector-borne transmission is highest.⁶ *T. cruzi* endemicity has

been established throughout the southern U.S., particularly in South Texas, where locally acquired human infections have been documented with increased frequency.⁷⁻¹⁰ Analysis of captured reduviid bugs on Joint Base San Antonio (JBSA), a large military installation in South Texas, as well as from surrounding Bexar County, indicate the potential for autochthonous cases,^{11,12} although a recent cross-sectional study of military trainees and instructors demonstrated no prevalent infections based on serologic and molecular testing.¹³

To prevent blood transfusion–related transmission, in keeping with national guidelines from the Blood Products Advisory Committee of the U.S. Food and Drug Administration, the JBSA–Lackland Blood

Donor Center screens all first-time blood donors for *T. cruzi* infection¹⁴ with a chemiluminescent immunoassay (ChLIA). Blood that screens positive is discarded before entering the blood supply. Although the ChLIA has a reported specificity exceeding 99%,¹⁵ its large-scale application in a low-prevalence population yields a significant number of false-positive results. For persons screening positive, the Centers for Disease Control and Prevention (CDC) recommends confirmatory testing with at least two separate, independent tests, which may include an antibody enzyme immunoassay (EIA), trypomastigote excreted-secreted antigen (TESA), radioimmunoprecipitation assay, and an enzyme-linked immunosorbent assay (ELISA). Regardless of the confirmatory assay used, those persons who confirm positive should undergo a complete history and physical examination, a resting electrocardiogram (ECG), and a 30-second lead II rhythm strip.¹⁶ This descriptive study was initiated to assess adherence to these recommendations among a population of military blood donors at JBSA.

METHODS

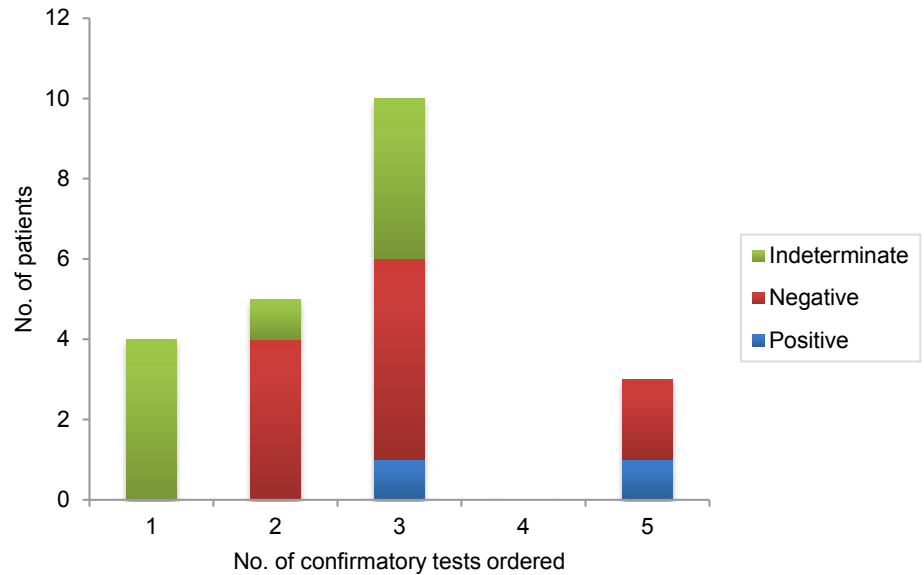
A retrospective chart review was performed on all service members who screened positive for *T. cruzi* on blood donation at the JBSA–Lackland Blood Donor Center between 1 January 2014 and 31 December 2016 facilitated by the Lackland Public Health Department (559 AMDS). Demographic information, results of confirmatory laboratory testing, and completion of recommended clinical workup were abstracted from each chart. Given variation in commercial ELISA tests, results were stratified by those capable of

detecting both anti-*T. cruzi* IgM and IgG antibodies and those restricted to IgG only. Per the CDC recommendations, an individual was considered positive for Chagas disease if at least two additional confirmatory serologic tests were positive.¹⁶ For this study, patients were considered negative if at least two additional tests were negative, and indeterminate if not meeting either the positive or negative criteria. This corresponds to CDC recommendations that discordant results on two tests should be considered indeterminate and clarified by a third assay. Repeat positive ChLIA tests were not considered confirmatory. Blood donor denominator data were provided by the JBSA-Lackland Blood Donor Center.

