JUNE 2020

Volume 27
Number 06

MSMR

MEDICAL SURVEILLANCE MONTHLY REPORT

CDC/James Gathany

A publication of the Armed Forces Health Surveillance Branch

Letter to the Editor: G6PD Deficiency in the Tafenoquine Era

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In the December 2019 issue of the *MSMR*, Lee and Poitras reported a 2.2% prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency among active duty U.S. service members between 2004 and 2018.[1] Their study utilized Health Level 7-formatted chemistry data archived in the Composite Health Care System (CHCS), but it did not stratify by quantitative or qualitative testing.

When tafenoquine was approved by the U.S. Food and Drug Administration in 2018 for chemoprophylaxis and radical cure of *Plasmodium vivax*,[2] the distinction between quantitative and qualitative testing became clinically significant. Formerly, primaquine was the only approved medication to treat hypnozoites, the dormant form of the parasite in the liver stage of malaria. Its use required a "normal" G6PD activity level, the threshold of which on qualitative tests was usually established at 30%–40%. Tafenoquine, with its longer half-life of 14 days (compared to 6 hours for primaquine), provides a far simpler dosing regimen for malaria chemoprophylaxis and radical cure, but it may precipitate hemolytic anemia at higher levels of G6PD activity. Consequently, the U.S. Centers for Disease Control and Prevention recommends a quantitative G6PD assessment before tafenoquine prescription[2] to ensure activity exceeding 70%.[3,4]

An X-linked genetic disorder, G6PD deficiency in males is usually severe (enzyme activity < 30%), meaning that a "deficient" result on qualitative testing contraindicates the use of both primaquine and tafenoquine. The same is true for females who are homozygous or double heterozygous for mutant alleles—both of which are rare. However, single heterozygous females usually have milder deficiency (enzyme activity 30%–80%),[3] meaning they would have a "normal" result on qualitative testing and could safely take primaquine but potentially not tafenoquine.

Universal G6PD deficiency screening is required across the U.S. Armed Forces, but current policy does not mandate quantitative testing.[5] Since tafenoquine may improve medication adherence and thus become a preferable antimalarial option, it is important to understand how many service members have only been qualitatively tested. In the U.S. Air Force, 167,945 active duty members had at least 1 G6PD test performed and recorded in the CHCS between 1 January 2015 and 31 December 2019. Of these, only 4,325 (2.6%), including 1,602 females, had a normal qualitative test with no quantitative result. This low percentage should continue to decrease since quantitative testing is standard protocol for all new recruits at U.S. Air Force basic military training as well as new officer accessions at the U.S. Air Force Academy and Officer Training School (email communication, Maj Dianne Frankel and Lt Col Kevin Baldovich, December 2019 and January 2020, respectively).

While the article by Lee and Poitras provides valuable information, G6PD deficiency surveillance in the tafenoquine era should incorporate quantitative values. These values should also be documented in service members' deployment readiness records. For example, the Aeromedical Services Information Management System, the U.S. Air Force's readiness platform, defines G6PD status as either "normal" or "deficient"—essentially as a qualitative test, even if a quantitative enzyme activity level is available in the electronic health record. This may lead to improper prescription of tafenoquine to airmen, particularly females, who are coded as having "normal" G6PD activity levels but whose levels are in fact intermediate.

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In reply: We appreciate the response by Drs. Sayers and Webber to our article published in the December 2019 issue of the *MSMR* on the prevalence of G6PD deficiency among active duty service members. We are in agreement that quantitative as well as qualitative testing for the genetic condition is imperative to prevent the potentially harmful side effects from the use of the 8-aminoquinoline (8-AQ) class of antimalarial drugs (tafenoquine and primaquine) for malaria chemoprophylaxis and radical cure. We applaud the Air Force for the implementation of quantitative screening of G6PD deficiency among new recruits.

Our article highlights the need for leadership awareness of G6PD deficiency diagnoses to reduce the possibility of adverse events from the use of the 8-AQ class of antimalarial drugs. The inclusion of quantitative G6PD testing is an important tool to further identify at-risk service members.

Respectfully,
MAJ Jangwoo Lee, PhD; Beth Poitras, MPH

Summary of the 2018–2019 Influenza Season Among Department of Defense Service Members and Other Beneficiaries

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The Armed Forces Health Surveillance Branch conducts weekly surveillance of influenza activity among Department of Defense (DoD) populations each influenza season. This report provides a summary of the data from the 2018–2019 influenza season. Ambulatory data for influenza-like illnesses (ILIs), influenza hospitalization data, and lab data for influenza-confirmed cases were used for the surveillance. The 2018–2019 season differed from past seasons in that it was much longer, had a later peak, and the predominant strain of influenza changed from influenza A(H1N1)pdm09 at the beginning of the season to influenza A(H3N2) in the middle of the season. Non-service member beneficiaries accounted for the majority of ILI-related encounters and hospitalizations. However, there were still 149 influenza-related hospitalizations among service members during the 2018–2019 season. Continued weekly surveillance of influenza among DoD populations is crucial to track increases in activity each season and the potential emergence of new and/or severe influenza subtypes.

WHAT ARE THE NEW FINDINGS?

The 2018–2019 influenza season was longer than the preceding 2 seasons. Unlike most prior seasons, 2 strains were common. Influenza A(H1N1)pdm09 was the most common strain early in the season, but influenza A(H3N2) predominated later in the season. Total influenza vaccine effectiveness was low during this season in part because the A(H3N2) strain was antigenically drifted from the vaccine strain.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Surveillance data about influenza disease inform the planning and strategy for efforts to reduce the future impact of influenza on the health and medical readiness of the Armed Forces. The data and findings in this report reinforce the importance of the use of up-to-date multivalent influenza vaccines that protect against several different specific virus strains that may become common in the coming influenza season.

Influenza infects an estimated 8% of the U.S. population annually, with children and the elderly at highest risk.[1] Service members may also be at a higher risk for exposure to influenza because of increased crowding and mixing in the recruit setting and duty assignments abroad where influenza subtypes may differ.[2] Each influenza season is different because of antigenic drift in the circulating influenza subtypes, the degree of match between vaccine subtypes and circulating subtypes, and vaccine coverage of the population. As such, it is important to conduct annual surveillance of each influenza season to identify the onset and patterns of activity, emergence of drifted or shifted subtypes, and severity of the season.

The Armed Forces Health Surveillance Branch of the Defense Health Agency utilizes electronic sources of ambulatory medical encounters, hospitalizations, and laboratory data to conduct annual influenza surveillance among all Department of Defense (DoD) beneficiaries across the world. Weekly reports are generated to provide near real-time influenza surveillance data for each of the DoD Combatant Commands. This report provides a summary of DoD influenza surveillance data for the 2018–2019 influenza season.

METHODS

Medical encounter and demographic data from the Defense Medical Surveillance System (DMSS) and Health Level 7 (HL7)-formatted laboratory data from the Navy and Marine Corps Public Health Center (NMCPHC) were used for this analysis. The HL7-formatted laboratory data are nonstandardized, so NMCPHC applies an algorithm to the data to identify influenza tests and standardize results. The surveillance period for the 2018–2019 influenza season was 30 September 2018 through 1 June 2019 (influenza weeks 40 through 22). Data from the 2016–2017 and 2017–2018 influenza seasons are also presented for comparison. The surveillance population included all individuals who were Military Health System (MHS) beneficiaries (i.e., active and reserve/guard component service members, retired service members, family members and other dependents of service members and retirees, and other authorized government employees and family members) who accessed care through either a military medical facility/provider or a civilian facility/provider (if paid for by the MHS). However, medical data from military treatment facilities (MTFs) that were using MHS GENESIS at the time of this surveillance (Naval Hospital Oak Harbor, Naval Hospital Bremerton, Air Force Medical Services Fairchild, and Madigan Army Medical Center) are not captured in the DMSS data. Therefore, medical encounter and laboratory data from these MTFs are not included in the analysis. For the analysis, populations were grouped as service members or other beneficiaries.

Outpatient medical encounters were classified as an influenza-like illness (ILI) encounter if they had an ILI diagnosis code (International Classification of Diseases, 10th Revision [ICD-10] codes B97.89, H66.9, H66.90, H66.91, H66.92, H66.93, J00, J01.9, J01.90, J06.9, J09, J09.X, J09.X1, J09.X2, J09.X3, J09.X9, J10, J10.0, J10.00, J10.01, J10.08, J10.1, J10.2, J10.8, J10.81, J10.82, J10.83, J10.89, J11, J11.0, J11.00, J11.08, J11.1, J11.2, J11.8, J11.81, J11.82, J11.83, J11.89, J12.89, J12.9, J18, J18.1, J18.8, J18.9, J20.9, J40, R05, R50.9) in any diagnostic position. The percentage of all outpatient encounters that were classified as ILI encounters was calculated for each week for each study population. Baseline ILI activity for the season was defined as the mean percentage of all outpatient encounters during noninfluenza weeks (weeks 22–39) over the prior 3 years.

Hospitalized influenza cases were defined as having a hospitalization with a diagnosis of influenza (ICD-10: J09, J10, J11) in any diagnostic position. The number of hospitalized influenza cases each week for each study population was calculated. For other beneficiaries, counts of influenza hospitalizations by age group (0–4, 5–9, 10–17, 18–35, 36–49, 50–64, 65+) were calculated.

