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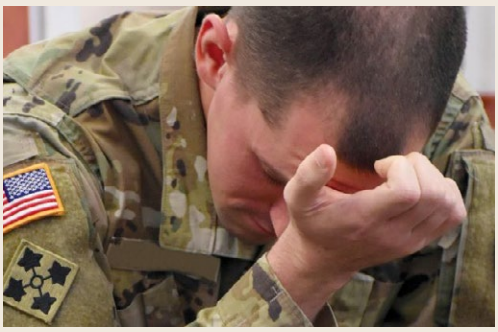

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Surveillance Trends for SARS-CoV-2 and Other Respiratory Pathogens Among U.S. Military Health System Beneficiaries, 27 September 2020–2 October 2021

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Laboratory-based respiratory pathogen surveillance for SARS-CoV-2 and other respiratory pathogens was conducted in the 2020–2021 surveillance season among U.S. Military Health System (MHS) beneficiaries through the Department of Defense Global Respiratory Pathogen Surveillance Program (DoDGRPSP). Sentinel and participating sites submitted 96,660 specimens for clinical diagnostic testing. A total of 12,282 SARS-CoV-2 positive cases were identified, and 7,286 of the associated viruses were successfully sequenced. Two overlapping waves of SARS-CoV-2 activity were observed during the season. The B.1.1.7 (Alpha) lineage was dominant during February 2021 through May 2021. By July 2021, and continuing through the rest of the season, B.1.617.2/AY.x (Delta) lineage predominated and by September 2021 comprised 100% of identified SARS-CoV-2 lineages. The emergence of SARS-CoV-2 coincided with substantial reductions in the circulation of seasonal influenza viruses and most other non-SARS-CoV-2 respiratory pathogens. A total of 4,426 non-SARS-CoV-2 respiratory pathogens were identified, including 71 influenza. Of the 71 influenza positives, 64 were successfully sequenced. The majority of influenza strains sequenced belonged to influenza A(H3N2) clades 3C.2a1b.2a2. The most common non-SARS-CoV-2 respiratory pathogen detected was rhinovirus/enterovirus (3,058).

WHAT ARE THE NEW FINDINGS?

DoDGRPSP data show that B.1.1.7 (Alpha) lineage was dominant during February 2021 through May 2021. B.1.617.2/AY.x (Delta) was the predominant lineage from July 2021 through September 2021. The emergence of SARS-CoV-2 corresponded with substantial reductions to the circulation of most other respiratory pathogens, including the influenza virus, among MHS beneficiaries.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

As SARS-CoV-2 cases continue to fluctuate, sequencing is crucial to characterize the diversity of variants impacting MHS beneficiaries. Additionally, as recent focus has shifted to SARS-CoV-2 detection, testing for other respiratory pathogens should still be performed in patients presenting with respiratory symptoms for the effective surveillance of other respiratory pathogens within the MHS. Such continued surveillance will enable installations to rapidly identify, control, and prevent further spread of respiratory pathogens in their communities and provide optimal treatment for MHS beneficiaries..

Respiratory pathogens, such as influenza and adenovirus, have been the main focus of the Department of Defense Global Respiratory Pathogen Surveillance Program (DoDGRPSP) since 1976.[1] However, DoDGRPSP also began focusing on SARS-CoV-2 when COVID-19 was declared a pandemic illness in early March 2020.[2] Following this declaration, the DoD quickly adapted and organized its respiratory surveillance program, housed at the U.S. Air Force School of Aerospace Medicine (USAFSAM), in response to this emergent virus. The DoDGRPSP began to track the incidences of COVID-19-like illness (CLI) or influenza-like illness (ILI) trends and provided data to the Centers for Disease Control and Prevention (CDC) and reported identified SARS-CoV-2 isolates among its beneficiaries. This report provides an overview of DoDGRPSP in addition to summarizing SARS-CoV-2 and other respiratory pathogen activity during the 2020–2021 surveillance season.

METHODS

Surveillance population

The Defense Health Agency/Armed Forces Health Surveillance Division–Air Force Satellite Cell (DHA/AFHSD–AF) and USAFSAM manage the surveillance program that includes 102 sentinel sites and many non-sentinel sites. DoDGRPSP requests that sentinel sites submit 6–10 respiratory specimens per week from U.S. Military Health System (MHS) beneficiaries who meet the CLI or ILI case definition. CLI or ILI were defined as the presence of a fever ≥100.4°F (≥38°C oral or equivalent) and cough, and 3 or more of the following symptoms: shortness of breath, chills, fatigue, body aches, headache, loss of taste/smell, sore throat, sinus congestion, runny nose, vomiting, chills with shaking, and diarrhea[3] within 72 hours of

symptoms onset. Demographic information for patients was collected through a self-reported questionnaire, the Composite Health Care System (CHCS), the Defense Enrollment Eligibility Reporting System (DEERS) and the Armed Forces Health Longitudinal Technology Application (AHLTA). Any specimens that the laboratory cancelled, rejected, did not test, or returned as an inconclusive test result were not included in the final study population.

Laboratory testing

Two laboratories processed the specimens: Landstuhl Regional Medical Center (LRMC) for all the U.S. European Command (EUCOM) and USAFSAM for all other locations. Non-SARS-CoV-2 respiratory pathogen selection and testing have been previously described.[1,4,5] SARS-CoV-2 testing was done through Real-Time Reverse Transcription Polymerase Chain Reaction amplification (RT-PCR, Cobas 8800 system, Roche Diagnostics or Thermo TaqPath COVID-19 Combo Kit) at USAFSAM or the Cepheid GeneXpert Xpress Flu/RSV (Flu/RSV/FluA-B), Luminex or BioFire at LRMC. Respiratory specimens were collected by nasal wash or nasopharyngeal swab and transported at -70°C. All tests were performed in accordance with the protocols available provided by the CDC and manufacturer's instructions for use. The laboratory-confirmed positive specimens for SARS-CoV-2 or influenza viruses were further genetically characterized via Illumina next-generation sequencing (NGS) technology and analyzed using the Cecret pipeline[6] and Pango[7] for SARS-CoV-2 and the CDC Iterative Refinement Meta-Assembler (IRMA) package[8], BioEdit software[9], and components of the DNASTAR Lasergene Core Suite[10] for influenza.

