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Early Identification of SARS-CoV-2 Emergence in the Department of Defense via Retrospective Analysis of 2019–2020 Upper Respiratory Illness Samples

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The first U.S. case of non-travel-related severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) infection was detected in late February 2020 in California, but the prevailing delay in diagnostic testing and initial stringent testing criteria made it difficult to identify those who could have acquired the virus through community spread. The emergence of the virus in the western Pacific region in late 2019 and the global distribution of Department of Defense (DoD) personnel present the risk that DoD members may have been exposed and contracted the virus earlier than U.S. detections. Here, a retrospective study from residual samples collected from a global DoD Respiratory Surveillance Program was conducted to establish a tentative timeline of when this virus began circulating in the DoD population. Quantitative real-time reverse-transcription polymerase chain reaction testing for SARS-CoV-2 was performed and the specimen collection dates of positive results were compared to the dates of the first infections previously identified in respective states and counties. Twenty-four positive samples were identified out of approximately 7,000 tested. Although this retrospective testing found early cases in 8 locations, there were no results indicative of circulation before late February.

WHAT ARE THE NEW FINDINGS?

The first reported confirmed SARS-CoV-2 infection in the U.S. was in Washington state on 21 January 2020 in an individual who had traveled to Wuhan, China. To determine if SARS-CoV-2 infections were present in the U.S. prior to that date, samples from a DoD respiratory surveillance program dating back to 1 December 2019, were evaluated for the presence of SARS-CoV-2 RNA. Viral RNA was not detected in any sample collected before 21 January 2020; however, positive samples were identified for several U.S. regions where the date of collection preceded the first reported infection for that region.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

The implementation of new and emerging pathogen detection assays into already established surveillance programs could detect community spread earlier, thereby reducing the spread of pathogen among vulnerable populations more effectively.

Although the first 2 decades of the 21st century were marked by the emergence of novel respiratory pathogens with pandemic potential (2003 SARS-CoV, 2009 Influenza A H1N1, and 2012 MERS-CoV), the recognition and spread of a highly infectious and unusually lethal strain of the human betacoronaviruses, i.e., severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in late 2019 caught the world's health systems by surprise. The emergent nature of the coronavirus disease 2019 (COVID-19) pandemic resulted in most of the scientific literature being released through the *medRxiv* preprint server prior to peer-review. As such, the authors recommend critical consideration of the referenced literature. Even the most technologically advanced countries with the greatest wealth, such as the U.S., did not have sufficient pandemic preparedness plans in place to adapt to this outbreak.[1] In fact, the lack of centralized planning was evident in the wide variation between states on recommendations for testing in the early outbreak period between March (when the virus first arrived in most states) and July 2020.[2] Even the Department of Defense (DoD), with its numerous world-class infectious disease research institutes and clinical surveillance programs, was caught off-guard. However, the DoD quickly adapted and put into place a surveillance approach leveraging its established Upper Respiratory Surveillance program housed at the U.S. Air Force School of Aerospace Medicine (USAFSAM). This response resulted in a massive capability increase and the DoD has remained ready to execute its global mission.

The gaps in early testing led to widespread underestimation of infected individuals, with some early sampling results suggesting nearly 5% of undiagnosed people in the U.S. were seropositive for prior exposure to the virus.[3] According to Kalish et al., this seropositivity rate translates to 5 undiagnosed infections per diagnosis between May and July 2020. An additional impact of the variable testing recommendations and the high infectivity of the virus was the emergence of local hotspots such as New Orleans during Mardi Gras,[4] where only a few individuals imported the virus but many exported it elsewhere.

In order to better prepare for the next major outbreak, a more detailed and thorough understanding of the early emergence of this pandemic in the U.S. and DoD-associated populations is required. To that end, a retrospective analysis was performed of clinical remnants from patients who reported to military medical treatment facilities during the winter of 2019–2020 complaining of upper respiratory infections. This paper reports the findings from that study and implications for increasing the DoD's readiness for the next pandemic.

METHODS

The Air Force Research Laboratory Institutional Review Board (Study number FWR20190037N) determined this study to be non-human subject research as part of a public health response activity and the study was conducted between March and June 2020.

Sample selection and testing

De-identified nasopharyngeal swab (NPS) samples were collected from a respiratory surveillance program that tracks influenza globally to aid in the yearly influenza vaccine development. Samples were stabilized in viral transport media prior to testing, covered the date range from 1 December 2019 to 3 June 2020, and originated from 86 military medical treatment facilities (MTFs) around the globe. USAFSAM (a DoD Reference Laboratory) previously tested these samples for upper respiratory infections using the Luminex Respiratory panel (Austin, TX) before being stored at -80º C. The Reference Laboratory provided the following metadata: date of collection, MTF, and coinfections.

Ribonucleic acid (RNA) was extracted from the NPS samples with Promega Maxwell 16 instruments using the Maxwell Total Viral RNA kit according to the manufacturer's instructions. Quantitative real-time reverse-transcription polymerase chain reaction (qRT-PCR) testing was performed using the SuperScript III RT-PCR master mix (ThermoFisher, cat. #204454) with the research-use only 2019-nCoV primer-probe kit (IDT DNA, cat. #10006605). Thermocycling conditions on the ABI 7500 FAST analyzer consisted of a 20-minute reverse transcription step at 50° C, a 10-minute hot-start activation step at 95° C, and 45 cycles of 95° C for 3 seconds followed by 55° C for 30 seconds.

Data analysis and statistics

In accordance with the approved Centers for Disease Control and Prevention (CDC) assay methodology, samples were positive for SARS-CoV-2 if the RNase P control passed (cycle threshold [Ct] < 40) and both primer sets N1 and N2 produced Ct values below 40. In the cases where RNase P did not amplify but both N1 and N2 were positive, those samples were called positive in accordance with the Food and Drug Administration-authorized instructions for use of the CDC 2019-nCoV RT-PCR Diagnostic Panel. Samples where only 1 of the 2 markers were detected were "inconclusive" and the test was repeated using the previously extracted RNA. Sample metadata and amplicon data, which had been stored separately, were combined by the Laboratory Director prior to analysis. MS Access 2013 (Microsoft Corporation, Redmond, WA) was used for data management and descriptive statistics such as number of positives, daily positive hit rate, and earliest detection.

RESULTS

The observed positivity rate was 0.3% (24 positive samples from 7,021 total samples). Of these samples, 14 were collected from patients prior to the first COVID-19 case clinically reported at 8 different installations **(Table 1)**. The first positive RT-PCR sample from Wright Patterson Air Force Base (AFB) in Ohio was collected a full month before the first laboratory-confirmed case at that installation (22 March 2020), and 2 days before the first laboratory-confirmed case in the DoD (26 February 2020 by U.S. Forces Korea).[6] A second PCR-positive specimen of significant interest was collected at Ellsworth AFB 46 days before the first case of COVID-19 reported from the installation in South Dakota.

Samples were received from installations in 3 geographic combatant commands **(Table 2)**: European Command (EUCOM), Pacific Command (PACOM), and Northern Command (NORTHCOM). The majority of test samples (89.3%) originated in NORTHCOM followed by PACOM (6.6%), and EUCOM (3.4%). An additional 47 samples originated in U.S. Coast Guard clinics (0.7%). Positive sample distribution included 20 from NORTHCOM (0.3% positive rate), 0 from PACOM, 4 from EUCOM (1.7% positive rate), and 0 from the Coast Guard.

The number of SARS-CoV-2 positives in this respiratory surveillance sample set increased logarithmically with time, mirroring the positivity rate observed in the larger pandemic **(Figure)**. Beginning in the week ending 29 February, an increasing number of positive tests was observed until the week ending 28 March. The decline at the end of March was due to the addition of SARS-CoV-2 clinical testing in the Air Force clinical test menu in early March. Therefore, most of the SARS-CoV-2 positive samples in March and beyond were evaluated directly by the clinical lab and not by the surveillance lab. The effect of clinical testing was also seen in that the peak sampling period was from mid-February to early March, when nearly one-third of all samples were collected. Notably, the effect was most dramatically seen in testing numbers between the weeks ending 21 March and 28 March, when 691 samples were tested compared with 90, respectively.