Laboratory-confirmed influenza cases were defined as having a positive polymerase chain reaction, viral culture, or rapid influenza assay result. Laboratory-confirmed influenza cases were stratified by influenza types/subtypes (influenza A (not subtyped), influenza A(H1N1)pdm09, influenza A(H3N2), influenza A and B coinfection, and influenza B. The total number of laboratory-confirmed influenza cases stratified by type/subtype and the percentage of all influenza laboratory tests performed that had positive test results were calculated for each week of the influenza season for service members and for other beneficiaries separately.

RESULTS

Virus surveillance

Among all beneficiaries, there were 149,254 respiratory specimens tested for influenza during the 2018–2019 influenza season **(data not shown)**. Of those, 30,464 (20.4%) were positive for influenza. Service members had a lower percentage of specimens testing positive for influenza (16.7%) compared to other beneficiaries (21.8%). Among all populations, influenza A (any subtype) predominated during this season, with 28,454 (93.4%) of all positive specimens testing positive for influenza A. The distribution of subtypes among influenza A positive specimens was 73.3% influenza A (not subtyped), 12.6% A(H3N2), and 7.5% A(H1N1)pdm09. The remaining specimens were positive for influenza B (1,805; 5.9%) or an influenza A/B coinfection (205; 0.7%). The distribution of subtypes was similar between service members and other beneficiaries **(data not shown)**.

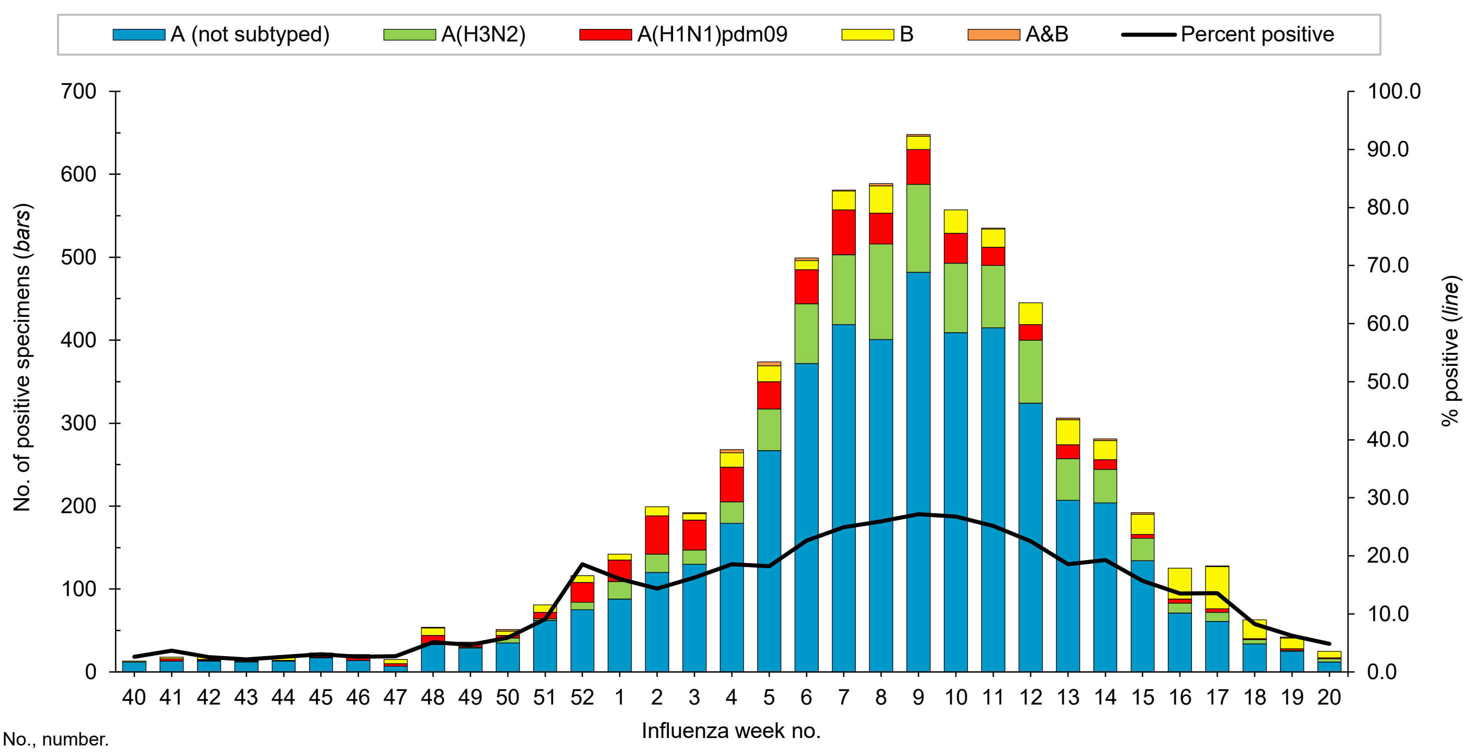
The distribution of influenza serotypes and the percentage of specimens positive for influenza by week are presented in **Figures 1a and 1b** for service members and other beneficiaries, respectively. Among subtyped influenza A specimens, A(H1N1) pdm09 predominated early in the season, but A(H3N2) was predominant after week 3. The highest numbers of positive specimens and the highest percentages of positives occurred during week 9 for service members and weeks 6 and 7 for other beneficiaries. These results indicate peak influenza activity for the season during the month of February 2019.

Outpatient encounter ILI surveillance

During the 2018–2019 season, the weekly percentages of outpatient encounters due to an ILI for service members were above baseline (2.1%) for 22 weeks (weeks 46–15) **(Figure 2a)**. A similar pattern was seen among other beneficiaries, for whom the percentages were above baseline (3.4%) for 20 weeks (weeks 47–14) **(Figure 2b)**. This pattern is similar to the percentage of outpatient encounters due to ILI during the prior 2 influenza seasons.

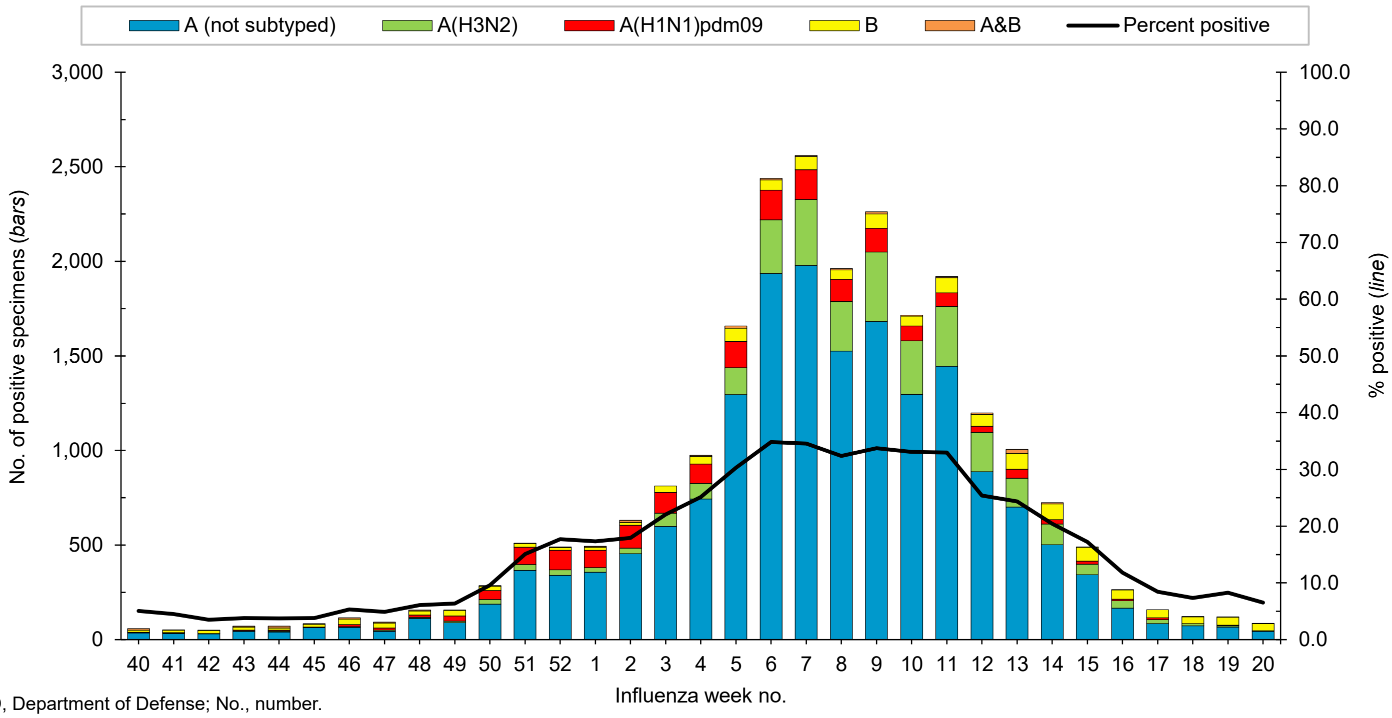
Earlier in the 2018–2019 season, between weeks 40–52, the trend and magnitude of the percentages of encounters due to ILI were also similar to those of the past 2 seasons **(Figures 2a and 2b)**. All seasons had peaks during weeks 52 and 1. This timing coincides with the end-of-year holiday period. Rather than a true peak in ILI activity though, this peak was being driven by a differential decrease in the total number of medical encounters and

FIGURE 1a. Numbers of laboratory-confirmed influenza specimens by serotype and percentages of respiratory specimens positive for influenza by surveillance week, service members, U.S. Armed Forces, 2018–2019 influenza season



No., number.