Statistical analysis

Data analysis was performed using SAS version 9.4 (2014, SAS Institute, Cary, NC). A p-value of <0.05 was considered statistically significant. Baseline characteristics of all pathogen detections were summarized by the frequency of specimens collected, number tested and the test positivity. The trends in positivity rate over time for both SARS-CoV-2 and non-SARS-CoV-2 respiratory pathogens were described by calculating the 14-day rolling average. Comparisons of the demographic characteristics (sex, age group, month of illness, and geographical combatant commands) and the clinical findings (patient symptoms) among the groups were performed using a chi-square or Fisher's exact test for categorical variables and a *t* test for continuous variables. Symptom evaluation was limited to those specimens with associated DoDGRPSP questionnaires.

RESULTS

SARS-CoV-2 and other respiratory pathogens surveillance

From 27 September 2020 through 2 October 2021, a total of 96,660 specimens were collected **(Table 1)**. The majority of specimens (61.0%) were collected and tested in the months of October through January, reflecting the most laboratory-positive SARS-CoV-2 cases identified in the same months (75.5%). The most confirmed non-SARS-CoV-2 positive cases were in September, October and November. By comparison, more non-SARS-CoV-2 respiratory pathogens were confirmed in the 2 prior seasons.[1,5] A declining trend was observed for SARS-CoV-2 during the months of February 2021 through June 2021 **(Table 1)**. Of the specimens tested, 64,298 (66.5%) were from male beneficiaries and 32,362 (33.5%) were from female beneficiaries. Additionally, 62,648 (64.8%) were from service members, 19,259 (19.9%) were from beneficiary adults (18–64 years), 13,723 (14.2%) were from children (0–17 years) and 1,030 (1.1%) were from seniors (65+ years). The largest share of the specimens came from beneficiaries aged 25–44 (44.3%; n=42,803). In this group, there were 5,551 positive specimens for SARS-CoV-2 and 1,277 positive for other respiratory pathogens. Additionally, the beneficiaries aged 0–17 had more specimens positive for non-SARS-CoV-2 respiratory pathogens than those in any other age group **(Table 1)**.

The collected specimens varied widely by the 4 geographical combatant commands. The U.S Northern Command (NORTHCOM) contributed 58,117 (60.1%) specimens, with 8,868 positive for SARS-CoV-2 and 3,003 positive for non-SARS-CoV-2 pathogens. The U.S European Command (EUCOM) contributed 37,108 (38.4%) specimens of which 3,313 were positive for SARS-CoV-2 and 1,117 were positive for other pathogens. The U.S Indo-Pacific Command (INDOPACOM) and U.S Central Command (CENTCOM) contributed 1,353 (1.4%) and 82 (0.08%) specimens, respectively.

To understand the distribution, dynamics and clinical profile of SARS-CoV-2 and non-SARS-CoV-2 respiratory pathogen transmission during the surveillance season, a detailed analysis of the data was performed. Among the 4,426 non-SARS-CoV-2 respiratory pathogens detected, 65 were positive for influenza A(H3N2) including 7 coinfections, 4 of which were positive for influenza B viruses with no lineage classification including 1 coinfection, and 2 were positive for influenza A(H1N1) pdm09 **(Table 2)**. The most common non-SARS-CoV-2 respiratory pathogen was rhinovirus/enterovirus (3,312), including 254 specimens positive for rhinovirus/enterovirus and another non-influenza virus **(data not shown)**. The respiratory pathogen panel includes tests for only 2 bacterial pathogens: *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*. *M. pneumoniae* was not detected; however, 2 specimens were confirmed positive for *C. pneumoniae* as compared to 60 in the prior season.[5] Overall, 12,282 specimens were positive for SARS-CoV-2 including 33 coinfections. These mixed infections included: 3 adenovirus, 2 coronavirus (seasonal), 2 RSV, 4 human metapneumovirus, 19 rhinovirus/enterovirus, 1 human bocavirus, 1 adenovirus and parainfluenza (triple coinfection) and 1 human metapneumovirus, parainfluenza and rhinovirus/enterovirus (quadruple coinfection).

SARS-CoV-2 testing began during week 10 (March 2020) of the 2019–2020 surveillance season **(Figures 1, 2)**. This is the same month that a national public health emergency was issued in response to SARS-CoV-2 pandemic by the U. S. government.[11] Subsequent declines in the number of non-SARS-CoV-2 respiratory pathogens and

TABLE 1. Characteristics of the surveillance population and sources of specimens for the MHS beneficiaries, 2020–2021 surveillance season

	SARS-CoV-2	Non-SARS-CoV-2[a]	No pathogen detected[b]	Negative[c]	Total
Total	12,282	4,426	8,057	71,895	96,660
Sex					
Male	8,510	2,602	4,735	48,450	64,298
Female	3,772	1,824	3,321	23,445	32,362
Age group (years)					
0–17	1,145	1,735	1,302	9569	13,751
18–24	4,031	1,232	2,674	21,991	29,928
25–44	5,551	1,277	3,089	32,886	42,803
45–64	1,387	141	816	6,804	9,148
65+	168	41	176	645	1,030
Month of collection					
September	629	755	838	4,635	6,857
October	1,784	701	943	11,979	15,407
November	3,500	532	1,405	15,448	20,885
December	2,361	264	1,015	9,544	13,184
January	1,629	164	716	6,990	9,499
February	424	180	436	4,339	5,379
March	405	216	615	5,125	6,361
April	398	254	463	4,230	5,345
May	142	252	304	2,741	3,439
June	78	207	213	1,973	2,471
July	283	453	407	1,639	2,782
August	649	448	702	3,252	5,051
U.S. combatant command					
CENTCOM	6	0	0	76	82
EUCOM	3,313	1,117	2,459	30,219	37,108
INDOPACOM	95	306	601	351	1,353
NORTHCOM	8,868	3,003	4,997	41,249	58,117
Beneficiary category					
Beneficiary adults	2,732	431	1,646	14,450	19,259
Child	1,145	1,722	1,292	9,564	13,723
Elderly	168	41	176	645	1,030
Service member	8,237	2,232	4,943	47,236	62,648
Data source					
LRMC	3,312	1,007	2,239	30,304	36,862
USAFSAM	8,970	3,419	5,818	41,591	59,798