In addition to observing an increase in testing, two peaks were detected in the positivity rates. For the week ending 29 February, one sample was positive out of 333 tests, a rate of 0.30%. The following two weeks remained below 1% positive rate (0.17% and 0.37%, respectively) before increasing to 1.45% with 10 detections out of 688 tests for the week ending 21 March, and peaking at 3.33% with three positive tests out of 90 samples during the final week of the study. The week ending 4 April had no positive tests, but then the next three weeks had positivity rates of 1.4%, 3.1%, and 3.8% before another week of no positive tests and finally a week with 2.0% positivity (1/49 tests). These observations are consistent with the observed increase in nationwide infection growth beginning during the week ending 14 March.[7]

EDITORIAL COMMENT

These results suggest that while the COVID-19 virus was present in the U.S. military population earlier than previously reported, the change in observed infection timing was minimal. Excluding the outlier from Ellsworth AFB, the initial positive specimens were collected approximately 2 weeks before the first cases were reported (average=11.6 days, range 2–27 days). These results are similar to the results of other retrospective testing studies that focused on PCR-based detection of residual samples.[8-10]

TABLE 1. Summary of SARS-CoV-2 positive samples

Sample no.	Installation	Collection date	Date first case identified	Gene targets of the CDC SARS-CoV-2 assay		
				N1[a]	N2[a]	RP[a]
439[b]	Wright-Patterson AFB, OH	24-Feb-20	22-Mar-20	29.8	36.6	24.2
2902	Robins AFB, GA	4-Mar-20	21-Mar-20	17.7	18.7	29.8
3488	Lakenheath AB, United Kingdom	12-Mar-20	20-Mar-20	23.6	24.7	25.5
3406	Little Rock AFB, AR	13-Mar-20	22-Mar-20	19.2	19.7	30.7
3343	Wright-Patterson AFB, OH	15-Mar-20	21-Mar-20	18.0	19.0	26.6
3732	Scott AFB, IL	16-Mar-20	31-Mar-20	23.8	23.6	27.4
4149	Langley AFB, VA	18-Mar-20	20-Mar-20	26.0	27.3	27.2
4207	Lakenheath AB, United Kingdom	18-Mar-20	20-Mar-20	25.2	26.1	28.9
3902	NH Beaufort, SC	18-Mar-20	21-Mar-20	27.8	29.4	28.0
4116	NH Beaufort, SC	19-Mar-20	21-Mar-20	29.9	32.6	20.0
4324	Lakenheath AB, United Kingdom	19-Mar-20	20-Mar-20	17.5	18.3	22.1
4089	Ellsworth AFB, SD	20-Mar-20	6-May-20	32.9	36.1	21.9
4087	NH Beaufort, SC	20-Mar-20	21-Mar-20	15.6	16.1	24.5
4086	NH Beaufort, SC	20-Mar-20	21-Mar-20	27.6	29.3	22.7
4326	JBSA-Lackland AFB, TX	23-Mar-20	[c]	33.3	36.7	23.5
4259	NH Beaufort, SC	23-Mar-20	21-Mar-20	18.1	19.8	22.6
4420	NH Beaufort, SC	24-Mar-20	21-Mar-20	24.8	29.1	18.8
6563	NH Camp Lejeune, NC	5-Apr-20	12-Mar-20	30.3	34.5	27.0
6675	Eglin AFB, FL	16-Apr-20	19-Mar-20	25.3	26.9	24.1
6692	Lakenheath AB, United Kingdom	16-Apr-20	20-Mar-20	33.4	35.2	24.9
6690	Keller ACH, NY	20-Apr-20	[c]	24.4	24.4	23.3
6753	USAMEDDAC Fort Drum, NY	23-Apr-20	17-Mar-20	20.7	21.4	27.8
6822	Blanchfield ACH, KY	7-May-20	26-Mar-20	20.4	21.6	23.3
6924	Eglin AFB, FL	24-May-20	19-Mar-20	35.3	39.0	25.5

[a]Gene targets of the CDC SARS-CoV-2 assay.
[b]Sample detected via SYBRgreen with primers synthesized in-house using CDC primer sequences.
[c]Early case data were not available for JBSA-Lackland and Keller ACH. JBSA-Lackland served as a quarantine site for evacuees from the Pacific as early as February 2020.
SARS-CoV-2, severe acute respiratory syndrome-coronavirus 2; No., number; CDC, Centers for Disease Control and Prevention; N1, SARS-CoV-2 N1; N2, SARS-CoV-2 N2; RP, human RNase P; AFB, Air Force Base; AB, Air Base; NH, Naval Hospital; JBSA, Joint Base San Antonio; USAMEDDAC, U.S. Army Medical Department Activity; ACH, Army Community Hospital.

Evaluation of residual specimens using antibody tests is still an on-going effort and may lead to different data as better assays become available.[11]

Collectively, the retrospective testing results worldwide demonstrate that the early testing response was inadequate. In the U.S., the lead for testing is the Centers for Disease Control and Prevention, guiding the development and deployment of diagnostic assays. In steady-state operations this is a fully acceptable arrangement; however, as has been seen during this outbreak, relying solely upon a single organization for direction has shortcomings. In contrast, the DoD's use of centralized control coupled with broad, decentralized execution provides the flexibility and adaptability that are necessary for early investigation of disease outbreaks.

When military planners return to the table to develop the next public health emergency preparedness plan, they should consider Joint doctrine and the wealth of expertise that the DoD has spread across its agency. The biological defense and public health enterprises centered around the Defense Threat Reduction Agency, the Defense Advanced Research Projects Agency, and the Armed Forces Health Surveillance Division utilize advanced molecular technology and deploy those capabilities across the services. Data from technologies such as next generation sequencing for detection could feed directly into the research labs so that diagnostics, vaccines, and therapeutics could be continually generated and transitioned to the industrial infrastructure at the first sign of outbreak. Technology is available and in wide use today that was not available in December 2019 for detecting the earliest positives, but even with these advances in technology, as the results reported here demonstrate, outbreaks could be identified a matter of a few weeks earlier. For the next pandemic, the challenge is to have technology innovators engaged globally, and to adequately resource government, academic, and industry research labs to make a one month sequence-to-diagnostics turn-around a reality.

While more than 7,000 samples were tested in this study, the number of independent test sites is small and heavily favored by one Service. As expected a high proportion of samples originated from NORTHCOM facilities, where most of the DoD MTFs are located, while the overseas samples originated from 10 Air Force installations and 1 Army installation. In a demonstration of multi-agency collaboration, samples were received from 6 Coast Guard clinics, too. No samples were received from Southern Command and less than 10 samples from Central Command, so the impact of the epidemic in military members stationed in those regions is unknown. In order to provide adequate surveillance during normal operations and epidemics, the Military Health System, and the Defense Health Agency by extension, must increase the participation of sentinel sites in the Respiratory Surveillance Program. With 475 military hospitals and medical clinics across the globe, the DoD is the only health care system that is equipped to monitor worldwide infectious diseases before they enter the homeland. The surveillance network for the DoD is primed to immediately add validated assays for new and emerging infections in parallel with the clinical assays that are deployed, to actively track community spread once a virus has been detected by the CDC early in a pandemic.

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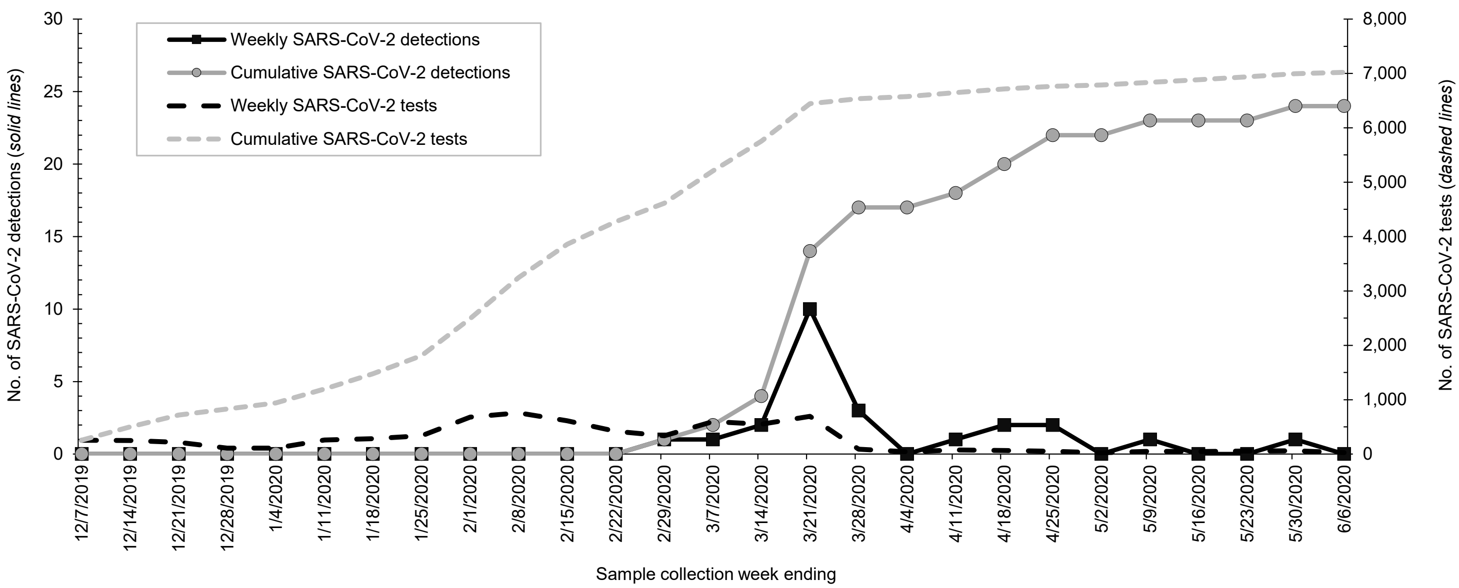
TABLE 2. Numbers of samples tested for SARS-CoV-2 and percentages positive, by month and region

Month and year samples received	Total		NORTHCOM		PACOM		EUCOM		Other	
	No. samples	No. positive (%)	No. samples	No. positive (%)	No. samples	No. positive	No. samples	No. positive (%)	No. samples	No. positive
Dec 2019	878	0	758	0	80	0	36	0	4	0
Jan 2020	1592	0	1435	0	85	0	48	0	24	0
Feb 2020	2,141	1 (0.0)	1,971	1 (0.1)	82	0	77	0	11	0
Mar 2020	1,924	16 (0.8)	1,746	13 (0.7)	109	0	61	3 (4.9)	8	0
Apr 2020	249	5 (2.0)	149	4 (2.7)	85	0	15	1 (6.7)	0	0
May 2020	219	2 (0.9)	195	2 (1.0)	21	0	3	0	0	0
Jun 2020	18	0	18	0	0	0	0	0	0	0
Total	7,021	24	6,272	20 (0.3)	462	0	240	4 (1.7)	47	0

SARS-CoV-2, severe acute respiratory syndrome-coronavirus 2; No., number; NORTHCOM, U.S. Northern Command; INDOPACOM, U.S. Indo-Pacific Command; U.S. EUCOM, European Command.