FIGURE 1b. Numbers of laboratory-confirmed influenza specimens by serotype and percentages of respiratory specimens positive for influenza by surveillance week, other DoD beneficiaries, 2018–2019 influenza season



DoD, Department of Defense; No., number.

ILI encounters during that time. Specifically, for the 2018–2019 season, the total number of outpatient medical encounters decreased 58% from week 51 to week 52; however, ILI encounters decreased only 36% between those 2 weeks. Therefore, this peak in ILI percentage is considered an artifact of the overall decline in total outpatient encounters and is not reflected in the peak influenza weeks for the season. After week 1, the 2018–2019 season ILI percentages began to diverge from the prior 2 seasons. Among service members, the percentage of encounters due to ILI had a later peak (week 8) than the prior 2 seasons (weeks 2 and 3), but the magnitude of the 2018–2019 peak was similar to that of the 2017–2018 peak **(Figure 2a)**. Among other beneficiaries, the trend was similar to the 2 prior seasons, with peak activity occurring during week 6 (2017–2018: week 5; 2016–2017: week 6), and the magnitude was similar to the 2016–2017 season **(Figure 2b)**.

Influenza-related hospitalizations

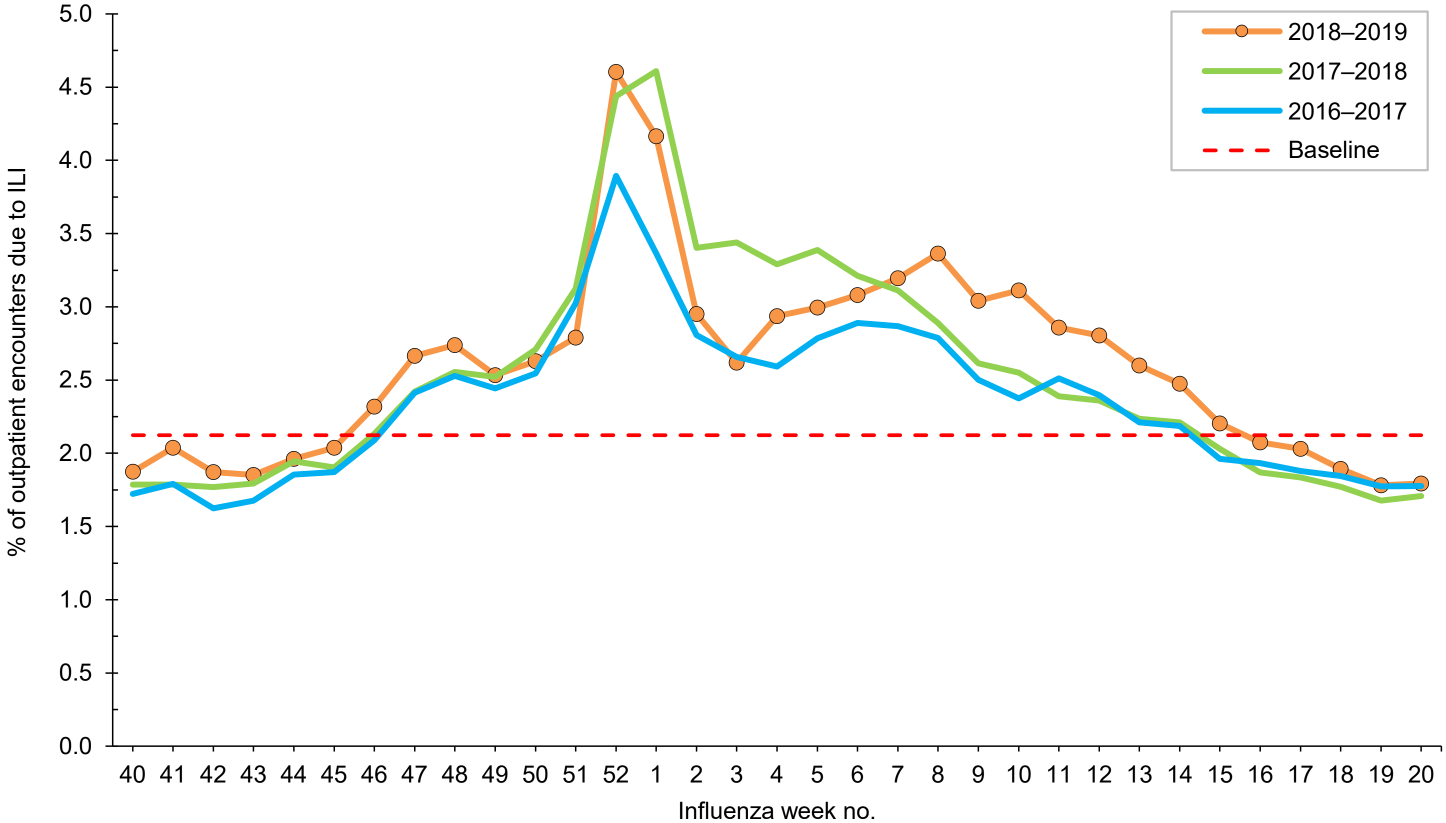
Of the total 5,847 influenza-related hospitalizations during the 2018–2019 season, 149 occurred among service members **(Figure 3)**. The majority of hospitalizations occurred among other beneficiaries (n=5,698; 97.5%). Hospitalizations peaked overall during week 11 (n=471), but service member hospitalizations peaked during week 10 (n=18) **(Figure 3)**. Among other beneficiaries, the majority of influenza-related hospitalizations occurred among those 65 years of age or older (n=3,778; 66.3%) **(Figure 4)**.

EDITORIAL COMMENT

The 2018–2019 influenza season among service members and other DoD beneficiaries was a longer season with a later peak compared to the prior 2 seasons. The season also differed from prior seasons in that the beginning of the season was predominated by influenza A(H1N1)pdm09 while influenza A(H3N2) predominated after week 3; most seasons have just 1 influenza A subtype predominating. As expected, the influenza season among DoD service members and beneficiaries was similar to the season among the general U.S. population.[3] Although the DoD influenza surveillance data include information from around the world, the majority of encounter and laboratory data came from the U.S. and to a lesser extent Europe, which also had an influenza season similar to that in the U.S.[4] As with the general U.S. population, the elderly (> 64 years of age) accounted for the majority of influenza hospitalizations among other beneficiaries. The elderly population accounted for 66% of all other beneficiary hospitalizations for the season compared to 47% among the general U.S. population.[3]

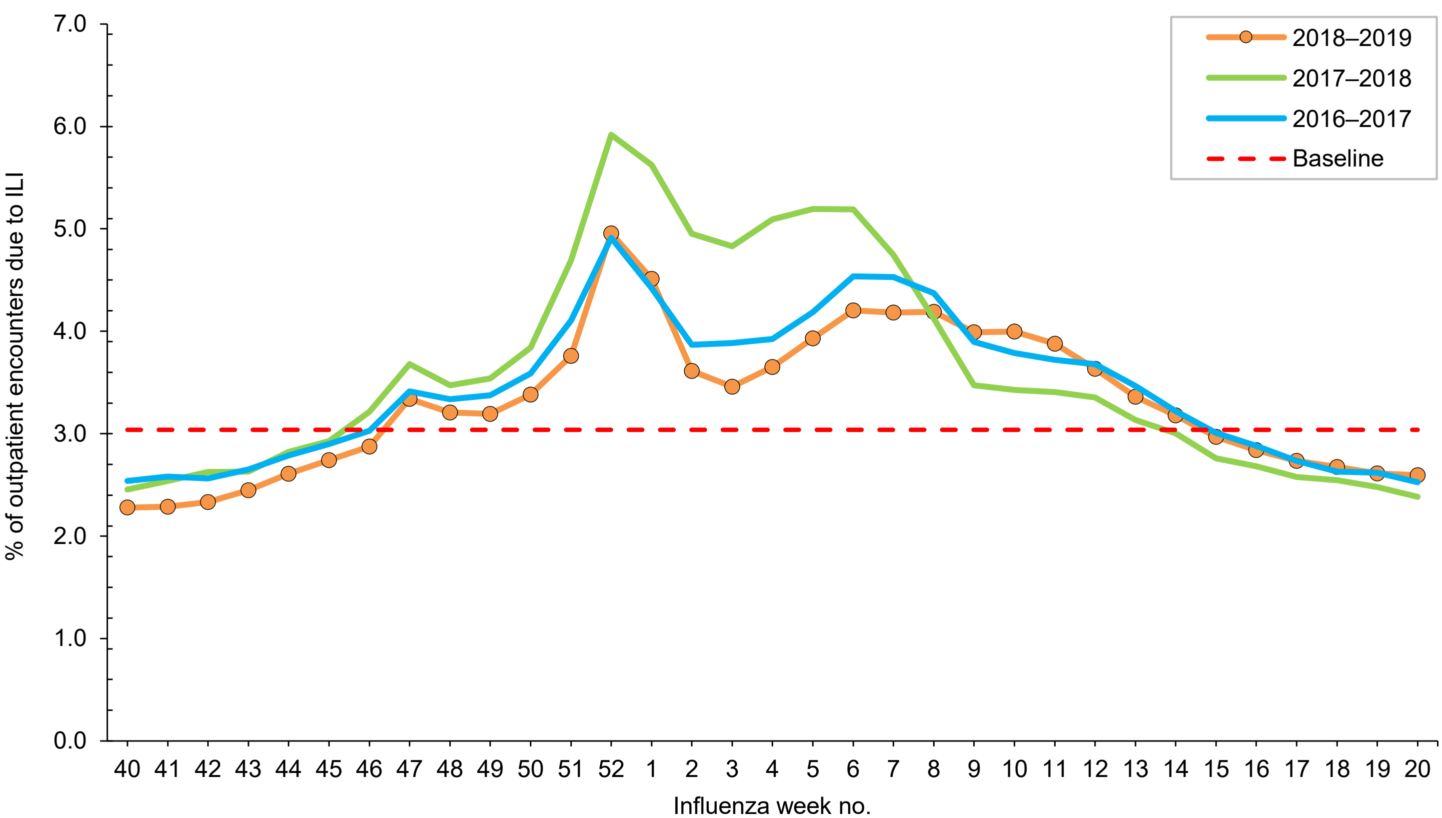
A seasonal influenza vaccine is still the best way to protect against influenza. Service members are required to receive a seasonal influenza vaccine annually. During the 2018–2019 season, DoD policy set a goal of 90% of service members vaccinated by 15 January 2019.[5] Although vaccination rates of service members were very high, influenza cases still occurred among this population during the 2018–2019 season. Cases of influenza among service members may be attributable to infections occurring before receipt of the influenza vaccine, within the 14 days following vaccination when the vaccine may not provide complete protection, or after vaccination because the vaccine is less than 100% effective. During the 2018–2019 season, vaccine effectiveness among the general U.S. population was particularly low because of the emergence of a drifted A/H3N2 (clade 3C.3a) circulating virus that differed from the vaccine strain.[6] Although the influenza vaccine is not 100% effective at preventing influenza infection, a recent study showed that vaccination also decreased the risk of hospitalization and admission to the intensive care unit and decreased severity of illness.[7] Continued vaccination of service members and other DoD beneficiaries is crucial to