RESULTS

Of the 43,402 persons who donated blood at JBSA-Lackland and were tested for *T. cruzi* infection during the 3-year surveillance period, 23 (0.05%) screened positive. Charts were available for all cases except one, a non-active duty member, who was excluded from the analysis. Among the 22 cases included in the study, the majority were male (82%) and in training status (77%), with a median age of 23.8 years (range: 18–60 years) (Table). Mean duration from the positive screening test to the first clinical evaluation was 7.6 days, and from the first evaluation to diagnostic workup completion was 53 days. Three service

FIGURE 1a. Numbers of patients who screened positive for *Trypanosoma cruzi* infection (N=22), Joint Base San Antonio–Lackland Blood Donor Center during 2014–2016, by Chagas disease status and number of confirmatory serologic tests ordered



members had a permanent change of station during the workup, so finalization of their evaluations occurred at their gaining installations.

Service members who screened positive underwent a mean of 2.7 (range: 1–5) additional serologic tests (Figure 1a), with significant heterogeneity among confirmatory tests ordered. A total of 17 service members (77%) were retested with ChLIA, making it the most commonly ordered assay, followed by EIA (55%) (Figure 1b). In total, 13 different combinations of confirmatory tests were ordered. Although all

service members had a history and physical, only 15 (68%) had an ECG and five (23%) had a 30-second rhythm strip (Figure 2). A total of 14 service members (64%) were referred to the infectious disease clinic at the local military treatment facility.

Two patients, both Texas natives, were confirmed positive for Chagas disease based on having two positive confirmatory tests. Both patients had at least a basic cardiac workup and declined treatment. One patient was diagnosed with Chagasic cardiomyopathy and underwent administrative separation from the military.¹⁰ For 11 (50%) patients, infection was ruled out with at least two negative assays. Nine (41%) individuals failed to meet either positive or negative criteria; among these indeterminate cases, four had only one confirmatory test performed, and the other five had a mix of positive and negative results, rendering their cases inconclusive based on chart review.

TABLE. Baseline characteristics of active duty service members who screened positive for *Trypanosoma cruzi* infection (N=22), Joint Base San Antonio–Lackland Blood Donor Center, 2014–2016

Characteristics	
Age, median (range)	23.8 (18–60 yrs)
Male sex, no. (%)	18 (82%)
In training status, no. (%)	17 (77%)
No. of days from positive screen to first evaluation, mean (range)	7.6 (1–19)
No. of days from first evaluation to workup completion, mean (range)	53 (8–147)
Diagnostic disposition	No. (%)
Positive (Chagas confirmed)	2 (9%)
Negative (Chagas ruled out)	11 (50%)
Indeterminate	9 (41%)

EDITORIAL COMMENT

In this population of first-time blood donors at the JBSA-Lackland Blood Donor Center between 2014 and 2016, one in 21,700 was diagnosed with Chagas disease.

FIGURE 1b. Numbers of patients who screened positive for *Trypanosoma cruzi* infection (N=22), Joint Base San Antonio–Lackland Blood Donor Center during 2014–2016, by Chagas disease status and type of confirmatory serologic test ordered