FIGURE. Weekly and cumulative counts of SARS-CoV-2 tests and detections, 1 December 2019–3 June 2020



Note: The first SARS-CoV-2 positive sample was identified on 24 February and the cumulative number of cases increased exponentially by week until clinical testing became widespread in the DoD.
SARS-CoV-2, severe acute respiratory syndrome-coronavirus 2; No., number.

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The Cost of Lower Extremity Fractures Among Active Duty U.S. Army Soldiers, 2017

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The estimated cost to the Army for lower extremity fractures in 2017 was approximately $116 million. Direct medical expenses totaled $24 million, and indirect medical costs totaled $92 million ($900 thousand lost duty; $91 million limited duty). Foot and toe fractures, along with lower leg and ankle fractures accounted for the majority of soldiers' initial visits for care (n=4,482; 91.6%), and more than $103 million (89.0%) of overall costs ($116 million). Costs varied by location of care. In outpatient settings, initial visits for foot and toe injuries accounted for the highest costs: $49 million overall. Direct medical costs totaled $1.2 million, and indirect medical costs (limited duty) were $48 million. Conversely, in inpatient settings, lower leg and ankle fractures accounted for slightly more than half of all costs (overall $9 million; $4.8 million in direct medical costs and $4.5 million in indirect medical costs). The finding that the majority of costs related to lower extremity fractures were due to estimated days of lost or limited duty and associated loss of productivity justifies the inclusion of indirect cost estimates as a part of overall injury cost calculations.

WHAT ARE THE NEW FINDINGS?

This study found that indirect medical costs (i.e., loss of return on personnel salary) cost the Army nearly 4 times the amount spent on direct medical care for soldiers' lower extremity fractures. This estimate assumes that lost duty time was equivalent to the number of days hospitalized for a lower extremity fracture and limited duty was equal to 120 days at 50% productivity for each lower extremity fracture. Study findings demonstrate the value of including indirect costs to obtain a comprehensive understanding of the financial burden of military injuries.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Injury costs estimates inform Army injury prevention initiatives and prioritization efforts. However, a standardized method for estimating Army injury costs is needed. The methodology developed for this analysis fills a critical gap in Army estimates of injury burden and provides the foundation for future expanded cost estimates.

Injuries have long been the leading challenge to the Army's ability to optimize medical readiness and soldier health.[1–3] The likelihood of a soldier experiencing an injury is high, with over half of soldiers experiencing a new injury annually.[4] Overall, there are over 1,800 new injuries diagnosed per 1,000 soldiers each year.[4] Many of these injuries are preventable, lead to costly medical encounters and lost productivity among military personnel, and account for the status of more than half of all medically non-deployable Army soldiers.[5–7]

This analysis is centered on acute fractures of the lower extremities. Acute fractures are considered "severe" injuries due to the frequent need for hospitalization and the amount of recovery time required before a soldier can return to work at full capacity. U.S. Army surveillance data from 2015 indicate that 45% of acute injury hospitalizations were due to fractures.[8]

Prior studies have estimated the number of lost duty days attributed to fractures to range from 73 to 120 days—compared to 35 days for dislocations, 18 to 30 days for sprains and strains, and 3 to 11 days for heat- and cold-weather related injuries.[9–11]

The purpose of this study was to develop a standardized methodology for estimating the direct and indirect medical costs of military injuries. The analyses focused on lower extremity fractures, in particular, because such injuries are considered by both the Army safety and health communities to be a high-visibility, high-priority concern.[12,13] No papers to date have addressed the costs of fractures to the Army or to other military services.

METHODS

Centering on factors of interest to the military (a military-societal perspective), a cost-of-illness approach was used to combine information on the number of injuries and the impact of their associated health care utilization into single estimates of cost.[14–17] A cross sectional, prevalence-based study design was employed. Therefore, all acute lower extremity fractures requiring medical care – both new and ongoing for calendar year (CY) 2017 – were included in the analysis. The resulting injury estimates provide the costs of lower extremity fractures in a single year, rather than recurrent costs of these injuries over the course of a soldier's career.

This study included injuries identified in the medical records from the active component of the U.S. Army. Army Reserve and National Guard members on active duty status at any time during CY 2017 were also included. These data represent injury-related care received in or paid for by the Military Health System (MHS) and were obtained from MHS Data Repository

(MDR) files including the Standard Inpatient Data Record (SIDR) (military treatment facility [MTF] inpatient data), the Comprehensive Ambulatory/Professional Encounter Record (CAPER) (MTF outpatient data), TRICARE Encounter Data-Institutional (TED-I) (inpatient data), and TED-Non-Institutional (NI) (records of outpatient purchased care) using the MHS Mart (M2) interface.

Lower extremity fractures were identified using International Classification of Disease, 10th Revision, Clinical Modification (ICD-10-CM) medical diagnostic codes. The listing of codes was identified using an ICD-10-CM Injury Mortality Diagnosis (IMD) Matrix.[18] The inclusion criterion for a case was any medical encounter with an ICD-10 diagnosis code of S72 (fracture of bones in hip or upper leg), S82 (fracture of bones in the knee, lower leg, or ankle), or S92 (fracture of bones in the feet or toes) recorded in the first or second diagnostic position. All extenders for the listed codes were captured and included in the analysis.

Inclusion of the first 2 diagnosis code positions varies from the methodology used in previous incidence and prevalence studies of Army injuries, which limited inclusion criteria to the first diagnosis code position only. A review of several case examples found that many fractures were not identified by a primary diagnosis because a diagnosis of "pain" in a lower extremity often preceded the fracture diagnosis. It was necessary to use the secondary diagnosis to more completely capture all fractures and associated direct costs for treatments and indirect costs via estimated days of lost duty. A 365-day incidence rule was applied by person and injury in order to reduce the effect of follow-up injury visits and potential overestimation of frequencies and rates. The rule states that multiple visits for the same 3-digit ICD-10-CM diagnosis within 365 days of the initial visit were counted as only 1 visit, allowing only 1 injury of the same type per year.

Comprehensive cost-of-illness metrics—both direct and indirect costs—were examined. Direct medical cost was defined as the cost of care associated with the fracture encounter paid for by the MHS. All direct medical cost data were extracted from the MDR and were included for each injury encounter. Two types of indirect medical costs were determined: (1) lost duty time, in which a soldier is not able/available to perform his/her duties due to health care (e.g., injury-related hospitalizations); and (2) limited duty time, in which a soldier either could not participate in his/her military occupational and physical training tasks and/or performed these tasks at diminished capacity due to the injury (e.g., working while injured). The amount of time lost (lost duty time) is based on hospital length of stay associated with a lower extremity fracture. Clinician visit duration or appointment time is not consistently captured across all outpatient settings. No assumptions were made for the length of time for visits and no lost duty time was estimated for time away from duties associated with these appointments. Given the incomplete capture of limited duty days in military medical records, the amount of limited time (limited duty days) for lower extremity fractures was based on estimates from existing literature.[9]

Data were extracted, downloaded, and analyzed using SAS/STAT software, version 9.4 (2014, SAS Institute, Cary, NC). Analyses of lower extremity fractures resulting in inpatient and outpatient treatment were stratified by body region and encounter type. The number of soldiers treated for lower extremity fractures (along with age, sex, and rank group characteristics), frequency of encounters, and estimated limited duty days were reported. Total cost was calculated as the sum of direct medical cost and indirect medical cost.

Direct medical cost, the full cost and/or total amount paid for an injury encounter, was summed respectively for the three fracture diagnosis codes (based on ICD-10 codes S72, S82, and S92). Data were reported in 2017 U.S. dollars by location of care (outpatient and inpatient) and by injury encounter type using available ICD-10-CM extension digits. Initial encounters (first occurrence) were indicated by a seventh digit of "A", "B", or "C", follow-up encounters by "D"–"R", and sequela encounters by "S".

Indirect medical cost, the costs associated with estimated lost duty time and limited duty time, were calculated by linking each soldier's rank from his/her initial encounter to military pay charts.[19] The 2 types of indirect medical costs are considered independent and an injury could be associated with both lost duty time and limited duty time. Indirect medical cost associated with lost duty time for inpatient stays was calculated as the number of days spent in the hospital multiplied by the salary associated with the soldier's rank at the time of the injury. No lost duty time was calculated for outpatient visits. Indirect medical cost associated with limited duty time, based on Ruscio's estimate,[9] was calculated only for the initial occurrence of each injury of interest.[9] The first occurrence of a fracture with an initial encounter indicator (i.e., an "A", "B", or "C") in the seventh position of the ICD code was first assumed to result in 120 days of limited duty.[9] Upon further consideration by injury subject matter experts, and to provide conservative estimates for this analysis, it was assumed that all 120 days were limited duty at 50% productivity. Therefore, the cost of 1 limited duty day was considered equal to half of a service member's daily pay. For 120 days of limited duty, the cost of an injury would equal 120 (days) x 50% of the soldier's daily salary.