FIGURE 2a. Percentages of outpatient encounters due to ILI, service members, U.S. Armed Forces, 2018–2019 influenza season



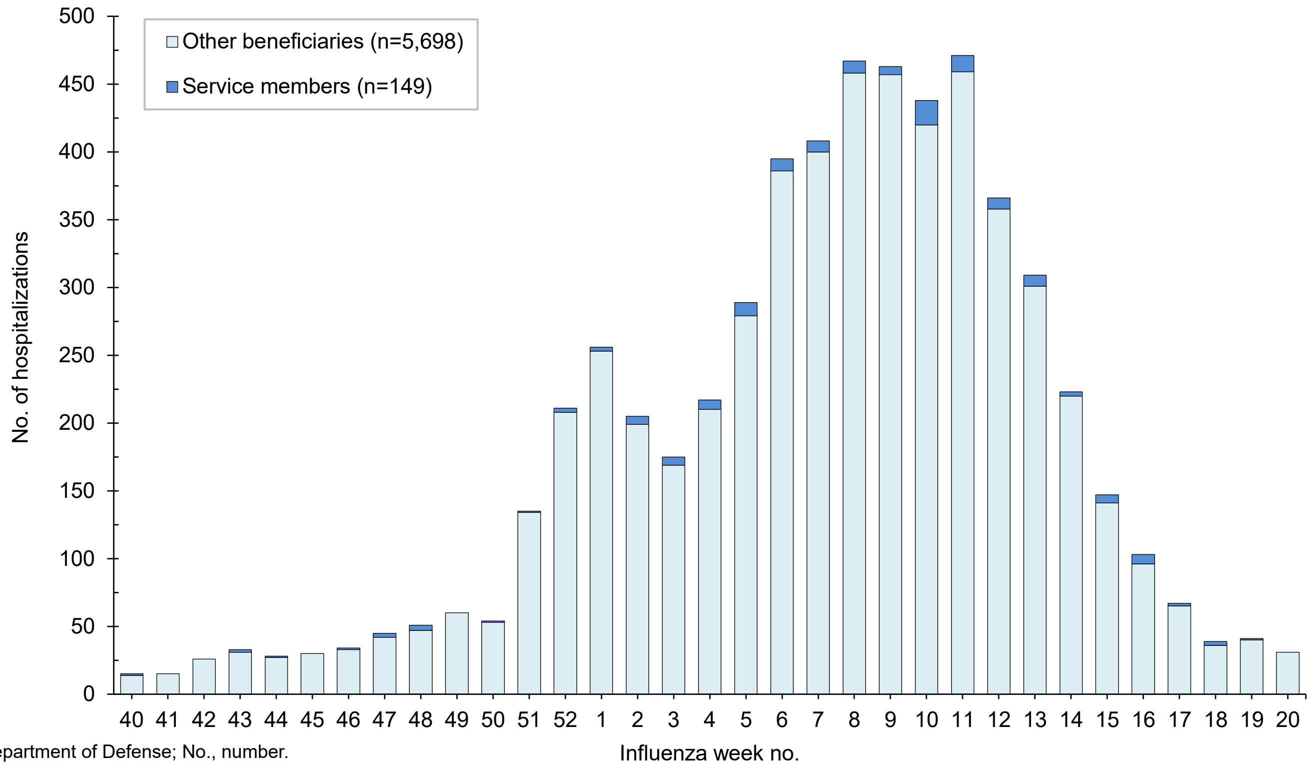
ILI, influenza-like illness; no., number.

FIGURE 2b. Percentages of outpatient encounters due to ILI, other DoD beneficiaries, 2018–2019 influenza season



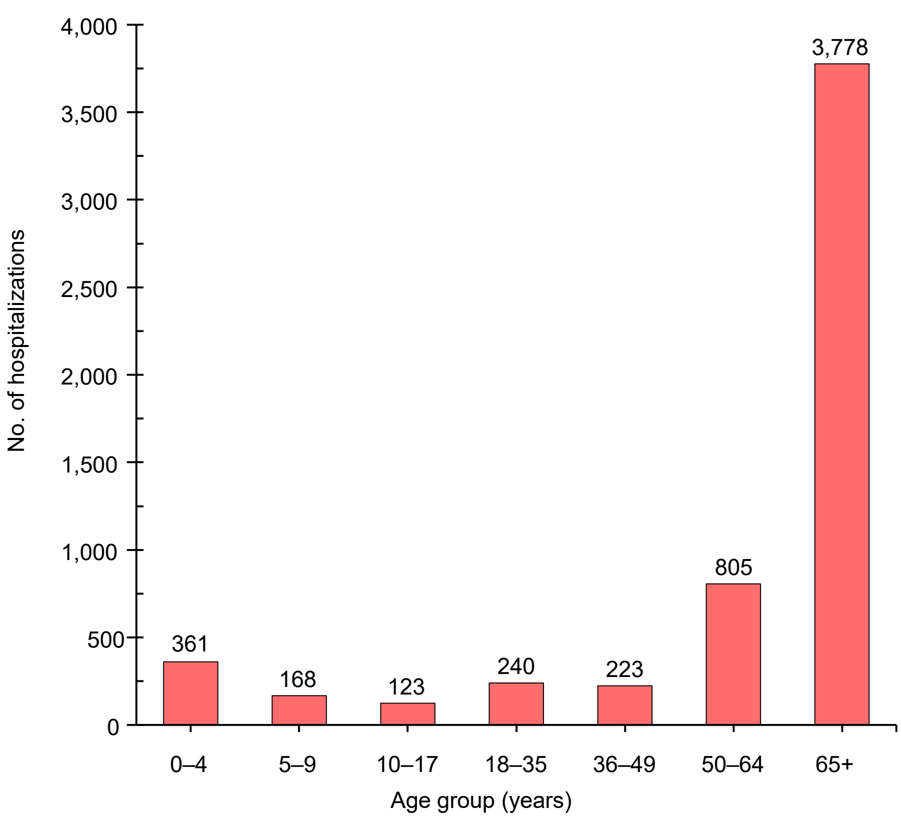
ILI, influenza-like illness; DoD; Department of Defense; no., number.

FIGURE 3. Influenza-related hospitalizations, service members and other DoD beneficiaries, 2018–2019 influenza season



DoD, Department of Defense; No., number.

FIGURE 4. Age distribution of beneficiaries with influenza-related hospitalizations, 2018–2019 influenza season



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combat influenza infections and lessen disease severity. This season also demonstrated the importance of annual influenza surveillance, as the seasons differ from year to year.

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Direct Care Cost of Heat Illness to the Army, 2016–2018

Lanna J. Forrest, PhD, MSPH; Alexis L. Maule, PhD; Ashleigh K. McCabe, MPH; Julianna Kebisek, MPH; Ryan A. Steelman, MPH; John F. Ambrose, PhD

Heat injury surveillance in the Department of Defense (DoD) includes the more severe conditions, heat exhaustion and heat stroke.[1] Hospitalization occurs more frequently among service members experiencing heat stroke; however, both conditions can result in hospitalization and may require follow-up medical care. Between 2014 and 2018, annual rates of heat illness have increased among U.S. active component members.[2] This report describes the total direct medical cost to the Army associated with heat exhaustion and heat stroke from 2016 through 2018.