[a]Non-SARS-CoV-2 - all Influenza and non-influenza broken out in Table 2.
[b]No Pathogen Detected - No pathogen was identified via multiplex testing and may not include SARS-CoV-2 testing.
[c]Negative - Specimen was negative for SARS-CoV-2 and only tested for SARS-CoV-2. LRMC, Landstuhl Regional Medical Center.
MHS, Military Health System; NORTHCOM, Northern Command; EUCOM, European Command; CENTCOM, Central Command;
INDOPACOM, Indo-Pacific Command; USAFSAM, U.S. Air Force School of Aerospace Medicine.

percent positivity likely resulted, at least in part, from non-pharmaceutical interventions implemented worldwide **(Figures 1, 2)**.

During the 2019–2020 season, the percent positivity rates for SARS-CoV-2 began to decrease in surveillance week 28 through week 34 (July–August 2020) and continued to decrease to near 0 in week 36 through week 37 (September 2020), before a relative increase in week 38 through week 39 (September 2020) of the surveillance year. A similar pattern was observed in the Health and Human Services Regions of the U.S., although, there was variability in some of the regions.[14]

Peak SARS-CoV-2 activity occurred during weeks 40 through 4 (September 2020–January 2021) **(Figure 1)**. Thereafter, the weekly detections steadily decreased until week 27 (June 2021) **(Figure 1)**. However, starting surveillance week 28 and continuing through week 33 (July–August 2021), an increasing trend was observed with the emergence of the Delta variant in the summer which may have been due to the virus's increased transmissibility and immune evasion.[15] The trend began to decrease after week 35, perhaps due to improved vaccination coverage in beneficiaries.

The percent positivity for non-SARS-CoV-2 respiratory pathogens was higher compared to the SARS-CoV-2 virus during the 2020–2021 surveillance season. Of note, the percent positives for SARS-CoV-2 and non-SARS-CoV-2 during the 2020–2021 surveillance season ranged from 3% to 26% and 15% to 55%, respectively **(Figure 2)**. It is unclear what factors may have contributed to the apparent change in the relative frequencies of identification of SARS-CoV-2 compared to the other usual potential respiratory pathogens.

Genetic characteristics of SARS-CoV-2 and influenza virus

For the period from 4 October 2020 through 3 October 2021, USAFSAM conducted next-generation sequencing and analysis on both influenza positive and SARS-CoV-2 positive specimens with the help of its partners, the Navy Medical Research Unit 2 (NAMRU-2) in Cambodia and the Armed Forces Research

TABLE 2. SARS-CoV-2, and non- SARS-CoV-2 respiratory pathogens, MHS beneficiaries, 2020–2021 surveillance season

Pathogen	No. of specimens	% of total
Total	96,660	100
SARS-CoV-2 detected	12,282	12.7
SARS-CoV-2 infection	12,249	12.7
SARS-CoV-2 coinfection[a]	33	0.0
Non-SARS-CoV-2 (influenza detected)	71	0.1
Influenza A(H1N1)pdm09	2	0.0
Single infection	2	0.0
Influenza A(H3N2)	65	0.1
Single infection	58	0.1
Coinfection[b]	7	0.0
B/lineage unclassified	4	0.0
Single infection	3	0.0
Coinfection[b]	1	0.0
Non-SARS-CoV-2 (non-influenza) detected	4,355	4.5
Adenovirus	55	0.1
Chlamydophila pneumoniae	2	0.0
Coronavirus (seasonal)	318	0.3
Human bocavirus	65	0.1
Human metapneumovirus	66	0.1
Mycoplasma pneumoniae	0	0.0
Parainfluenza	295	0.3
Respiratory syncytial virus (RSV)	210	0.2
Rhinovirus/enterovirus	3,058	3.2
Non-Influenza viral coinfection[c]	286	0.3
Other	79,952	82.7
No pathogen detected[d]	8,057	8.3
Negative[e]	71,895	74.4

[a]SARS-CoV-2 coinfection includes infection with non-influenza respiratory pathogen.
[b]Influenza coinfections included infection with an influenza and a non-influenza respiratory pathogen.
[c]Non-Influenza viral coinfection included 2 or more infection with non-influenza respiratory pathogen except *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae*.
[d]No pathogen was identified via multiplex testing.
[e]Specimen was negative for SARS-CoV-2 and only tested for SARS-CoV-2.
MHS, Military Health System.

Institute of Medical Sciences (AFRIMS) in Thailand. In total, 64 of 71 influenza specimens were successfully sequenced and analyzed. Among those, 63 were influenza A(H3N2) with 11 clade 3C.2a1b.2a1 (17.5%) specimens collected from Cambodia and Thailand between September 2020 and December 2020, one clade 3C.2a1b.1a (1.6%) specimen collected from the Philippines in December 2020, and 51 clade 3C.2a1b.2a2 (80.9%) specimens collected from Germany and Maryland in September 2021 **(Figure 3a)**. One influenza A(H1N1) pdm09 specimen from North Dakota was identified as being of swine origin and had hemagglutinin (HA) and neuraminidase (NA) genes that closely resembled human origin A(H1N1) viruses. However, the internal gene segments closely resembled swine origin A(H1N1) viruses. This specimen, designated as an influenza A(H1N1) variant, or A(H1N1)v, was collected from a 5 year old patient who had visited a state fair, and had contact with livestock, 3 days prior to symptom onset and specimen collection. No further cases of this influenza variant were detected, suggesting the absence of human-to-human transmission.