RESULTS

Characteristics of lower extremity fractures

Table 1 shows there were 5,287 soldiers who experienced at least 1 lower extremity fracture in CY 2017 (83.3% men, 16.7% women). Over two-fifths (44.1%) of those with lower extremity fractures were 30 years of age or older and 44.0% were less than E–5 in rank. More than half (54.5%) of soldiers with lower extremity fractures experienced fractures to the foot and toes (n=2,880), and 37.1% experienced fractures to the lower leg and ankle (n=1,962); all other anatomical sites for the lower extremity accounted for the remaining 8.9% of fractures (n=445).

TABLE 1. Demographic characteristics and ranks of active duty Army soldiers with at least 1 lower extremity fracture-related medical encounter,[a] calendar year 2017

	Lower extremity specific anatomical sites											
	Overall		Foot and toes		Hip		Knee		Lower leg and ankle		Upper leg and thigh	
	n	%	n	%	n	%	n	%	n	%	n	%
At least 1 medical encounter[b]	5,287	100.0	2,880	54.5	157	3.0	136	2.6	1,962	37.1	152	2.9
Sex												
Female	885	16.7	496	56.0	67	7.6	17	1.9	285	32.2	20	2.3
Male	4,402	83.3	2,384	54.2	90	2.0	119	2.7	1,677	38.1	132	3.0
Age group (years)												
17–19	422	8.0	188	44.5	37	8.8	6	1.4	174	41.2	17	4.0
20–24	1,426	27.0	735	51.5	49	3.4	43	3.0	551	38.6	48	3.4
25–29	1,106	20.9	586	53.0	24	2.2	33	3.0	432	39.1	31	2.8
30+	2,333	44.1	1,371	58.8	47	2.0	54	2.3	805	34.5	56	2.4
Rank/grade												
Junior enlisted (E1–E4)	2,325	44.0	1,165	50.1	100	4.3	66	2.8	917	39.4	77	3.3
Senior enlisted (E5–E9)	2,037	38.5	1,147	56.3	34	1.7	55	2.7	739	36.3	62	3.0
Officer (01–09)	720	13.6	458	63.6	16	2.2	13	1.8	222	30.8	11	1.5
Warrant officer (W01–W06)	164	3.1	89	54.3	5	3.0	2	1.2	66	40.2	2	1.2
Other	41	0.8	21	51.2	2	4.9	0	0.0	18	43.9	0	0.0

[a]Initial inpatient and outpatient medical encounters only.
[b]Soldiers experienced at least 1 initial outpatient and/or inpatient lower extremity fracture-related encounter.

Cost of inpatient care for lower extremity fractures

A total of 433 soldiers received inpatient care for lower extremity fractures **(Table 2)**. The number of soldiers hospitalized for lower leg and ankle fractures (n=278) was 5 times the number hospitalized for upper leg and thigh fractures (n=55), the second most common fracture location. Lower leg and ankle fractures accounted for the highest number of limited duty days associated with inpatient treatment (n=33,744; 64.5%). Lower leg and ankle fractures also accounted for the highest direct medical costs, just over $6.4 million (59.8% of total direct medical inpatient costs); the highest lost duty cost, slightly more than $550 thousand (59.6% of the cost associated with bed days); and the highest limited duty cost, about $4.2 million (66.4% of the cost associated with lost productivity). Of the estimated $18.1 million in inpatient cost reported in **Table 2**, $11.2 million (62.1%) was associated with lower leg and ankle fractures.

Cost of outpatient care for lower extremity fractures

Table 3 shows that 5,247 soldiers received outpatient care for lower extremity fractures. More soldiers made initial visits for foot and toe fractures (n=2,875; 54.8%) than for lower leg and ankle fractures (n=1,944; 37.0%). A smaller number of soldiers experienced lower extremity fractures in other anatomical sites (n=428; 8.2%).

The highest direct medical costs resulted from lower leg and ankle fractures ($7.2 million; 55.0%), followed by foot and toe fractures ($4.9 million; 37.3%). The highest indirect costs—lost or limited productivity costs due to limited duty time—resulted from foot and toe fractures ($47.6 million; 56.1%). Likewise, the highest total costs associated with outpatient encounters were for foot and toe fractures ($52.4 million; 53.6%), followed by lower leg and ankle fractures ($37.9 million; 38.7%).

Cost of inpatient and outpatient care for lower extremity fractures

Table 4 shows that 5,287 soldiers received care for lower extremity fractures in inpatient and/or outpatient sites in CY 2017; 40 soldiers received care in an inpatient setting only **(data not shown)**. More soldiers made initial visits for fractures of the foot and toe (n=2,880; 54.5%) than for fractures of the lower leg (n=1,962; 37.1%). Far fewer soldiers sought initial medical encounters for the other

TABLE 2. Cost[a] of active duty Army soldiers with at least 1 lower extremity fracture treated in inpatient settings, by lower extremity–specific anatomical site and visit type, calendar year 2017

Lower extremity fractures		Soldiers with 1 or more encounters[b]		Estimated limited duty days[c]		Medical Cost							
						Direct medical cost		Indirect medical cost				Total cost	
								Lost duty[d]	Limited duty	Total indirect medical cost			
Specific anatomical site	Encounter type	n	%	n	%	Cost	%	Cost	Cost	Cost	%	Cost	%
Foot and toes	Initial	48	11.1	5,760	99.9	$660,113	71.4	$29,616	$612,384	$642,000	93.3	$1,302,113	
	Follow-up	10	NA	4	0.1	$257,239	27.8	$45,350	$0	$45,350	6.6	$302,589	
	Sequela	1	NA	0	0.0	$7,204	0.8	$627	$0	$627	0.1	$7,831	
	Total	NA	NA	5,764	11.0	$924,556	8.6	$75,593	$612,384	$687,977	9.4	$1,612,533	8.9
Hip	Initial	39	9.0	4,680	100.0	$1,011,490	83.0	$55,093	$613,882	$668,975	88.1	$1,680,465	
	Follow-up	15	NA	1	0.0	$194,821	16.0	$85,583	$0	$85,583	11.3	$280,404	
	Sequela	1	NA	0	0.0	$12,307	1.0	$4,640	$0	$4,640	0.6	$16,947	
	Total	NA	NA	4,681	8.9	$1,218,618	11.3	$145,316	$613,882	$759,198	10.4	$1,977,816	10.9
Knee	Initial	13	3.0	1,560	100.0	$200,609	85.2	$8,473	$163,262	$171,735	96.9	$372,344	
	Follow-up	4	NA	0	0.0	$34,872	14.8	$5,409	$0	$5,409	3.1	$40,281	
	Sequela	0	NA	0	0.0	$0	0.0	$0	$0	$0	0.0	$0	
	Total	NA	NA	1,560	3.0	$235,481	2.2	$13,882	$163,262	$177,144	2.4	$412,625	2.3
Lower leg and ankle	Initial	278	64.2	33,720	99.9	$4,811,993	74.7	$251,886	$4,237,327	$4,489,213	93.8	$9,301,206	
	Follow-up	70	NA	24	0.1	$1,601,269	24.9	$286,251	$0	$286,251	6.0	$1,887,520	
	Sequela	3	NA	0	0.0	$28,723	0.4	$12,726	$0	$12,726	0.3	$41,449	
	Total	NA	NA	33,744	64.5	$6,441,985	59.8	$550,863	$4,237,327	$4,788,190	65.6	$11,230,175	62.1
Upper leg and thigh	Initial	55	12.7	6,600	99.9	$1,257,765	64.4	$62,566	$746,978	$809,544	91.5	$2,067,309	
	Follow-up	25	NA	5	0.1	$694,865	35.6	$75,357	$0	$75,357	8.5	$770,222	
	Sequela	0	NA	0	0.0	$0	0.0	$0	$0	$0	0.0	$0	
	Total	NA	NA	6,605	12.6	$1,952,630	18.1	$137,923	$746,978	$884,901	12.1	$2,837,531	15.7
Total		433	100.0	52,354	100.0	$10,773,270	100.0	$923,577	$6,373,833	$7,297,410	100.0	$18,070,680	100.0

[a]Reported in 2017 dollars. Data include military treatment facility and purchased care information.
[b]Soldiers with at least 1 initial outpatient and/or inpatient lower extremity fracture-related encounter.
[c]For each unique fracture, 120 days of duty at 50% productivity were assumed. Soldiers with only subsequent or sequela encounters were not assigned limited duty days.
[d]Hospital bed days multiplied by the individuals pay rate.
NA, not applicable.

categories of lower extremity fracture (hip, n=157, 3.0%; upper leg and thigh, n= 152, 2.9%; knee, n=136, 2.6%).

Fractures to the foot and toes resulted in more days of limited duty than any other anatomical site of the lower extremities: 359,284 days (51.3% of the total days). The second greatest number of limited duty days was for lower leg and ankle fractures: 275,664 (39.4%) of the total days of limited duty.