METHODS

The Weather-Related Injury Repository (WRIR) contains clinical data and medical event reports for heat and cold weather injuries in Army soldiers.[3] The WRIR health encounter and admission data used in this analysis were derived from DoD military medical treatment facility medical records and paid TRICARE claims for beneficiaries at civilian facilities. Heat illness was identified using International Classification of Diseases, 10th Revision (ICD-10) codes for heat stroke (T67.0*) and heat exhaustion (T67.3*, T67.4*, T67.5*) in the primary or secondary diagnostic code positions.[1] For the purposes of this study, heat illness hospital admissions and outpatient encounters from 1 January 2016 through 31 December 2018 were extracted from the WRIR for Army active component and active and inactive National Guard and Reserve soldiers. Demographic characteristics were assigned according to the first encounter or admission during the analysis timeframe for each soldier.

Direct medical costs from the medical record and claims files were used to represent the cost of care paid for by the Military Health System (MHS). Variables for these costs have been included in the WRIR for each encounter since its implementation. For inpatient admissions to facilities owned and operated by the military, the direct cost of the care is captured in a variable identified as "full cost," which includes the cost of clinician salary, ancillary laboratory and radiology, ancillary salary, and intensive and surgical care units. For outpatient visits associated with these facilities, the direct cost of care captured in the same full cost variable includes clinician salary, professional salary, laboratory, radiology, pharmacy, ancillary, support, and other costs. For contracted care provided in civilian or network facilities, the direct medical cost represents the amount paid by TRICARE. This variable, tracked in the patient's medical record, has been used to estimate the total cost of each medical encounter in other reports evaluating medical costs for soldiers in the MHS.[4–6]

To determine the total direct medical cost, all hospital admission and outpatient encounter records with a heat exhaustion or heat stroke diagnosis meeting inclusion criteria were examined and the full cost and/or total amount paid for each heat illness encounter were summed by soldier and the date of care. Total direct medical care cost includes the cost of care associated with follow-up visits. The heat illness type was assigned based on the ICD-10 code in the primary or secondary position. The record was designated a heat stroke when either of the fields had a heat stroke diagnosis. Data were reported by clinical setting (outpatient and inpatient) and by heat illness type (heat exhaustion and heat stroke).

RESULTS

During the study period, 5,291 soldiers—1,027 (19.4%) females and 4,264 (80.6%) males—had 1 or more clinical records associated with heat stroke or heat exhaustion events **(Table 1)**. The majority were enlisted soldiers (88.1%) and younger than 35 years old (90.8%). Of the soldiers who received care for a heat illness, 1 in 4 were members of the National Guard/Reserve.

The 5,291 soldiers had 13,087 records of encounters for heat illnesses that resulted in an average of 2.5 medical encounters per soldier **(Table 2)**. The majority of the soldiers' records indicated heat exhaustion diagnoses (69.3%), of which 98.0% were recorded during outpatient encounters. Similarly, 91.4% of heat stroke diagnoses were made during outpatient encounters. The number of heat stroke admissions was nearly double that of heat exhaustion; the number of hospital bed days associated with heat stroke admissions (786 bed days) was 3 times the number associated with heat exhaustion admissions (263 bed days) **(data not shown)**.

The total direct care cost to the Army for heat stroke and heat exhaustion encounters was $7.3 million, or $559 per encounter. Even though approximately 70% of the medical encounters were related to heat exhaustion, cost was almost evenly divided between heat exhaustion and heat stroke encounters ($3.7 million and $3.6 million, respectively). The total cost of outpatient encounters was approximately 20% higher than the cost of inpatient admissions ($3.9 million and $3.3 million, respectively). An inpatient heat stroke encounter ($7,453/encounter) was more than 10-fold as costly as the aggregate cost per encounter ($559/encounter).

EDITORIAL COMMENT

This is the first report in the literature summarizing the direct medical costs associated with heat illness diagnoses among U.S. Army soldiers. A major strength of this study is its inclusion of all active Army and active and inactive National Guard/Reserve soldiers diagnosed with heat illnesses in outpatient and inpatient settings at both military treatment and civilian facilities. For example, in 2015, DeGroot and colleagues[7] found an overall treatment cost of $408,074 for heat injuries occurring among 128 of the 10,580 soldiers attending Army Ranger School, which is held at 1 military installation. The DeGroot and colleagues study, which included only Army Ranger trainees, found that the cost per encounter for heat exhaustion treated at the Ranger aid station ranged from $176 to $216 per encounter. The authors estimated that the cost per encounter ranged

TABLE 1. Demographic and military characteristics of soldiers with heat illness encounters, U.S. Army, 2016–2018

Characteristic	No.	% total
Sex		
Female	1,027	19.4
Male	4,264	80.6
Age group (years)		
<25	3,168	59.9
25–34	1,633	30.9
35–44	374	7.1
45+	116	2.2
Component		
Active Duty	3,856	72.9
Active Guard/Reserve	952	18.0
Inactive Guard/Reserve	483	9.1
Rank		
Junior enlisted (EJ)	3,700	69.9
Senior enlisted (ES)	961	18.2
Cadet	53	1.0
Junior officer (OJ)	434	8.2
Senior officer (OS)	46	0.9
Warrant officer (WO)	27	0.5
All others	70	1.3
Total	5,291	100.0

No., number.

TABLE 2. Medical encounters and direct care costs associated with heat illness, U.S. Army, 2016–2018

Heat illness	Care location	Total heat encounters	% total encounters	Total direct care cost	% total direct care cost	Per encounter cost
Any heat illness[a]	All	13,087	100.0	$7,321,719	100.0	$559
Heat exhaustion	All	9,074	69.3	$3,720,542	50.8	$410
	Inpatient	186	2.0	$761,413	20.5	$4,094
	Outpatient	8,888	98.0	$2,959,129	79.5	$333
Heat stroke	All	4,013	30.6	$3,601,177	49.2	$897
	Inpatient	344	8.6	$2,563,740	71.2	$7,453
	Outpatient	3,669	91.4	$1,037,436	28.8	$283

[a]Includes heat exhaustion and heat stroke.

from $3,024 to $4,327 for heat exhaustion treated but not admitted to a hospital (outpatient), while the cost of an encounter for heat stroke, as indicated by a hospital admission (inpatient), ranged from $5,000 to $6,878 per encounter.[7] Using more precise encounter and hospitalization data from 5,291 U.S. Army soldiers with a heat injury over a 3-year period, the current study found a total direct care cost of $7,321,719 for heat injuries. The cost per encounter was $410 for heat exhaustion and $897 per heat stroke encounter.

Direct medical costs are only a portion of the total cost associated with heat illness. Indirect costs of illness account for costs associated with absenteeism, lost productivity, and decreased performance.[8–10] In the military, there are lost productivity costs to the Army in the form of 1) lost duty days (or absenteeism), where the soldier is paid but is not able to perform the relevant duties because of health-related reasons, such as hospitalization, and 2) limited duty days, in which a soldier performs the relevant duties but at diminished capacity following an illness or injury.[4,6] This analysis notes a total of 1,049 bed days (or lost duty days) due to heat illness diagnoses. Based on average soldier pay for the study timeframe and assuming the loss of 8 hours per day, these lost duty days total $356,000 in lost cost to the Army.

While data for medical profiles associated with heat illness were not available, the indirect costs of the lost and limited duty time associated with medical profiles have been estimated at almost 80% of the total cost of other injuries.[4,6] If we assume this cost ratio for heat illness, indirect costs could reach $36 million. A future analysis should incorporate lost and/or limited duty heat illness profile data in order to provide a better estimate of the total cost of these conditions to the Army.

There were 2 main limitations to the study. The surveillance period for this report covered the period 1 January 2016 through 31 December 2018, so it is possible that some initial costs occurring before January 2016 and some follow-up and sequelae visits occurring after December 2018 were not accounted for in the full care cost for each heat illness event. Additionally, the cost assigned by the MHS to heat injury as a primary diagnosis reflects the intensity and complexity of care for other illnesses or injuries (e.g., gastroenteritis, stress fracture) that may be present at the time of the encounter.[11]

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Animal-Related Injuries in Veterinary Services Personnel, U.S. Army, 2001–2018

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Limited data exist on animal-related injuries in the U.S. Army veterinary service (VS). The purpose of this study was to determine the incidence of animal-related injuries and the associated risk factors in VS personnel. A retrospective cohort study was conducted using military healthcare surveillance data on animal-related injuries in VS personnel from 2001–2018. Yearly incidence of medically diagnosed animal-related injuries ranged from 25–50 injuries per 1,000 person-years from 2001–2018. Linear regression showed no significant trend in the incidence rate per year over the study period (R^2=0.005). Bites were the most common injury (86.5%), with dog bites (44.3%) being the most common injury type and dogs the most common species implicated. After controlling for sex, age group, race/ethnicity group, and occupation, adjusted incidence rate ratios (AIRRs) showed significantly elevated risk for animal-related injuries among females compared to males (AIRR=1.69; 95% confidence interval [CI]: 1.45–1.99), soldiers aged 17–29 compared to those aged 30 years or older (AIRR=2.55; 95% CI: 2.12–3.08), and technicians compared to veterinarians (AIRR=1.57; 95% CI: 1.30–1.89). Unlike the majority of published literature on veterinary occupational health and safety, this study showed a clear increased risk of diagnoses of injury among females compared to males.