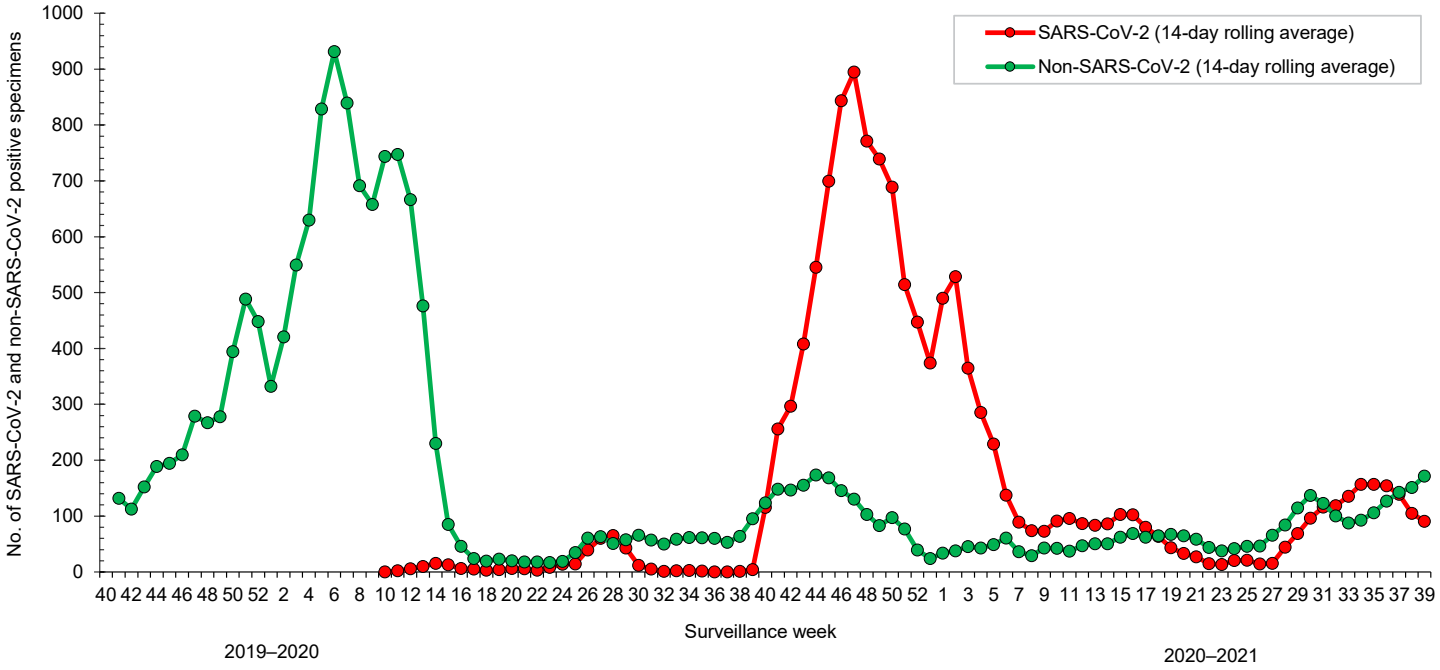
In addition, 7,286 out of 12,282 SARS-CoV-2 positive specimens were sequenced, analyzed and 5,070 were assigned to PANGO lineages. As of December 2020, the World Health Organization (WHO) characterized genetic variants under the classifications Variants of Concern (VOC), Variants of Interest (VOI), and Variants under Monitoring (VUM). The VOC identified included 809 B.1.1.7 (Alpha), 18 B.1.351 (Beta), 41 P.1 (Gamma), and 3,237 B.1.617.2/AY (Delta). The VOI included 11 B.1.621 (Mu). The VUM included nine B.1.1.318, two B.1.525 (Eta), and 56 B.1.526 (Iota) **(Figure 3b)**.

SARS-CoV-2 infection analysis

Data were limited to specimens that were tested for SARS-CoV-2 virus without coinfections and those that submitted a DoDGRPSP questionnaire. There were 86,057 specimens tested for SARS-CoV-2, of which 12,249 were positive and classified as cases; 73,808 were negative and classified as non-cases **(Table 3)**. Male beneficiaries made up 8,493 (69.3%) of the cases and 49,514 (67.1%) of the non-cases. Female beneficiaries made up 3,756 (30.7%) of the cases and 24,294 (32.9%) of the non-cases. In addition, when comparing the proportions of cases to non-cases, statistically significant differences were observed for the following demographic characteristics: sex, age, month of illness, and geographical combatant commands **(Table 3)**.