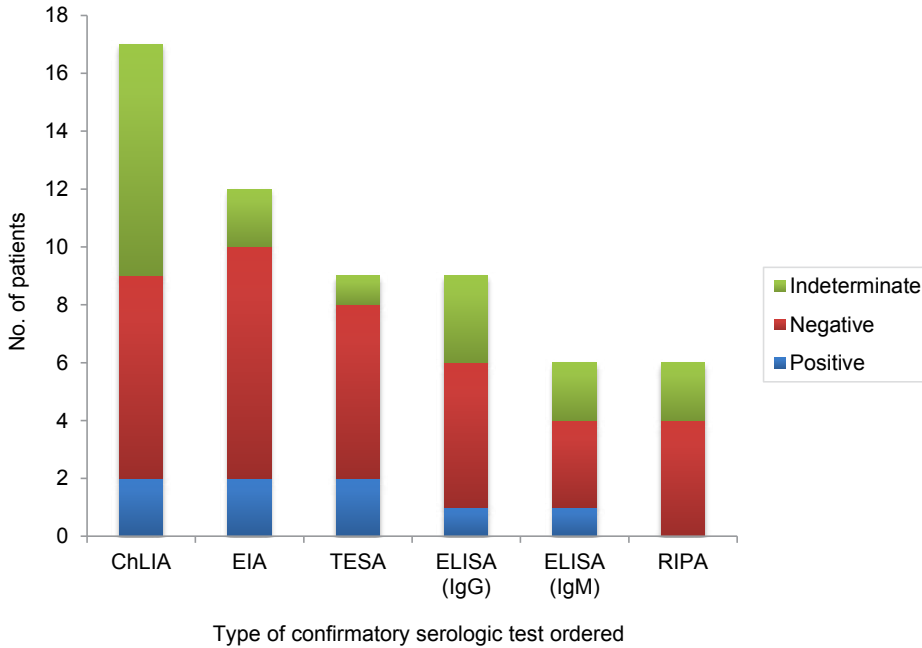
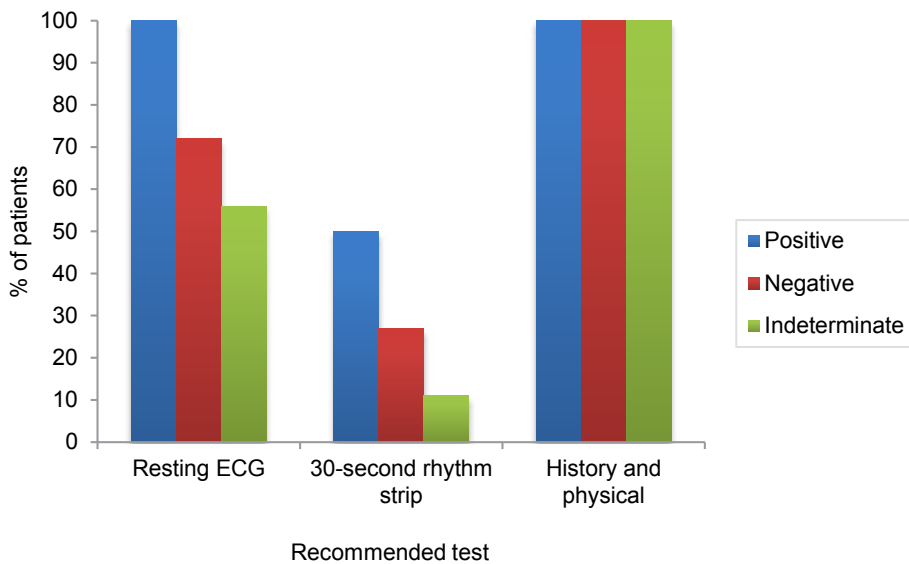


FIGURE 2. Percentages of patients who screened positive for *Trypanosoma cruzi* infection (N=22) at Joint Base San Antonio–Lackland Blood Donor Center during 2014–2016, by Chagas disease status and type of recommended diagnostic evaluation received



This figure is lower than the one-in-6,500 prevalence among donors at five civilian blood banks in Texas. However, the JBSA population is more representative of the entire nation than any one state. Furthermore, the Texas blood donor study confirmed patients with only a single

confirmatory test, a criterion that may have included patients who might have been labeled indeterminate per the parameters of this study.⁹

Among the 22 active duty members who screened positive for *T. cruzi* infection, diagnostic evaluation varied considerably.

Laboratory testing, which often included unnecessary repetition of the screening test, was far from uniform, even when the entire workup was completed at one military treatment facility. Although the two patients diagnosed with Chagas disease received the appropriate baseline cardiac evaluation, the majority of patients with indeterminate dispositions did not—a key consideration given the inability of current antiparasitic treatment to reverse cardiomyopathy, and thus the importance of early detection.¹⁷ Of note, patients who tested negative were more likely to receive a cardiac workup than the patients who were indeterminate. This observation likely reflects that some indeterminate cases had fewer interactions with providers and fewer tests ordered.

Given the operational requirement for a safe and sizable blood supply in the armed forces, healthcare providers in the Military Health System may need to evaluate patients who have screened positive for *T. cruzi* infection during blood donation. These providers, most of whom rarely encounter Chagas disease in their usual practice, should follow the clinical practice guideline developed by Bern and colleagues, which specifies the requirements for confirmatory testing and cardiac screening.¹⁶ Military treatment facilities that operate or support blood banks should consider designating a clinical lead for evaluating TRICARE beneficiaries who have screened positive for communicable diseases during blood donation. This may enhance standardization of care and improve communication between the clinic, blood bank, and installation public health department. Ideally, every donor who screens positive for *T. cruzi* should undergo a complete history and physical, a resting ECG, a 30-second lead II rhythm strip, and a uniform laboratory workup (e.g., EIA and TESA). Although laboratory confirmation should include at least two different confirmatory tests run in parallel, the exact tests may vary based on the laboratory capabilities of the particular military treatment facility. If infectious disease consultation is unavailable, a provider suspecting Chagas disease may submit specimens directly to the CDC Reference Diagnostic Laboratory using a Form 50.34; instructions and contact information are available at

<https://www.cdc.gov/laboratory/specimen-submission/help-faqs.html>.

Disclaimer: The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense and its Components.

Author affiliations: San Antonio Military Medical Center, San Antonio, TX (Lt Col Yun, Capt Marcus); Wilford Hall Ambulatory Surgical Center, San Antonio, TX (Maj Webber, Dr. Cropper, Maj Wilson).

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