WHAT ARE THE NEW FINDINGS?

The yearly incidence of animal-related injuries to U.S. Army VS personnel did not change significantly from 2001–2018. Dog bites were the most common type of animal-related injury. Being female, younger, and a veterinary technician were all associated with an increased risk for animal-related injury.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Risk of injury among VS personnel varied by sex, age, and occupation. Leaders within the VS must ensure that there are no disparities in training or equipping the veterinary force to handle animals properly and that animal-related injury prevention measures are in place and prioritized.

The U.S. Army veterinary service (VS) comprises enlisted soldiers serving as animal care specialists and veterinary food inspection specialists, veterinary corps officers (VCOs: veterinarians and food safety officers), and Department of the Army civilians. The VS serves as the lead organization for the animal health mission within the Department of Defense (DoD). This mission includes, but is not limited to, the clinical and surgical care of military working dogs (MWDs), DoD-owned animals used in research, and the privately owned pets of DoD service members and their beneficiaries.

Because of the broad responsibilities and specialized skill sets of veterinarians and veterinary technicians, there are unique occupational risks related to animal exposure. Physical injuries from an animal by a bite, scratch, or other physical strike during restraint, treatment, or handling are the most common circumstances for veterinary occupational injuries. In the civilian community, animal-related injuries to veterinarians and technicians have been well documented.[1–7] Data on the prevalence or incidence and associated risk of animal-related injuries to U.S. Army VS personnel are limited, however. Between 2001 and 2010, 433 (2.1%) of the approximately 20,000 animal bites to service members were to VS personnel.[8] In a more recent publication, of the approximately 22,000 animal bite cases among reserve and active component service members during 2011–2018, 537 (2.4%) were among VS personnel. The crude incidence rate of animal bites in VS personnel was 438 per 100,000 person-years (p-yrs) from 2011 through 2018. This incidence rate was second only to the rate of animal bites among service members working in military law enforcement.[9] These data on U.S. Armed Forces pertained to animal bites only and did not show specific incidence rates for demographic, occupational, or military subgroups of service members within the VS (i.e., age groups, sex, veterinarians vs. technicians, junior enlisted vs. senior enlisted).

In the veterinary profession, animal bites and scratches can be frequent and their severity can range from requiring only basic first aid to necessitating hospitalization. Furthermore, these injuries have a high probability of causing secondary wound infections and/or long-term disabilities.[1,2,4] It has been estimated that between 50%–67% of veterinarians and up to 98% of veterinary technicians have had an animal-related injury during their careers.[4] Musculoskeletal diseases and other conditions secondary to or indirectly related to animal exposure and work are also common within the veterinary community. These exposures may include heavy lifting, repetitive motions, anesthetic gases, x-rays, needle stick injuries, and a variety of toxic pesticides and therapeutic agents.[10–12]

For the purposes of this study, animal-related injuries were limited to those caused by mammalian species and do not include injuries from venomous reptiles or arthropods. The specific type of animal-related injury varies by frequency and risk, depending upon the predominant mammalian species with which a veterinary professional is working. Overall, the most dangerous animals to work around are cattle and horses. Injuries caused by these large mammalian species account for the most human fatalities and are responsible for many serious crush and kick injuries.[2,5] One survey-based study of members of the American Association of Swine Practitioners reported that needle stick injuries were the most common type of animal-related injury and that 22% of swine practitioners reported having a diagnosis of hearing impairment.[13] Small animal practitioners' animal-related injuries are mostly confined to dog and cat bites and/or scratches. However, there is variability between studies on the prevalence and severity of dog vs. cat bites and/or scratches.[1–7]

VS personnel have the most experience and are the subject matter experts in animal handling and animal-related safety for the DoD. To maintain their expertise in this field, and in order to train others on safe animal handling practices, the VS needs to ensure that their methods are as safe and effective as possible. Increasing the overall readiness of VS soldiers requires a targeted training approach for risk mitigation of animal-related injuries. Determining the most at-risk members of the VS population could inform the development, refinement, and targeted implementation of prevention strategies to further reduce animal-related injuries within the VS.

The purpose of this study was to determine the incidence of medically documented animal-related injuries among active component VS personnel from 2001 through 2018 and the associated risk factors. Based on a review of the published literature and experience in the VS, it was hypothesized that young age, male sex, and occupation as a technician would be associated with an increased risk for animal-related injuries within this population.

METHODS

This report describes a retrospective cohort study of active component VS soldiers and VCOs from 1 January 2001 through 31 December 2018. Deidentified demographic and medical encounter data were provided by the Armed Forces Health Surveillance Branch of the Defense Health Agency. Institutional Review Board (IRB) approval was obtained from the Uniformed Services University IRB. Service members with U.S. Army military occupational specialty (MOS) codes 91T and 68T (animal care specialists, hereafter referred to as technicians) and all 64 series (64A, 64B, 64C, 64D, 64E, 64F, 64Z, hereafter referred to a veterinarians) constituted the population of interest.

Animal-related injury events (cases) were identified from inpatient and outpatient encounter data among garrison-stationed VS personnel and did not include deployed or in-theater cases. Each active component VS member with a medical encounter that included a diagnostic code indicative of an animal-related injury (i.e., nonvenomous mammal bite, scratch, or other nonvenomous mammalian-related injury type) in any diagnostic position within the described surveillance period was defined as a case. Case-defining codes included International Classification of Diseases, 9th Revision (ICD-9) codes E906.0, E906.1, E906.3, E906.5, E906.8, and E906.9 and International Classification of Diseases, 10th Revision (ICD-10) codes W53.*, W54.*, and W55.*.

After a diagnosis met the definition of a case, any subsequent diagnosis of an animal-related injury was not counted as an incident case unless at least 90 days had passed since the prior diagnosis with the same animal-related injury–defined ICD code or the subsequent ICD code was different from the prior animal-related injury ICD code. This criterion reduced the likelihood of double counting cases who were receiving follow-up care for the original injury. Person-time sums for the populations of technicians and veterinarians during the study period were calculated overall, by year, and by demographic variables. The demographic variables describing each member of the cohort were the following: MOS (91T/68T or 64 series), age group (17–19, 20–29, 30–39, and 40+ years), sex (male or female), and race/ethnicity group (non-Hispanic white, non-Hispanic black, Hispanic, Asian/Pacific Islander, American Indian/Alaska Native, and other/unknown), and rank/grade (junior enlisted [E1–E4], senior enlisted [E5–E9], junior officer [O3–O4], and senior officer [O5–O10]).

Grade/rank was not included as a variable for calculating risk because the definitions of the rank categories are not appropriate to the ranks of VCOs. Because of relatively small cell sizes in the youngest and the oldest age groups, combined age groups of 17–29 years and 30 years or older were created. Similarly, the "non-Hispanic black" and "other/unknown" race/ethnicity groups were combined to allow for comparison to the non-Hispanic white group. This simplification allowed for a binomial assessment of all demographic parameters (i.e., male vs. female, veterinarian vs. technician, old vs. young, and white vs. non-white).

Descriptive statistics were used to analyze the incidence rates of animal-related injuries according to the demographic variables within the populations of technicians and veterinarians. Animal bites with ICD-9 codes that were not indicative of a dog or rat (ICD-9: E906.3 and E906.5) or with ICD-10 codes that were not indicative of a dog, rat, cat, horse, cow, hoof stock, pig, or raccoon (ICD-10: 55.81*) were classified as "other." Each type of animal-related injury was totaled by species and injury type to the highest specificity allowed by ICD coding. Injury counts by type and species were presented as totals and percentages of all injuries in the cohort during 2001–2018. Yearly incidence rates for the study period were calculated by dividing the total number of incident cases for each year by the sum of p-yrs for that year. Incidence rates were calculated as incident animal-related injury diagnoses per 1,000 p-yrs. The linear trendline function in Microsoft Excel for Office 365 was used to assess the fit (R^2) of a regression line to the annual incidence rates over time (2018, Microsoft Corporation, Redmond, WA).

Multivariable Poisson regression models were used to calculate adjusted incidence rate ratios (AIRRs) and 95% confidence intervals (CIs) controlling for sex, combined age group, combined race/ethnicity group, and occupation. Statistical significance was defined as $p < .05$. With the exception of the simple trendline assessment, statistical analyses were carried out using Stata/IC, version 15 (2015, StataCorp LLC, College Station, TX).

RESULTS

A total of 772 incident animal-related injury diagnoses were ascertained among VS personnel from 2001 through 2018, resulting in an overall incidence rate of 37.7 per 1,000 p-yrs **(Table 1)**. The subgroup with the highest crude incidence rate was technicians aged 17–19 years, at 91.8 injuries per 1,000 p-yrs. During the surveillance period, approximately 43 incident animal-related injuries were diagnosed per year among VS personnel, with the lowest counts of injuries in 2001 (n=26) and the highest in 2017 (n=58) **(Figure 1)**. Examination of crude incidence rates of animal-related injury diagnoses over time showed no linear trend (R^2=0.005); annual rates fluctuated between 50.1 per 1,000 p-yrs in 2013 and 24.4 per 1,000 p-yrs in 2018 **(data not shown)**. Compared to their respective counterparts, technicians, females, those in younger age groups, non-Hispanic white VS personnel, and junior enlisted soldiers had the highest crude rates for animal-related injuries **(Table 1)**.