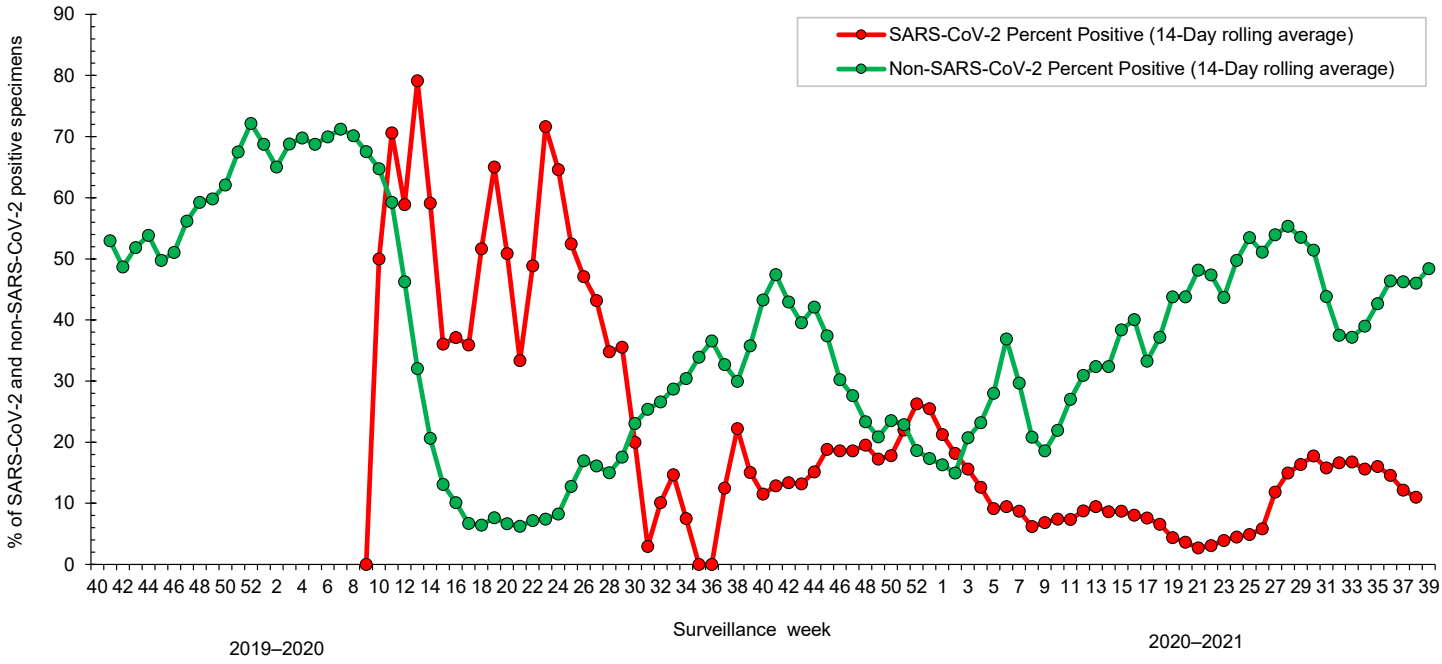
Symptomatic evaluation was further limited to those with a DoDGRPSP questionnaire and who met the case definition criteria. Among the 86,057 specimens tested for SARS-CoV-2, 1,306 specimens had DoDGRPSP questionnaires **(Table 4)**. Univariate analysis showed that out of the 14 symptoms evaluated, 10 had statistically significant differences between the cases and the non-cases ($p<.05$). The most common symptoms among the confirmed cases were cough (75.4%), sinus congestion (66.3%), headache (64.9%), and body aches (57.3%). Additionally, cough (59.6%), sinus congestion (55.5%) and headache (55.6%) were the

FIGURE 1. Number of SARS-CoV-2, non-SARS-CoV-2 positive specimens by surveillance week, MHS beneficiaries, 2019–2020 and 2020–2021 surveillance seasons (14-day rolling average)



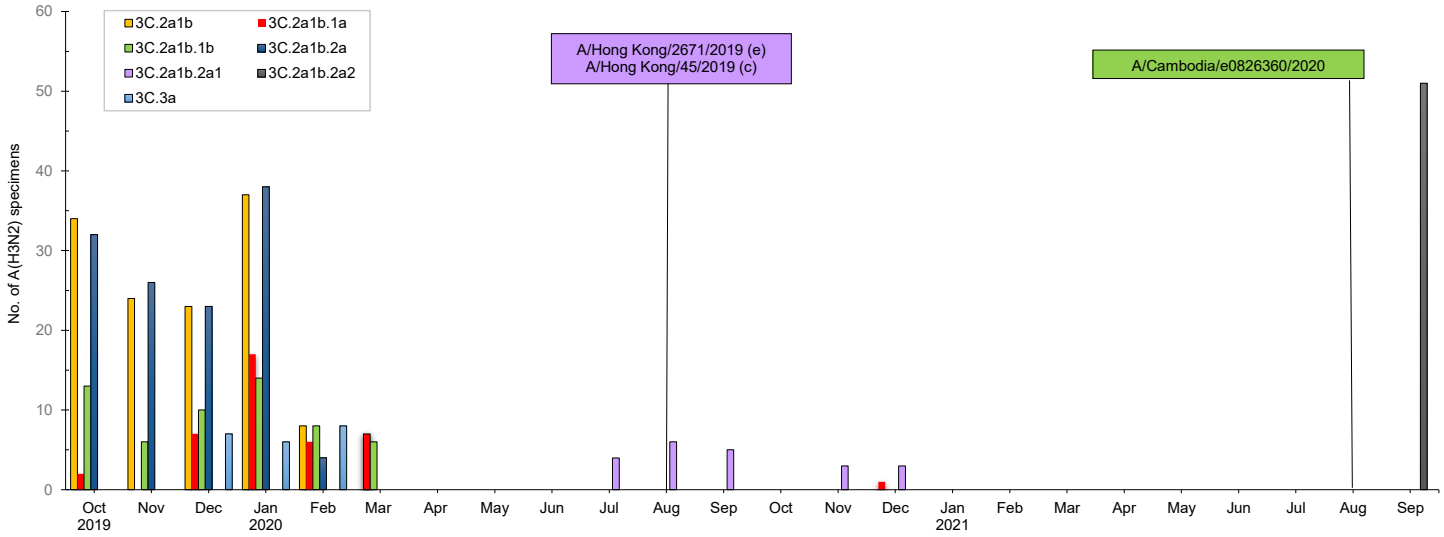
MHS, Military Health System, No., number.

FIGURE 2. Percentage of SARS-CoV-2, non-SARS-CoV-2 positive specimens and surveillance week, MHS beneficiaries, 2019–2020 and 2020–2021 surveillance season (14-day rolling average)