The highest total costs for lower extremity fractures were associated with foot and toe fractures ($54.1 million; 46.6%), followed by the cost of lower leg and ankle fractures ($49.1 million; 42.4%). These 2 anatomical sites accounted for 89.0% of total costs.

EDITORIAL COMMENT

In a single year (CY 2017), lower extremity fractures—the most common cause of hospitalization among military service members—cost the Army an estimated $116 million in direct and indirect medical cost, and more than 5,000 active

TABLE 3. Cost[a] of active duty Army soldiers with at least 1 lower extremity fracture treated in outpatient settings, by lower extremity–specific anatomical site and visit type, calendar year 2017

Lower extremity fractures		Soldiers with 1 or more encounters[b]		Estimated limited duty days[c]		Medical Cost							
						Direct medical cost		Indirect medical cost				Total cost	
								Lost duty[d]	Limited duty	Total indirect medical cost			
Specific anatomical site	Encounter type	n	%	n	%	Cost	%	Cost	Cost	Cost	%	Cost	%
Foot and toes	Initial	2,875	54.8	353,520	100.0	$1,236,961	25.3	$0	$47,561,396	$47,561,396	100.0	$48,798,357	
	Follow-up	2,786	NA	0	0.0	$3,537,952	72.5	$0	$0	$0	0.0	$3,537,952	
	Sequela	274	NA	0	0.0	$104,842	2.1	$0	$0	$0	0.0	$104,842	
	Total	NA	NA	353,520	54.5	$4,879,755	37.3	$0	$47,561,396	$47,561,396	56.1	$52,441,151	53.6
Hip	Initial	150	2.9	18,240	100.0	$42,200	23.5	$0	$2,175,903	$2,175,903	100.0	$2,218,103	
	Follow-up	194	NA	0	0.0	$129,919	72.3	$0	$0	$0	0.0	$129,919	
	Sequela	32	NA	0	0.0	$7,639	4.2	$0	$0	$0	0.0	$7,639	
	Total	NA	NA	18,240	2.8	$179,758	1.4	$0	$2,175,903	$2,175,903	2.6	$2,355,661	2.4
Knee	Initial	134	2.6	16,560	100.0	$105,553	28.6	$0	$2,117,602	$2,117,602	100.0	$2,223,155	
	Follow-up	141	NA	0	0.0	$255,535	69.3	$0	$0	$0	0.0	$255,535	
	Sequela	24	NA	0	0.0	$7,418	2.0	$0	$0	$0	0.0	$7,418	
	Total	NA	NA	16,560	2.6	$368,506	2.8	$0	$2,117,602	$2,117,602	2.5	$2,486,108	2.5
Lower leg and ankle	Initial	1,944	37.0	241,920	100.0	$1,024,152	14.2	$0	$30,642,565	$30,642,565	100.0	$31,666,717	
	Follow-up	2,118	NA	0	0.0	$6,014,572	83.4	$0	$0	$0	0.0	$6,014,572	
	Sequela	375	NA	0	0.0	$169,556	2.4	$0	$0	$0	0.0	$169,556	
	Total	NA	NA	241,920	37.3	$7,208,280	55.0	$0	$30,642,565	$30,642,565	36.2	$37,850,845	38.7
Upper leg and thigh	Initial	144	2.7	17,880	100.0	$66,027	14.4	$0	$2,207,845	$2,207,845	100.0	$2,273,872	
	Follow-up	212	NA	0	0.0	$345,991	75.4	$0	$0	$0	0.0	$345,991	
	Sequela	52	NA	0	0.0	$47,010	10.2	$0	$0	$0	0.0	$47,010	
	Total	NA	NA	17,880	2.8	$459,028	3.5	$0	$2,207,845	$2,207,845	2.6	$2,666,873	2.7
Total		5,247	100.0	648,120	100.0	$13,095,327	100.0	$0	$84,705,311	$84,705,311	100.0	$97,800,638	100.0

[a]Reported in 2017 dollars. Data include military treatment facility and purchased care information.
[b]Soldiers with at least 1 initial outpatient and/or inpatient lower extremity fracture-related encounter.
[c]For each unique fracture, 120 days of duty at 50% productivity were assumed. Soldiers with only subsequent or sequela encounters were not assigned limited duty days.
[d]No lost duty time was estimated for outpatient visits.
NA, not applicable.

duty soldiers experienced 1 or more lower extremity fractures in CY 2017. Even though lower extremity fractures are considered "serious" injuries, the largest percentage of associated costs ($97.8 million; 84.4%) was incurred by fractures treated in outpatient settings. Overall, 5,247 soldiers had outpatient encounters for lower extremity fractures. The majority of soldiers treated in outpatient settings for lower extremity fractures had encounters for fractures to foot and toes (54.8%), followed by fractures to lower leg and ankle (37.0%). Although more serious, the costs of lower extremity fractures requiring hospitalization were only $18.1 million, or 15.6% of the total costs. However, the costs per case for fractures treated in inpatient settings was 9 times the cost of those treated on an outpatient basis ($30,628 per case versus $3,370 per case [Encounter data reported in the full technical report[21]]). Among the 433 soldiers hospitalized for lower extremity fractures, 64.2%

TABLE 4. Cost[a] of active duty Army soldiers' encounters for lower extremity fractures treated in both inpatient and outpatient settings, by lower extremity-specific anatomical sites and visit type, calendar year 2017

Lower extremity fractures		Soldiers with 1 or more encounters[b]		Estimated limited duty days[c]		Medical Cost							
						Direct medical cost		Indirect medical cost				Total cost	
								Lost duty[d]	Limited duty	Total indirect medical cost			
Specific anatomical site	Encounter type	n	%	n	%	Cost	%	Cost	Cost	Cost	%	Cost	%
Foot and toes	Initial	2,880	54.5%	359,280	100.0	$1,897,074	32.7	$29,616	$48,173,780	$48,203,396	100.0	$50,100,470	
	Follow-up	2,787	NA	4	0.0	$3,795,191	65.4	$45,350	$0	$45,350	0.1	$3,840,541	
	Sequela	275	NA	0	0.0	$112,045	1.9	$627	$0	$627	0.0	$112,672	
	Total	NA	NA	359,284	51.3	$5,804,310	24.3	$75,593	$48,173,780	$48,249,373	52.4	$54,053,683	46.6
Hip	Initial	157	3.0%	22,920	100.0	$1,053,690	75.4	$55,093	$2,789,785	$2,844,878	97.0	$3,898,568	
	Follow-up	197	NA	1	0.0	$324,740	23.2	$85,583	$0	$85,583	3.0	$410,323	
	Sequela	33	NA	0	0.0	$19,946	1.4	$4,640	$0	$4,640	0.0	$24,586	
	Total	NA	NA	22,921	3.3	$1,398,376	5.9	$145,316	$2,789,785	$2,935,101	3.2	$4,333,477	3.7
Knee	Initial	136	2.6%	18,120	100.0	$306,162	50.7	$8,473	$2,280,865	$2,289,338	100.0	$2,595,500	
	Follow-up	142	NA	0	0.0	$290,406	48.1	$5,409	$0	$5,409	0.0	$295,815	
	Sequela	24	NA	0	0.0	$7,418	1.2	$0	$0	$0	0.0	$7,418	
	Total	NA	NA	18,120	2.6	$603,986	2.5	$13,882	$2,280,865	$2,294,747	2.5	$2,898,733	2.5
Lower leg and ankle	Initial	1,962	37.1%	275,640	100.0	$5,836,146	42.8	$251,886	$34,879,891	$35,131,777	99.0	$40,967,923	
	Follow-up	2,124	NA	24	0.0	$7,615,842	55.8	$286,251	$0	$286,251	1.0	$7,902,093	
	Sequela	376	NA	0	0.0	$198,279	1.5	$12,726	$0	$12,726	0.0	$211,005	
	Total	NA	NA	275,664	39.4	$13,650,267	57.2	$550,863	$34,879,891	$35,430,754	38.5	$49,081,021	42.4
Upper leg and thigh	Initial	152	2.9%	24,480	100.0	$1,323,792	54.9	$62,566	$2,954,824	$3,017,390	98.0	$4,341,182	
	Follow-up	214	NA	5	0.0	$1,040,856	43.2	$75,357	$0	$75,357	2.0	$1,116,213	
	Sequela	52	NA	0	0.0	$47,010	1.9	$0	$0	$0	0.0	$47,010	
	Total	NA	NA	24,485	3.5	$2,411,658	10.1	$137,923	$2,954,824	$3,092,747	3.4	$5,504,405	4.8
Total		5,287	100%	700,474	100.0	$23,868,597	100.0	$923,577	$91,079,145	92,002,722	100.0	$115,871,319	100.0

[a]Reported in 2017 dollars. Data include military treatment facility and purchased care information.
[b]Soldiers with at least 1 initial outpatient and/or inpatient lower extremity fracture-related encounter.
[c]For each unique fracture, 120 days of duty at 50% productivity were assumed. Soldiers with only subsequent or sequela encounters were not assigned limited duty days.
[d]Inpatient stays only: Hospital bed days multiplied by the individual's pay rate.
NA, not applicable.

were hospitalized for fractures to lower legs and ankles, followed by upper leg and thigh fractures (12.7%). Overall, the indirect costs of fractures ($92.0 million) were approximately 4 times greater than costs associated with direct medical expenses ($23.9 million). These indirect costs were clearly driven by the cost associated with limited duty days ($91.1 million of the $92.0 million). This study estimated that more than 700,000 limited duty days were associated with lower extremity fractures in 2017; 648,000 days were related to soldiers treated in outpatient settings, and 52,000 days were related to soldiers who were hospitalized.