Of all injuries counted, 668 (86.5%) were bites from a variety of species **(Table 2, Figure 2)**. Of all the animal-related injuries, dog bites were the single most common type, with a total of 342 (44.3%). "Other" bites accounted for 34.7% (n=268) of the total. Only 11 recorded injuries were caused by large-bodied mammal species. Of the 772 total injuries, 553 (71.6%) were sustained by veterinary technicians, while only 219 (28.4%) were sustained by veterinarians. The majority of animal-related injuries were among females (n=515; 66.7%) **(Table 1)**. Of the technicians' injuries, 435 (78.7%) were in junior enlisted soldiers, and of the veterinarians' injuries, 214 (97.7%) were in junior officers. More than three-quarters (78.1%) of the animal-related injuries were among non-Hispanic white soldiers.

Unadjusted IRRs revealed a more than 2-fold increased risk in sustaining a diagnosis of an animal-related injury for females vs. males (IRR=2.17; 95% CI: 1.87–2.52), technicians vs. veterinarians (IRR=2.52; 95% CI: 2.15–2.94), and those 17–29 years old vs. those 30+ years old (IRR=3.54; 95% CI: 3.03–4.13) **(Table 3)**. After adjustment for sex, age, race/ethnicity, and occupation, these differences in rates remained statistically significant. Even after combining minority race/ethnicity categories, non-Hispanic white soldiers showed a 56% increased incidence of animal-related injury compared with the combined non-Hispanic black/other/unknown group in the adjusted model (AIRR=1.56; 95% CI: 1.31–1.86) **(Table 3)**.

EDITORIAL COMMENT

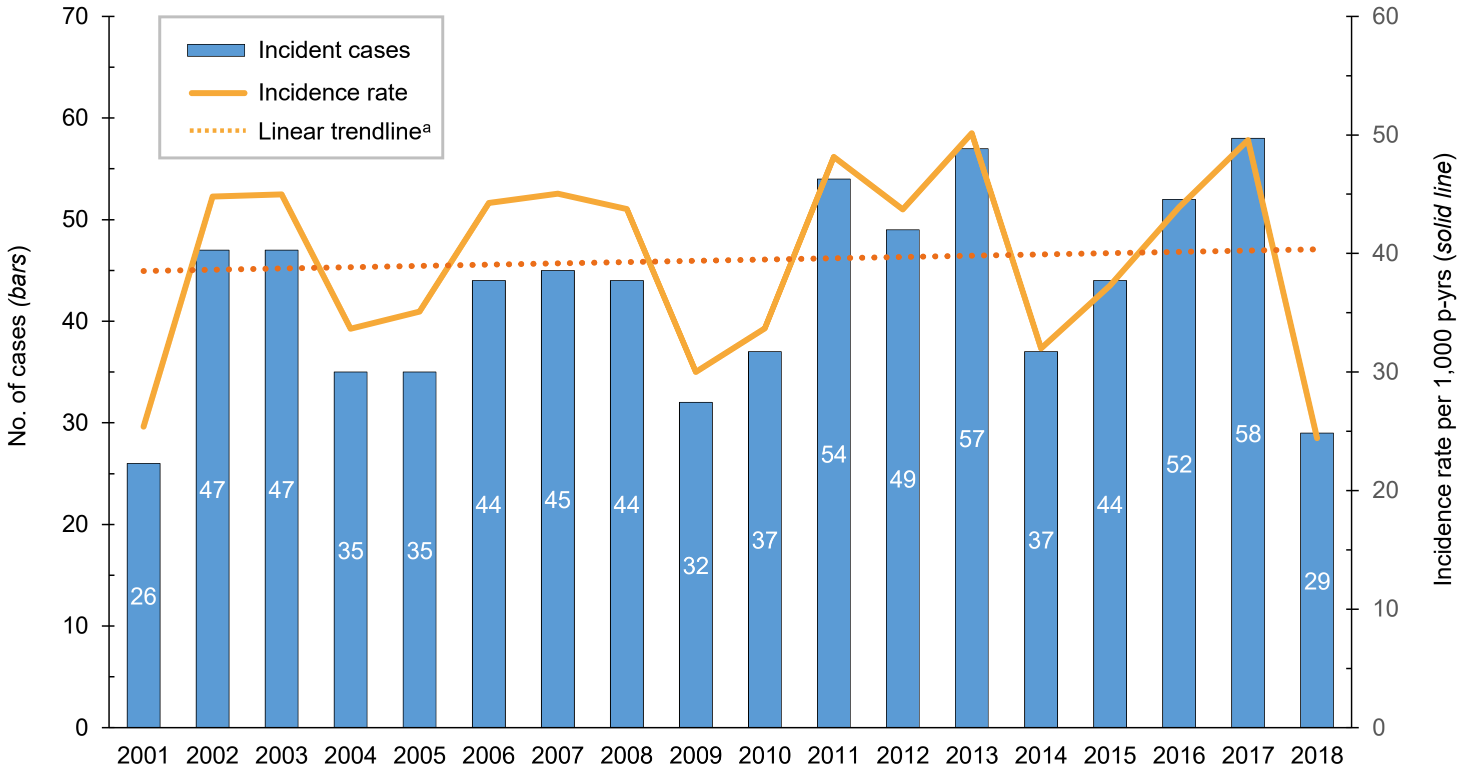
The results of this study indicate that technicians, females, and younger soldiers were at a higher risk of sustaining an animal-related injury when compared to veterinarians, males, and older soldiers, respectively. Even in the adjusted analysis, there was at least a 50% increase in risk for younger individuals, technicians, and females when compared to older individuals, veterinarians, and males, respectively **(Table 3)**. The explanation for the increased risk observed in females compared to males is not immediately apparent. In VS clinical operations, males are frequently selected for riskier tasks involving

TABLE 1. Animal-related injury cases, by demographic and military characteristics, U.S. Army VS personnel, 2001–2018

	No. injuries[a]			P-yrs[b]		Incidence rate[c]	
	Total	Technicians	Veterinarians	Technicians	Veterinarians	Technicians	Veterinarians
Total	772	553	219	10,196.4	10,280.7	54.2	21.3
Sex							
Male	257	200	57	4,896.3	5,742.8	40.8	9.9
Female	515	353	162	5,300.1	4,538.0	66.6	35.7
Age group (years)							
17–19	95	95	---	1,034.7	---	91.8	---
20–29	453	358	95	5,892.0	1,444.1	60.8	65.8
30–39	169	86	83	2,724.4	4,288.6	31.6	19.4
40+	55	14	41	545.3	4,548.0	25.7	9.0
Race/ethnicity group							
Non-Hispanic white	603	412	191	6,447.5	8,403.5	63.9	22.7
Non-Hispanic black	53	47	6	1,709.2	571.3	27.5	10.5
Other/unknown	116	94	22	2,039.8	1,306.0	46.1	16.8
Rank/grade							
Junior enlisted (E1–E4)	435	435	---	5,771.5	---	75.4	---
Senior enlisted (E5–E9)	118	118	---	4,425.0	---	26.7	---
Junior officer (O1–O5)	214	---	214	---	9,603.2	---	22.3
Senior officer (O6–O10)	5	---	5	---	677.5	---	7.4

[a]Counts are for animal-related injuries in technicians and veterinarians by demographic variable.
[b]Counts are for the total person-time as p-yrs for the cohort over the entire study period of 2001–2018 by demographic variable.
[c]Rate per 1,000 p-yrs.
VS, veterinary service; No., number; P-yrs, person-years.

FIGURE 1. Incident diagnoses and incidence rates of animal-related injury in all VS personnel, by year, U.S. Army, 2001–2018



[a]R^2=0.005 indicating no linear trend.
VS, veterinary service; No., number; p-yrs, person-years.

the handling of aggressive animals because of physical stature or strength. Furthermore, the "white male effect" has been previously described in risk perception literature, showing that white males tend to perceive less risk than women and minorities.[14] If the perception of risk is higher in females than in males in the VS cohort described here, it was not reflected in a decreased rate of animal-related injuries for females. An additional potential explanation for the increased risk of injury to female compared to male VS personnel may be related to differences in their healthcare-seeking behavior. Health behavior literature cites that females are more likely to utilize healthcare services than males, and it is possible that the increased incidence of injuries in females is a reporting bias due to their increase in healthcare seeking behavior.[15]

TABLE 2. Animal-related injury type, by occupation, U.S. Army VS personnel, 2001–2018