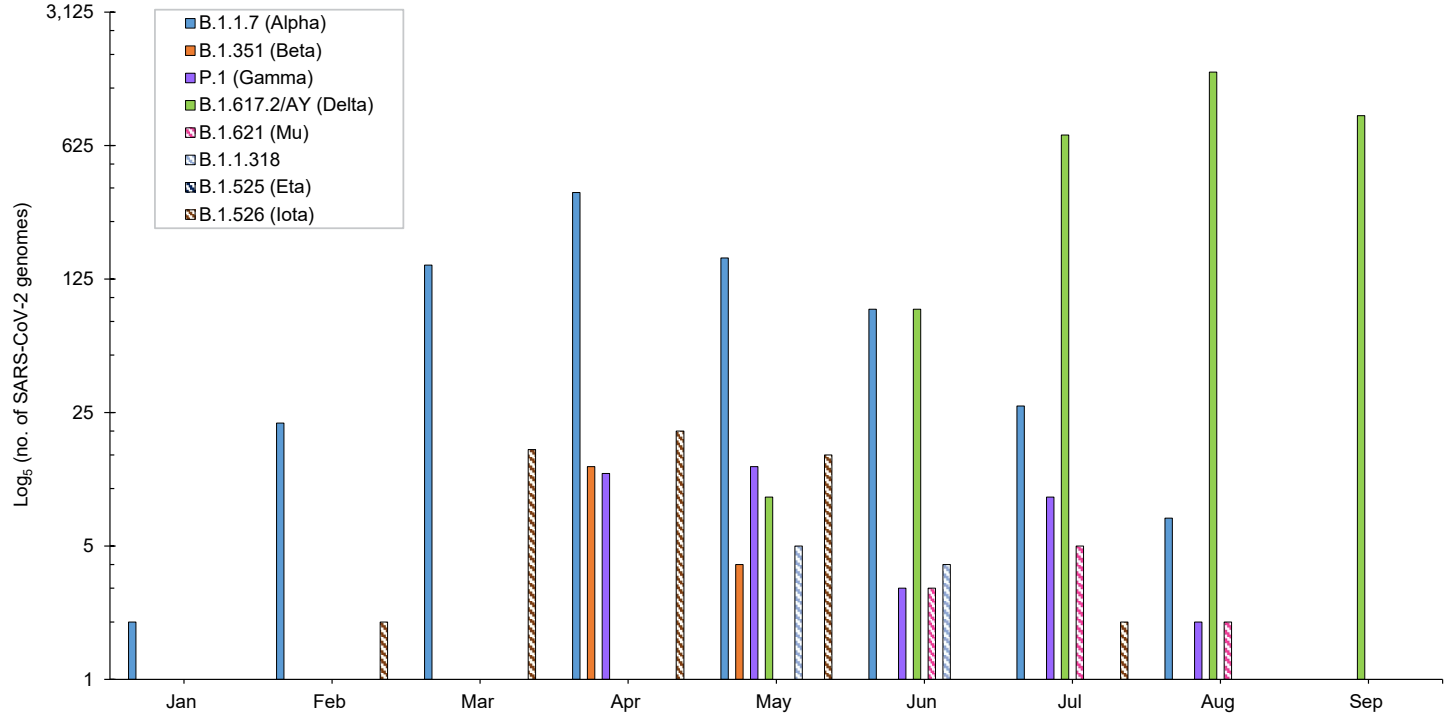
MHS, Military Health System

FIGURE 3a. Influenza A(H3N2) clade proportions across 2 seasons, 2019–2020 and 2020–2021 (n=64), MHS beneficiaries



Note: Changes to the influenza vaccine A(H3N2) component are shown in text boxes, color coordinated with the vaccine strain clade.
MHS, Military Health System, No., number.

FIGURE 3b. SARS-CoV-2 VOC, VOI, and VUM lineages identified from January 2021[a] through September 2021 (n=7,286), MHS beneficiaries



[a]No VOC/VOI/VUM were identified prior to January 2021.
MHS, Military Health System; VOC, variants of concern; VOI, variants of interest; VUM, variants under monitoring; No., number.

TABLE 3. Demographic characteristics of the laboratory-confirmed SARS-CoV-2 cases and non-cases, 2020–2021 surveillance season, MHS beneficiaries

Demographic	Cases		Non-cases		p-value
	No.	%	No.	%	
Total	12,249	14.2	73,808	85.8	
Sex					
Male	8,493	69.3	49,514	67.1	<.001
Female	3,756	30.7	24,294	32.9	
Age group (years)					
0–17	1,131	9.2	10,172	13.8	<.001
18–24	4,025	32.9	22,420	30.4	
25–44	5,542	45.2	33,548	45.5	
45–64	1,384	11.3	7,001	9.5	
65+	167	1.4	667	0.9	
Month of illness					
September	626	5.1	4,944	6.7	<.001
October	1,780	14.5	12,179	16.5	
November	3,497	28.5	15,755	21.3	
December	2,352	19.2	9,718	13.2	
January	1,625	13.3	7,151	9.7	
February	422	3.5	4,407	6.0	
March	405	3.3	5,256	7.1	
April	398	3.3	4,403	6.0	
May	141	1.2	2,841	3.9	
June	77	0.6	2,027	2.8	
July	280	2.3	1,727	2.3	
August	646	5.3	3,400	4.6	
U.S. combatant command					
USCENTCOM	6	0.1	76	0.1	<.001
USEUCOM	3,309	27.0	31,048	42.1	
USINDOPACOM	95	0.8	351	0.5	
USNORTHCOM	8,839	72.2	42,333	57.4	

MHS, Military Health System; NORTHCOM, Northern Command; EUCOM, European Command; CENTCOM, Central Command; INDOPACOM, Indo-Pacific Command; No., number.

most frequent symptoms observed in the non-cases, aside from sore throat (55.9%). The odds ratios calculated ranged from 0.80 (shortness of breath; 95%CI: 0.51–1.25) to 3.31 (change in sense of taste/smell; 95%CI: 2.31–4.74). The cases and non-cases did not differ significantly by the following symptoms: runny nose, shortness of breath, sore throat, and fatigue (p>.05) **(Table 4)**.

EDITORIAL COMMENT

The 2020–2021 season showed low non-SARS-CoV-2 respiratory pathogen activity. The predominant non-SARS-CoV-2 pathogen circulating during the 2020–2021 surveillance season was rhinovirus/enterovirus. Only 0.6% of non-SARS-CoV-2 respiratory specimens tested by the DoDGRPSP were positive for influenza viruses as compared with 19.6% in the 2019–2020 season.[5] Among the 71 confirmed cases of influenza, the majority were attributed to an outbreak at the U.S. Naval Academy in Annapolis, Maryland in September 2021. Overall, these numbers are substantially lower than those reported in 2019-2020,[5] contributing to an unprecedented 2020-2021 surveillance season for non-SARS-CoV-2 pathogens.