While the cost of fractures has not been previously reported, the diagnosis, distribution, and anatomical locations of these acute injuries for outpatient cases were similar to those seen previously among military service members.[2] The distribution of lower extremity fractures treated in hospitals in this study was also similar to the distributions reported among service members[2] and among medical evacuation cases during Operation Iraqi Freedom/Operation Enduring Freedom.[20]

This study estimated both direct and indirect medical costs attributed to a specific type of injury more precisely than any prior study. While days of lost duty and limited duty were estimated to determine the indirect costs, these costs were segregated by complete loss of duty time (such as due to hospital or bed restriction) and the cost of restricted abilities (represented as productivity loss). A study innovation involved inclusion of the secondary diagnosis in the case definition after study investigators noted a diagnosis of "pain" in a lower extremity often precedes the fracture diagnosis for these injuries. As a result, an additional 531 injuries of interest were appropriately identified. Methodological details are documented in an earlier APHC public health information paper.[21]

As an initial study, some limitations are acknowledged. Study estimates may overestimate costs associated with fractures where comorbid conditions (i.e., other injuries or conditions) contributed to the cost of the encounters. Additional analysis should be conducted to better understand the likelihood and magnitude of this concern. The basis for estimation of limited duty of 120 days was from information in the literature and not actual profile days assigned by providers, and therefore may lack precision. Additionally, these estimates are not differentiated by type of injury and could overestimate the cost for fractures where the number of limited duty days for a specific injury type were less than the estimated 120 days (e.g., toe fractures and metatarsal fractures). While the researchers addressed this concern by assuming that all 120 days were limited duty at 50% productivity; the productivity cutoff was based on the experience of injury prevention subject matter experts. Sensitivity analysis could be conducted to confirm the efficacy of this decision. The cost for fractures may be underestimated where visits preceding the fracture diagnosis (e.g., for pain) were not included in cost estimates. Appointment time is also lost duty time but was not available for all data sources and was not included in this analysis. Not all costs were captured since fractures recorded in diagnostic positions 3–10 were not included. Lower extremity fracture costs associated with outpatient surgeries (e.g., Current Procedural Terminology [CPT] codes 27600–27899, surgical procedures to the leg and ankle), may not have been captured especially where these costs were attached to visits preceding the fracture diagnosis. Costs for care paid by insurers outside the MHS as well as the cost for other care, such as informal care, were not included and are a source of underestimation as well.

Study findings support the methodological value of estimating Army injury costs. Specifically, the results demonstrate that the majority of costs of lower extremity fractures result from the indirect costs associated with limited duty time. This finding and the methods used to calculate the associated indirect and direct costs address a gap which has previously existed in the study and surveillance of military injuries.

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Brief Report

Medical Encounters for Snakebite Envenomation, Active and Reserve Components, U.S. Armed Forces, 2016–2020

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Of the approximately 3,000 known snake species in the world, about 20% (i.e., 600 species) are venomous.[1] Snakebite envenomation (SBE) occurs when venom is injected into a human or animal via a snake's fangs, or much less frequently, via spitting venom into a victim's eye or open wound. Not all snakebites result in envenomation; an estimated 25% to 50% of snakebites are "dry bites" in which an insufficient amount of venom is injected to cause clinical symptoms.[2,3] Clinical effects of snake envenomation can range from mild local effects (e.g., superficial puncture wounds, pain and swelling) to more severe complications including permanent disability and death.[3]

SBEs are a significant public health issue especially in the tropical and subtropical areas of Africa, Asia, and Latin America.[4] In 2017, the World Health Organization (WHO) identified SBE as a neglected tropical disease. WHO estimates between 1.8–2.7 million SBEs occur annually, resulting in an estimated 81,410 to 137,880 deaths.[5] Each year in the U.S., there are an estimated 5,000–10,000 SBEs and fewer than 10 associated deaths.[6]

Although rare, SBEs are an occupational hazard for military members worldwide. The recent published literature on SBE in military members is sparse. During contingency operations in Iraq and Afghanistan, self-reported incidence of snakebite in U.S. troops was 4.9 snakebites per 10,000 person-months.[7] A recent review of snakebites treated between 2015–2017 by the French military health service in overseas locations identified only two soldiers (1 French, 1 Dutch) treated for SBE in Mali, both of whom were treated with antivenom and recovered fully.[8] A 2018 summary of snakebites in UK personnel focused on Europe and Africa and reported on an envenomation in a UK service member bitten by a horned viper in Croatia. This summary also highlighted that the majority of SBE cases treated by military medical providers occurred among local civilians.[9] The only death attributed to SBE in a U.S. service member that was reported in the lay press occurred in 2015 in Kenya.[10]

No comprehensive summary of all medically diagnosed SBEs in U.S. service members worldwide has been published. This analysis summarizes the incidence of SBE in active and reserve component service members identified through review of administrative medical data. This analysis also provides a breakdown of SBEs by demographic and military characteristics including the country and combatant command in which the SBEs were treated.

METHODS

The surveillance period was from 1 January 2016 through 31 December 2020. The surveillance population included all individuals who served in the active or reserve component of the U.S. Army, Navy, Air Force, or Marine Corps at any time during the surveillance period. The Defense Medical Surveillance System (DMSS) was searched for all inpatient, outpatient and/or theater medical encounters that contained any of the ICD-10 codes falling under the parent code T63.0 ("Toxic effect of snake venom") in any diagnostic position. Because ICD-9 diagnoses still appear in the theater medical encounter data, service members could also qualify as a case if they had a diagnosis of ICD-9: 989.5 ("Toxic effect of venom") or E905.0 ("Venomous snakes and lizards causing poisoning and toxic reactions"). The patient assessment field was reviewed for these ICD-9 coded records to determine whether the injury was caused by a snake and only the records for injuries that were caused by snakes were retained. A service member could be counted as an incident case once per year. The location of the SBE was determined by mapping the treating facility for the SBE to a specific country and combatant command.

RESULTS

During the 5-year surveillance period, a total of 345 SBEs were diagnosed in U.S. service members. Approximately 90% of cases were among male service members and about 45% occurred in soldiers. More than three-quarters of SBEs were diagnosed among active component service members **(Table)**. The majority of cases occurred in service members in the 20–29 year old age group. Service members in the repair/engineering and combat-specific occupational groups were the most frequently affected by SBEs and constituted over half of all SBEs during the period **(Table)**.

The annual numbers of SBEs were at their highest in 2017 (n=83); this peak represented a 9.2% increase in SBEs over the prior year. Total SBEs declined by 22.6% in 2018 and a further 9.4% in 2019; 2019 had the lowest number of incident cases of SBE during the surveillance period (n=58). Incident cases increased by 10.3% in 2020 (n=64) which was the same level as 2018 (**Figure 1**). Overall, 59.4% (n=205) of the cases occurred between the months of June and September **(Figure 2)**.

Most SBE cases (96.2%) were diagnosed in the U.S.; consequently, almost 96% of cases occurred in the U.S. Northern Command **(Table)**. Cases diagnosed in Hawaii are attributed to the U.S. Indo-Pacific Command. Counts of cases by specific location were 1 in Puerto Rico, 330 in the U.S. (excluding Hawaii), 5 in Guam, 4 in Japan, 2 in Korea, 2 in Hawaii, and 1 with an unknown location.

TABLE. Demographic and military characteristics of incident cases of snakebite envenomation, U.S. Armed Forces, 2016–2020

	Total (2016–2020)	
	No.	%
Total	345	100.0
Sex		
Female	33	9.6
Male	312	90.4
Age group (years)		
17–19	19	5.5
20–29	183	53.0
30–39	92	26.7
40+	51	14.8
Race/ethnicity group		
Non-Hispanic White	253	73.3
Non-Hispanic Black	22	6.4
Hispanic	46	13.3
Other/unknown	24	7.0
Service		
Army	155	44.9
Navy	40	11.6
Air Force	79	22.9
Marine Corps	71	20.6
Component		
Active	264	76.5
Reserve	81	23.5
Rank		
E1–E4 (Junior enlisted)	135	39.1
E5–E9 (Senior enlisted)	153	44.3
O1–O3; W1–W3 (Junior officer)	33	9.6
O4–O10; W4–W5 (Senior officer)	24	7.0
Military occupation		
Combat-specific[a]	87	25.2
Motor transport	15	4.3
Pilot/air crew	13	3.8
Repair/engineering	94	27.2
Communications/intelligence	55	15.9
Veterinarian	3	0.9
Health care (not including veterinarian)	14	4.1
Other/unknown	64	18.6
Combatant Command		
AFRICOM	0	0.0
CENTCOM	0	0.0
EUCOM	0	0.0
NORTHCOM	331	95.9
INDOPACOM	13	3.8
SOUTHCOM	0	0.0
Unknown/missing	1	0.3
Country		
Guam	5	1.4
Japan	4	1.2
Republic of Korea	2	0.6
Puerto Rico	1	0.3
U.S. (including Hawaii)	332	96.2
Unknown/missing	1	0.3