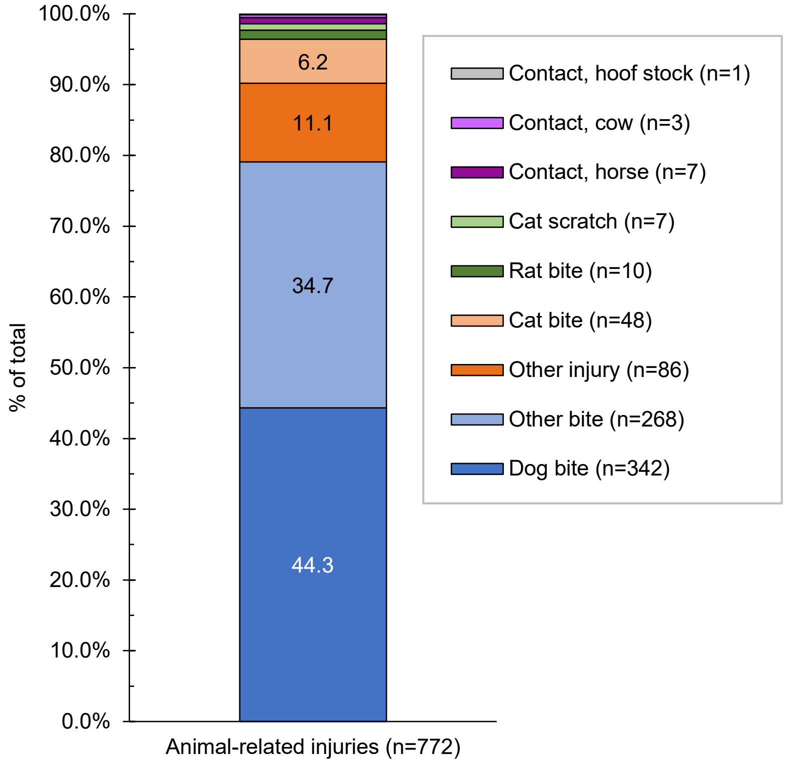
Injury type	Technicians (n=553)		Veterinarians (n=219)		Total (n=772)	
	No.	%	No.	%	No.	%
Type of biting animal						
Dog	242	43.8	100	45.7	342	44.3
Cat	26	4.7	22	10.0	48	6.2
Rat	9	1.6	1	0.5	10	1.3
Other[a]	213	38.5	55	25.1	268	34.7
Other injury						
Other	54	9.8	32	14.6	86	11.1
Cat scratch	5	0.9	2	0.9	7	0.9
Contact, horse	3	0.5	4	1.8	7	0.9
Contact, cow	1	0.2	2	0.9	3	0.4
Contact, hoof stock	---	---	1	0.5	1	0.1

[a]Other animal except arthropod.
VS, veterinary service; No., number.

One survey of Canadian veterinarians showed an increase in the odds of injury for females compared to males.[10] However, in an Australian veterinary injury study, Lucas and colleagues found that even with the increase in female veterinarians in the profession, a larger percentage of animal-related injuries was found in males.[2] To date, a literature search has not found a study describing the relationship of sex with animal-related injuries among veterinary technicians. Nordgren and colleagues[6] discussed work-related risk factors for animal-related injuries in certified veterinary technicians. However, they were unable to include sex in their statistical models because 97% of the study participants were female.

An increased risk for technicians to sustain an injury in the VS is conceivable, as technicians work with many more animals and would have more animal contact than a veterinarian. An increased risk of an

FIGURE 2. Percentages and counts of animal-related injuries, by type, U.S. Army VS personnel, 2001–2018



VS, veterinary service.

TABLE 3. IRRs of animal-related injuries, U.S. Army VS personnel, 2001–2018

Demographic characteristics	Rate[a]	IRR	95% CI	p-value	AIRR[b]	95% CI	p-value
Sex							
Female	52.3	2.17	1.87–2.52	<.001	1.69	1.45–1.99	<.001
Male	24.2	ref	.	.	ref	.	.
Age group (years)							
17–29	65.5	3.54	3.03–4.13	<.001	2.55	2.12–3.08	<.001
30+	18.5	ref	.	.	ref	.	.
Race/ethnicity group							
Non-Hispanic white	40.6	1.35	1.14–1.60	<.001	1.56	1.31–1.86	<.001
Non-Hispanic black/ other/unknown	30.0	ref	.	.	ref	.	.
Military occupation							
Technician	54.2	2.52	2.15–2.94	<.001	1.57	1.30–1.89	<.001
Veterinarian	21.3	ref	.	.	ref	.	.

[a]Rate per 1,000 person-years.
[b]Controlling for sex, combined age group, race/ethnicity group, and occupation.
IRR, incidence rate ratio; VS, veterinary service; CI, confidence interval; AIRR, adjusted incidence rate ratio.

animal-related injury for technicians when compared to veterinarians is well documented in the published literature.[1,3,4]

Several previous studies have shown that younger age increases the risk of sustaining an animal-related injury.[6,8,9,12] Regarding the increased rate of animal-related injuries in younger service members, this finding could be related to experience and work type. Junior enlisted soldiers and junior officers generally have more direct animal contact than their superiors. The frequency of animal contacts decreases dramatically as a VS soldier increases in rank (and consequently age), and the chance of injury is simply decreased as a result. Furthermore, those who have served in their career field longer may be less likely to suffer injuries or to seek medical care for injuries because they perceive them as minor. Moreover, junior soldiers might be directed or required to seek care for an injury by their superiors, whereas a more senior soldier may be able to more readily decline medical attention.

Previous research has described the type of animal-related injury by species and veterinary practice type.[4,5,7,10,13] VS clinical operations can be described as a mostly "small animal practice" for civilian veterinary clinic comparisons. In the civilian population, Fowler and colleagues[4] found that cats were the most likely species to cause an injury in small animal practice.[4,6] However, other studies have found that the highest incidence of animal-related injuries in small animal clinics is attributable to dogs.[2,16] The number of cat-related injuries in the VS cohort during 2001–2018 was 55 (48 bites and 7 scratches). Unfortunately, the granularity of ICD-9 codes were unable to indicate cats as a species type. The incident cases of cat-related injuries counted in this study were counted from 2015–2018, following the introduction of ICD-10 coding into the Military Health System. As a result, many "other" bites from before 2015 may have been cat bites that were not identifiable as such.

The present study had a very specific population definition that is demographically unique compared to civilian small animal veterinary clinics. The uniqueness of this population makes it difficult to generalize the results and make statistical comparisons to other cohort, case control, or cross-sectional studies regarding animal-related injuries in veterinary professionals. The most significant differences between this study and published literature on the topic are the roughly equal numbers of females and males within the population studied and the identification of female gender as a risk factor. Therefore, the analysis discussed here is unique in that gender was able to be evaluated as a risk factor in animal-related injuries within the veterinary profession.

Unfortunately, there is no way to know the number of animal-related injuries for which the VS personnel did not seek healthcare. Presumably, most animal-related injuries in VS service members are very minor, and the medically diagnosed incidence rates calculated here are very likely to be an underestimation of the true injury burden.[9] Self-treatment and lack of injury reporting in veterinary professionals have been previously described.[1,4,13,17,18] The change in ICD coding from ICD-9 to ICD-10 in 2015 altered the categorical or species type of some injuries and made it difficult to determine total and accurate risk by animal species for the entire surveillance period. Another limitation regarding animal information would be the "type" of species with respect to VS-specific mission sets. For example, of the 342 dog bites found in this study, it is unknown how many of those bites were from MWDs or other government-owned animals compared to privately owned animals. The type of species causing most animal-related injuries in VS personnel is a key piece of information that needs to be studied in order to effectively focus training on mitigation strategies and policies for improved workplace safety.

No inferences can be made about specific VS billets and their risk (i.e., garrison VS duties vs. lab animal research vs. a field unit). ICD-10 coding contains occupational injury codes that could have been utilized in the inclusion criteria. However, this could have possibly excluded many cases, and that designation did not exist for all ICD-9 codes. Therefore, occupational codes were not used in this analysis and there was no definitive way to determine if the injury was truly occupational in nature. In addition, there may be a significant differential misclassification bias if many more females than males reported animal-related injuries. This bias could result in falsely increasing the strength of association found.

The present study showed that there is an increased risk for diagnosed animal-related injury in females compared to males, young soldiers compared to older, and technicians compared to veterinarians in the VS population. VS leadership should utilize these data to ensure that there are no gender disparities in the training programs for animal care specialists (MOS 68T). Furthermore, leadership should ensure that there are no disparities in the duty assignments of female VS personnel or in the onsite training and task management of new female technicians. Additional research needs to be completed, along with task-specific and MOS-specific military injury data, in order to determine if changes need to be made for the entry requirements of the 68T MOS. Commanders and VCOs should utilize this information to ensure that their technicians, especially young female service members, utilize the appropriate personal protective measures and follow all safety protocols and standard operating procedures in order to mitigate animal-related injury risk.

Acknowledgments: The authors would like to thank Ms. Sorana Raiciulescu and MAJ Craig Calkins for their masterful spreadsheet and statistical support, without which this project would certainly not have been possible.

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Medical Surveillance Monthly Report (MSMR)
Armed Forces Health Surveillance Branch
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MEDICAL SURVEILLANCE MONTHLY REPORT (MSMR), in continuous publication since 1995, is produced by the Armed Forces Health Surveillance Branch (AFHSB). AFHSB is a designated public health authority within the Defense Health Agency. The *MSMR* provides evidence-based estimates of the incidence, distribution, impact, and trends of illness and injuries among U.S. military members and associated populations. Most reports in the *MSMR* are based on summaries of medical administrative data that are routinely provided to the AFHSB and integrated into the Defense Medical Surveillance System for health surveillance purposes.

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ISSN 2158-0111 (print)
ISSN 2152-8217 (online)