Beginning in December 2020, the WHO began characterizing SARS-CoV-2 lineages as VOC and VOI, and later added the category VUM.[16] Two overlapping waves of SARS-CoV-2 variant activity were observed throughout the 2020-2021 season. The B.1.1.7 (Alpha) lineage predominated February 2021 through May 2021. By July 2021, and continuing through the rest of the season, B.1.617.2/AY.x (Delta) predominated and by September 2021 made up 100% of the identified SARS-CoV-2 lineages. Other VOC, VOI and VUM were also observed, but in much smaller proportions (**Figure 3b**). The rapid shift in SARS-CoV-2 genetic diversity within a single surveillance season emphasizes the need for continued sequence surveillance of new and emerging SARS-CoV-2 variants.

As more studies continue to elucidate the impact of the COVID-19 pandemic on MHS beneficiaries,[17] surveillance of all respiratory pathogens is imperative in order to document changes in incidences of other diseases aside from COVID-19. Enhanced patient management and treatment, while reducing the time patients are in isolation, particularly for those infected with other common respiratory pathogen, is of extreme importance.

The findings in this study are subject to at least three limitations. First, if multiple specimens were submitted from an individual, only one specimen was retained in order to prevent duplication. If multiple specimens were submitted from a single individual, the first positive test result was recorded or in the case of all negative results, the first negative result was recorded. Second, the self-reporting nature of some of our data, specifically the symptoms, could have affected the statistical significance in

TABLE 4. Comparison of symptoms between cases and non-cases, MHS beneficiaries, 2020–2021 surveillance season

Symptoms	Cases		Non-cases		p-value	Odds ratio (OR)	OR 95% CI
	No.	%	No.	%			
Change in taste/smell	71	31.7	88	12.3	<.001	3.31	(2.31–4.74)
Chills	123	47.5	241	29.5	<.001	2.16	(1.62–2.87)
Cough	214	75.4	538	59.6	<.001	2.07	(1.53–2.79)
Shaking	33	15.6	40	5.7	<.001	3.06	(1.88–5.00)
Body aches	149	57.3	349	41.7	<.001	1.87	(1.41–2.48)
Fever	145	48.5	333	35.6	<.001	1.70	(1.31–2.22)
Sinus congestion	169	66.3	475	55.5	.002	1.58	(1.18–2.11)
Vomit	70	24.6	364	40.4	.004	2.59	(1.32–5.08)
Headache	168	64.9	479	55.6	.008	1.48	(1.11–1.97)
Diarrhea	28	13.7	148	20.4	.031	1.62	(1.41–2.49)
Runny nose	108	44.6	332	40.4	.245	1.19	(0.89–1.59)
Shortness of breath	28	13.7	118	16.5	.329	0.80	(0.51–1.25)
Sore throat	141	54.4	467	55.9	.688	0.94	(0.71–1.25)
Fatigue	126	50.0	412	49.4	.868	1.02	(0.77–1.36)

MHS, Military Health System; No., number.

the analysis because, it could have been underestimated or overestimated during the time of recall. Third, the low submission rate of the DoDGRPSP questionnaires reduced the amount of CLI or ILI information available for analysis. This low submission may be attributed to the non-pharmaceutical measures implemented across the installations such as distancing and limiting contact time. Nevertheless, all specimens submitted to the program are requested to meet the CLI or ILI criteria; however, physician diagnosed specimens were accepted (the patient did not meet the CLI/ILI criteria, but testing was determined necessary by the physician). Those without a questionnaire were assumed to be physician diagnosed specimens.

Although strong interventions were in place to prevent and contain the spread of the SARS-CoV-2 pandemic within the MHS, more work is needed to determine if those interventions effectively delayed the spread of SARS-CoV-2 virus.

This report analyzed the epidemiological trends of SARS-CoV-2 and non-SARS-CoV-2 respiratory pathogens and found a high infection rate of both SARS-CoV-2 and non-SARS-CoV-2 in patients presenting with CLI or ILI. Although the current pandemic constitutes a serious public health concern, many other pathogens cause respiratory tract infections among the MHS beneficiaries. Therefore, continued testing of those with respiratory symptoms using a multiplex PCR assay is the most effective means for surveillance and to identify the transmission patterns within MHS beneficiaries for optimal treatment and to inhibit the rapid spread of all respiratory pathogens.

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REFERENCES

1. Kersellius GD, Gruner WE, Fries AC, DeMarcus LS, Robbins AS. Respiratory pathogen surveillance trends and influenza vaccine effectiveness estimates for the 2018–2019 season among Department of Defense beneficiaries. *MSMR*. 2020;27(1):17–23.
2. The World Health Organization. Director-General's opening remarks at the media briefing on. COVID-19 -11 March 2020. Accessed 11 September 2021. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
3. The World Health Organization. Public health surveillance for COVID-19: Interim guidance. Accessed 11 September 2021. https://www.who.int/publications/i/item/who-2019-nCoV-surveillance-guidance-2020.8
4. DeMarcus LS, Shoubaki L, Federinko S. Comparing influenza vaccine effectiveness between cell-derived and egg-derived vaccines, 2017–2018 influenza season. *Vaccine*. 2019; 37(30):4015–4021.
5. Hu W, Gruner WE, DeMarcus LS, et al. Influenza Surveillance Trends and Influenza Vaccine Effectiveness Among Department of Defense Beneficiaries During the 2019–2020 Influenza Season; *MSMR*. 2021;28(3):2–8.
6. Young, EL. Technical Outreach and Assistance for States Team 2021. Cecret Workflow for SARS-CoV-2 Assembly and Lineage Classification.protocols.io. Accessed 8 December 2021.https://www.protocols.io/view/cecret-workflow-for-sars-cov-2-assembly-and-lineag-by72pzqe.
7. O'Toole A, Scher E, Underwood A, et al. Assignment of epidemiological lineages in an