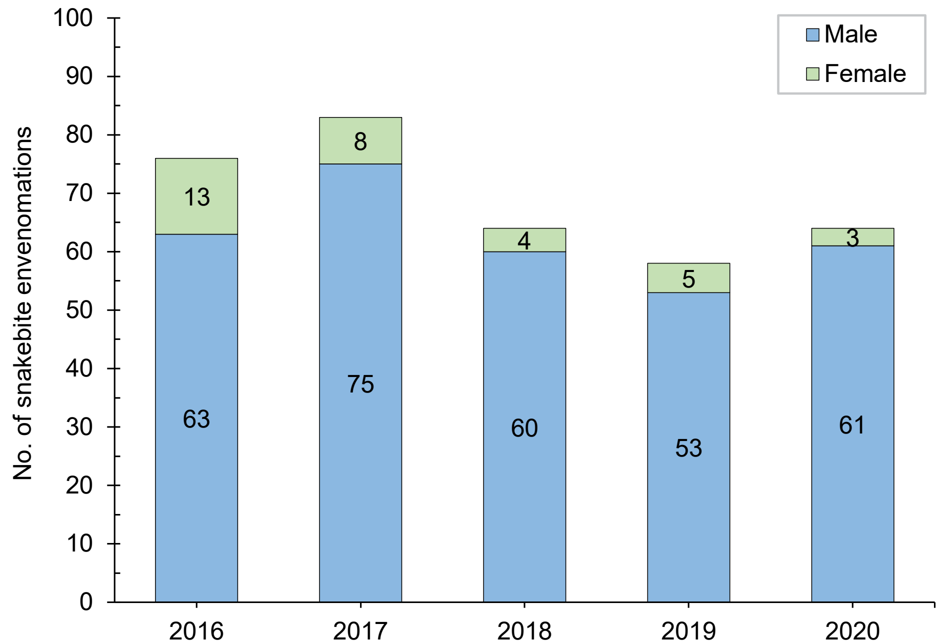
[a]Infantry/artillery/combat engineering.
No., number; AFRICOM, U.S. Africa Command; CENTCOM, U.S. Central Command; EUCOM, U.S. European Command; NORTHCOM; U.S. Northern Command; INDOPACOM, U.S. Indo-Pacific Command; SOUTHCOM, U.S. Southern Command.

EDITORIAL COMMENT

This analysis demonstrates that the vast majority of medically diagnosed SBEs in U.S. service members during 2016–2020 occurred in the U.S. In accordance with the findings of a recent report on the epidemiology of snakebites in the U.S., male service members were disproportionately affected by SBEs.[6]

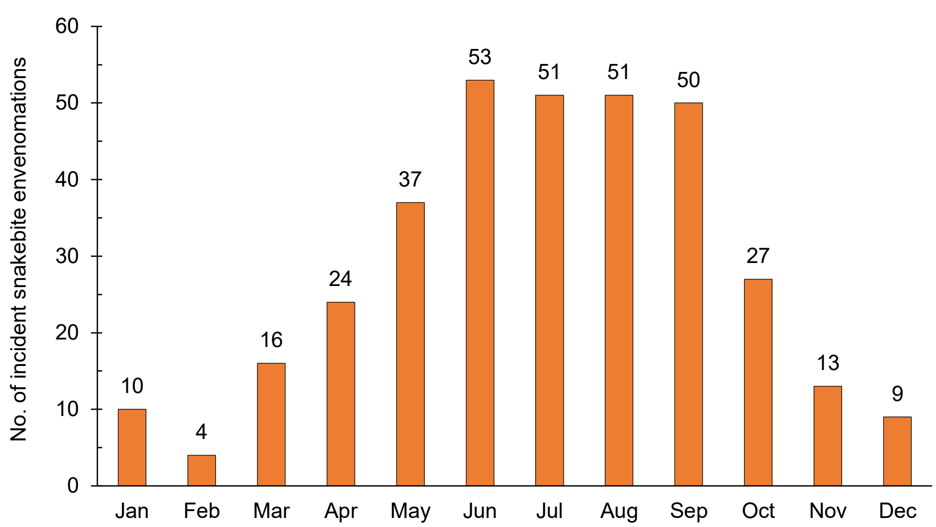
This analysis is subject to the same limitations as any analysis of administrative medical data. Only SBEs that were

FIGURE 1. Annual counts of incident cases of snakebite envenomations, by sex, active and reserve component service members, U.S. Armed Forces, 2016–2020



No., number.

FIGURE 2. Cumulative number of incident snakebite envenomations, by month, active and reserve component service members, U.S Armed Forces, 2016–2020



No., number.

diagnosed by a medical provider and entered into a service member's electronic medical record could be included in this analysis. An SBE could also be missed due to miscoding or because medical care for an SBE was not documented in the medical record.

In the U.S., service member SBEs occur more frequently during warm weather months. Preventive measures for avoiding SBE include precautions such as avoiding snakes in the wild, wearing long pants or boots when working or walking outdoors, and wearing gloves when handling brush or reaching into areas that might house snakes. Anyone bitten by a snake should seek medical attention as soon as possible.[11,12]

Although this analysis demonstrates that the majority of service members' SBEs occur in the U.S., appropriate precautions should be taken to avoid SBE during deployment outside of the U.S. Planning for deployment should include education in the medically important snake species and the appropriate medical management of snakebites specific to deployment location. In 2020, the Joint Trauma System published a Clinical Practice Guideline for Global Snake Envenomation Management (CPG ID:81) which provides a comprehensive guide to snakebite management by combatant command.[12]

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Department of Defense Mid-Season Vaccine Effectiveness Estimates for the 2019–2020 Influenza Season

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This report provides mid-season vaccine effectiveness (VE) estimates from the Armed Forces Health Surveillance Division (AFHSD), the DoD Global Respiratory Pathogen Surveillance (DoDGRS) program, and the Naval Health Research Center (NHRC) for the 2019–2020 influenza season. Using a test-negative case-control study design, the AFHSD performed a VE analysis for active component service members while the DoDGRS program and NHRC collaborated to perform a VE analysis for DoD beneficiaries and U.S.–Mexico border civilians. Among active component service members, there was low to moderate protection against influenza B, moderate protection against A(H3N2), and non-statistically significant low protection against influenza A overall and A(H1N1). Among DoD beneficiaries and U.S.–Mexico border civilians, there was statistically significant moderate protection against influenza B, influenza A overall, A(H1N1), and A(H3N2).

WHAT ARE THE NEW FINDINGS?

The 2019–2020 influenza vaccine provided moderate protection against influenza for beneficiary and civilian populations within the Department of Defense (DoD) and low to moderate protection against influenza for active component service members.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Components of the influenza vaccine can change each season and novel influenza strains can appear and circulate among active component and DoD beneficiary populations. Conducting VE studies every year can assist vaccine policy makers in making their decisions on strain selection for the influenza vaccine for the subsequent season, thus creating the most effective influenza vaccine, which can reduce morbidity and improve military readiness.

Historically, military populations have been stationed in congregate settings that predispose them to acute respiratory infections, resulting in significantly increased morbidity, which has impacted military readiness.[1] In previous seasons, it was estimated that 300,000 to 400,000 active component service members had medical encounters for respiratory infections.[2] Specifically, influenza has had a significant impact on the military population for over a century. During the influenza pandemic of 1918, 43,000 U.S. service members were killed due to the H1N1 pandemic strain that was circulating at the time, constituting approximately 40% of all U.S. war deaths during World War I.[3] On a yearly basis, the U.S. military requires influenza vaccination among active component personnel, with a goal of exceeding 90% immunization by mid-December of each year.[2]

Despite the high vaccination rate among the military population, vaccine breakthrough cases still occur. From 2007 through 2012, the Armed Forces Health Surveillance Division (AFHSD) reported 7,000–25,000 cases of influenza infections to the Military Health System each week of the influenza seasons, 3,000 to 16,000 of which were military personnel.[2,4,5] The Department of Defense (DoD) conducts year-round influenza surveillance for military health beneficiaries and civilian populations, and the DoD uses these data to estimate mid-season influenza vaccine effectiveness (VE), which is submitted annually to the Food and Drug Administration Vaccine and Related Biological Advisory Committee meeting. This report presents the mid-season VE estimates from the DoD 2019–2020 influenza season surveillance.

METHODS

Two separate analyses were performed to produce mid-season DoD VE estimates, both using a test-negative, case-control study design. The study population for the AFHSD analysis consisted of active component service members from the Army, Air Force, Navy, and Marine Corps stationed in the U.S. and abroad who were tested for influenza. Subjects were identified using the Defense Medical Surveillance System Health Level 7 data from the Navy and Marine Corps Public Health Center, and service member data from the Naval Health Research Center (NHRC) for specimens collected for influenza testing from 1 November 2019 to 15 February 2020. The AFHSD identified cases by either a positive reverse transcription polymerase chain reaction (RT-PCR), viral culture, or rapid test. Cases were laboratory-confirmed influenza positives and controls were influenza test negatives. Active component service members with a negative rapid test were excluded. Influenza vaccination status was ascertained through documentation in medical records. Subjects were considered vaccinated if the laboratory specimens were collected 14 days or more days after vaccination. Crude and adjusted

VE estimates were calculated using odds ratios (ORs) and 95% confidence intervals (CIs) obtained from multivariable logistic regression models. VE estimates were adjusted for sex, age category, and month of specimen collection. VE was calculated as (1–OR) × 100. Results were stratified by influenza subtype. Due to differences in the timing of circulating influenza strains this season, the influenza B and influenza A(H3N2) analyses used specimens from the entire period of 1 November 2019 to 15 February 2020, whereas the influenza A overall and influenza A(H1N1) analyses were restricted to the peak influenza A circulation period of 1 January 2020 to 15 February 2020. Influenza A(H3N2) cases were few and sporadic throughout the season, which is why the entire period was used. All vaccinated populations were restricted to subjects who received inactivated influenza vaccine because the live attenuated influenza vaccine was not routinely used among active component service members during the 2019–2020 season.

The DoD Global Respiratory Pathogen Surveillance (DoDGRS) program and NHRC combined their surveillance data to estimate VE among DoD beneficiaries and civilians whose specimens were collected from 3 November 2019 to 15 February 2020. Active component members were excluded from this analysis. Data from the DoDGRS program pertained to DoD dependents who visited military treatment facilities and whose specimens were sent to and tested at the U.S. Air Force School of Aerospace Medicine (USAFSAM). NHRC's data pertained to civilian populations who visited clinics near the U.S.–Mexico border and outpatient DoD beneficiaries in Southern California and Illinois. Cases were patients whose laboratory tests confirmed the presence of influenza virus, and controls were patients whose influenza tests were negative. Cases and controls were identified by RT-PCR and/or viral culture. Vaccination status was determined through electronic immunization records from the Air Force Complete Immunization Tracking Application or self-report from questionnaires. Individuals were considered vaccinated if they received the vaccine at least 14 days prior to their specimen collection date. Those whose vaccination status could not be ascertained or those who were vaccinated within 14 days prior to their illness were excluded. Crude and adjusted VE estimates for this analysis were also calculated using ORs and 95% CIs obtained from multivariable logistic regression models. VE estimates were adjusted for age group, time of specimen collection, location, and sex. VE was calculated as (1–OR) × 100. Results were stratified by influenza subtype and population (all dependents, aged 2–17 years, and aged 18 years or older) **(Table 1)**. Because of insufficient data, a sub-analysis for the elderly population (aged 65 years or older) was not possible.

RESULTS

For AFHSD's active component service member influenza B and A(H3N2) analysis (November to February), there were 2,033 and 37 laboratory-confirmed cases of influenza B and A(H3N2), respectively, and 4,982 test-negative controls. For AFHSD's active component service member influenza A (any subtype) and A(H1N1) analysis (January to February), there were 1,911 and 347 laboratory-confirmed cases of influenza A (any subtype) and A(H1N1), respectively, and 2,222 test-negative controls. Although the crude VE estimate for influenza B was not statistically significantly different from zero, the adjusted VE estimate was statistically significant at 31%. The crude and adjusted VE estimates for influenza A(H3N2) were statistically significant at 49% and 58%, respectively. The adjusted VE estimates for influenza A (any subtype) and A(H1N1) did not reach statistical significance at 12% and 28%, respectively. The confidence intervals for crude and adjusted VE estimates are shown in the **Table**.

For the USAFSAM/NHRC DoD beneficiary and civilian analysis, there were 1,595 confirmed cases and 2,150 controls. With the exception of influenza A(H3N2) in adults, all adjusted VE estimates were statistically significantly different from zero. Moreover, the VE estimates were substantially higher for influenza B (unadjusted and adjusted) and influenza A(H3N2) (adjusted) than for influenza A(H1N1) and all influenza A subtypes.

EDITORIAL COMMENT

Among active component service members, the mid-season 2019–2020 estimates of influenza vaccine effectiveness indicated moderate protection against A(H3N2) (58%), low to moderate protection against influenza B (31%), and non-statistically significant low protection against influenza A overall (12%) and A(H1N1) (28%). Estimates for the DoD beneficiaries and civilian population indicate a statistically significant moderate protection against overall influenza diagnosis (54%), influenza B (51%), influenza A (any subtype) (45%), A(H1N1) (42%), and A(H3N2) (60%). Mid-season VE estimates for active component service members were higher and statistically significant compared with the previous season.[7] This could potentially be due to the 2019–2020 season being more severe and having a higher volume of testing, which resulted in a larger sample size and improved statistical power of the analyses. VE estimates for the DoD beneficiaries and civilian populations were similar to interim estimates from the Centers for Disease Control and Prevention's VE analysis for the 2019–2020 influenza season.[8]

There were limitations to these analyses. Results for the active component service member analysis are for medically attended illnesses that were tested for influenza; therefore, the result may not be applicable to less severe illnesses that did not result in a medical encounter for the 2019–2020 influenza season. Among the active component service member population, influenza vaccination is mandatory, so this population is highly immunized. This could have a negative impact on VE, with potential statistical issues and biological effects such as attenuated immune response with repeated exposures. The DoD beneficiaries and civilians analysis was unable to calculate VE estimates for the elderly population due to insufficient data. Additionally, self-reported data from the questionnaire could result in potential recall bias on the analysis. However, this bias was curtailed for self-reported vaccination status by excluding those whose status could not be ascertained and electronic immunization records were used instead, if available.

TABLE. Mid-season crude and adjusted influenza VE estimates, by influenza subtype and population, 2019–2020 influenza season

Influenza type/ subtype	Population	Vaccination status	Cases No.	Cases %	Controls No.	Controls %	Crude VE % (95% CI)	Adjusted VE % (95% CI)
Active component service members (AFHSD and NHRC)[a]								
Influenza A (any subtype)	Total	Vaccinated	1,732	91	2,038	92	13 (-8–30)	12 (-10–30)
		Unvaccinated	179	9	184	8		
A(H1N1)	Total	Vaccinated	308	89	2,038	92	29 (-3–51)	28 (-5–51)
		Unvaccinated	39	11	184	8		
A(H3N2)	Total	Vaccinated	22	59	3,699	74	49 (2–74)	58 (9–80)
		Unvaccinated	15	41	1,283	26		
Influenza B	Total	Vaccinated	1,515	75	3,699	74	-1 (-14–10)	31 (20–40)
		Unvaccinated	518	25	1,283	26		
Non-active component DoD beneficiaries and civilians (USAFSAM/AFHSD-AF satellite and NHRC)[b]								
Overall	Total	Vaccinated	690	18	1,205	32	40 (32–48)	54 (46–60)
		Unvaccinated	905	24	945	25		
	2–17 yrs	Vaccinated	459	21	632	29	39 (28–49)	47 (35–56)
		Unvaccinated	588	27	493	23		
	18+ yrs	Vaccinated	228	15	564	36	42 (29–53)	48 (35–59)
		Unvaccinated	317	20	452	29		
Influenza A (any subtype)	Total	Vaccinated	367	13	1,205	42	25 (11–36)	45 (33–54)
		Unvaccinated	383	13	945	33		
	2–17 yrs	Vaccinated	204	13	632	42	14 (- 8–32)	38 (20–52)
		Unvaccinated	186	12	493	33		
	18+ yrs	Vaccinated	162	12	564	41	34 (16–48)	55 (42–66)
		Unvaccinated	197	14	452	33		
A(H1N1)	Total	Vaccinated	336	12	1,205	43	23 (9v36)	42 (29–52)
		Unvaccinated	344	12	945	33		
	2–17 yrs	Vaccinated	188	13	632	43	11 (-14–30)	31 (9–48)
		Unvaccinated	164	11	493	33		
	18+ yrs	Vaccinated	147	11	564	42	35 (16–49)	56 (43–67)
		Unvaccinated	180	13	452	34		
A(H3N2)	Total	Vaccinated	29	1	1,205	54	39 (-1–62)	60 (33–76)
		Unvaccinated	37	2	945	43		
	2–17 yrs	Vaccinated	15	1	632	54	44 (-9–72)	73 (43–87)
		Unvaccinated	21	2	493	42		
	18+ yrs	Vaccinated	15	1	591	55	Unable to perform analysis[c]	
		Unvaccinated	16	1	452	42		
Influenza B	Total	Vaccinated	323	11	1,205	40	51 (43–59)	51 (41–59)
		Unvaccinated	522	17	945	32		
	2–17 yrs	Vaccinated	255	14	632	35	51 (40–59)	54 (43–63)
		Unvaccinated	402	23	493	28		
	18+ yrs	Vaccinated	66	5	564	47	56 (39–68)	52 (31–67)
		Unvaccinated	120	10	452	38		

[a]VE adjusted for age group, month of diagnosis, and sex
[b]VE adjusted for age group, time of specimen collection, location, and sex
[c]Due to insufficient data, an analysis for influenza A(H3N2) 18+yrs was not performed.
No., number; DoD, Department of Defense; VE, vaccine effectiveness; CI, confidence interval; USAFSAM/AFHSD-AF, U.S. Air Force School of Aerospace Medicine/Armed Forces Surveillance Division-Air Force; NHRC, Naval Health Research Center; AFHSD, Armed Forces Health Surveillance Division; E&A, Epidemiology and Analysis section.

Because of the rapidly changing nature of the influenza virus, it is imperative for researchers to continue to assess the effectiveness of the influenza vaccine, as well as to enhance methods of VE analyses for more accurate estimates, and to take waning immunity and repeated vaccinations into account. Future research on these concepts could bring forth benefits and have an influence on decision-making for vaccination policies, especially for the military.

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