emerging pandemic using the pangolin tool. *Virus Evolution.* 2021;07(2):veab064.
8. Shepard SS, Meno S, Bahl, J, et al. Viral deep sequencing needs an adaptive approach: IRMA, the iterative refinement meta-assembler. *BMC Genomics* 2016;17(1):708.
9. Hall TA. BioEdit: a user-friendly biological sequence alignment editor and analysis program for Windows 95/98/NT. *Nucl Acids Symp Ser.*1999;41:95–98.
10. DNASTAR: Lasergene Core Suite (RRID:SCR_000291).
11. National Archives and Records Administration. Accessed on 3 January, 2022. https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/.
12. Lyu W, Wehby GL. Community Use Of Face Masks And COVID-19: Evidence From A Natural Experiment Of State Mandates In The US. *Health Aff (Millwood)*. 2020;39(8):1419–1425.
13. Al Jazeera News. Which countries have made wearing face masks compulsory? Accessed 15 February 2022. https://www.aljazeera.com/news/2020/8/17/which-countries-have-made-wearing-face-masks-compulsory
14. Center for Disease Control and Prevention. A weekly surveillance summary of U.S.COVID-19 activity for 2020-2021 season. Accessed 8 December 2021. https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/past-reports/08282020.html
15. Bushman M, Kahn R, et al. Population impact of SARS-CoV-2 variants with enhanced transmissibility and/or partial immune escape. *Cell*. 2021;184(26):6229–6242.
16. Mullen JL, Tsueng G, Latif AA, et al. The Center for Viral Systems Biology outbreak.info. Accessed 4 November 2021. https://outbreak.info/
17. Richard SA, Pollett SD, et al. COVID-19 Outcomes Among US Military Health System Beneficiaries Include Complications Across Multiple Organ Systems and Substantial Functional Impairment; *Open Forum Infectious Diseases*. 2021:8(12):ofab556.
18. World Health Organization. Recommended composition of the influenza virus vaccines for use in the 2021–2022 northern hemisphere influenza season. Accessed 6 September 2022. https://www.who.int/publications/i/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2021-2022-northern-hemisphere-influenza-season

Establishment of SARS-CoV-2 Genomic Surveillance Within the Military Health System During 1 March–31 December 2020

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This report describes SARS-CoV-2 genomic surveillance conducted by the Department of Defense (DoD) Global Emerging Infections Surveillance Branch and the Next-Generation Sequencing and Bioinformatics Consortium (NGSBC) in response to the COVID-19 pandemic. Samples and sequence data were from SARS-CoV-2 infections occurring among Military Health System (MHS) beneficiaries from 1 March to 31 December 2020. There were 1,366 MHS samples sequenced from 10 countries, 36 U.S states or territories, and 5 Geographic Combatant Commands, representing approximately 2% of DoD cases in 2020. Genomes from these samples were compared with other public sequences; observed trends were similar to those of Centers for Disease Control and Prevention national surveillance in the U.S. with B.1, B.1.2, and other sub-lineages comprising the dominant variants of SARS-CoV-2. Sequence data were used to monitor transmission dynamics on U.S. Navy ships and at military training centers and installations. As new variants emerge, DoD medical and public health practitioners should maximize the use of genomic surveillance resources within DoD to inform force health protection measures.

WHAT ARE THE NEW FINDINGS?

From 1 March through 31 December 2020, 1,366 MHS SARS-CoV-2 sequences were generated from 36 U.S. states or territories, 10 countries, and 9 naval vessels. Dominant lineages detected were B.1.2 (17%), B.1 (14%) and B.1.1 (8%). The first MHS case of a variant of concern (Epsilon) was identified in December 2020.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

As demonstrated by the emergence of multiple SARS-CoV-2 variants, sequencing is needed to monitor viral evolution and inform mitigation strategies in DoD settings, including troop movement and hygiene measures. Genomic surveillance supports the development of diagnostics, therapeutics, and vaccines and can help monitor their effectiveness over time.

In 2020, approximately 138,000 probable COVID-19 cases, including more than 87,000 polymerase chain reaction-(PCR)-confirmed cases, were reported among U.S. service members, dependents, and retirees (Shauna Stahlman, PhD, email communication, December 2021). During the early pandemic, SARS-CoV-2 transmission had dramatic impacts on Department of Defense (DoD) operations in the U.S. and overseas, with outbreaks limiting personnel movement in South Korea, sidelining U.S. Navy ships, and curtailing training on installations.[1-3] Significant time and resources were required for COVID-19 surveillance and mitigation of its impacts on DoD operations and Military Health System (MHS) beneficiaries.

COVID-19 is caused by SARS-CoV-2, which is a member of family Coronaviridae, genus *Betacoronavirus*. The virus contains a roughly 30 kilobase positive-sense RNA genome encoding 4 structural and 16 non-structural viral proteins. Since the beginning of the pandemic, viral sequencing has been a critical component of the response.[4-6] The first sequenced and publicly released SARS-CoV-2 genomes helped guide development of diagnostic assays and eventually vaccines.[7] Genomic data have also become critical components of epidemiology and outbreak response. These data can provide information about large-scale epidemics, such as the approximate date when SARS-CoV-2 was first introduced to North America,[8] and can also be used to characterize localized outbreaks, such as in congregate living facilities[9] and on cruise ships.[10] SARS-CoV-2 genomic epidemiology has also been used to examine transmission events within military recruit and trainee settings[11] and to detect introductions of novel variants from international military deployments.[12]

Genomic surveillance using whole-genome sequencing (WGS) is an important tool that can be used to detect changes in the SARS-CoV-2 viral genome. These changes may affect diagnostic sensitivity, vaccine efficacy, monoclonal antibody efficacy, or viral transmission and virulence.[13] More recently, the impacts of emerging SARS-CoV-2 variants, collectively known as variants of concern (VOC) and variants being

monitored (VBM), have been observed with respect to the effectiveness of medical countermeasures and, in the case of Alpha, Delta, and Omicron, with respect to displacement of other variants.[14,15]

To establish SARS-CoV-2 sequencing and genomic surveillance capabilities for the DoD, the Armed Forces Health Surveillance Division (AFHSD) Global Emerging Infections Surveillance (GEIS) Branch leveraged existing partnerships with Army, Navy, and Air Force public health and medical research laboratories as part of the Next Generation Sequencing and Bioinformatics Consortium (NGSBC). This Consortium was established in 2017 to work with GEIS partner DoD medical research and public health laboratories to coordinate and improve pathogen sequencing and analysis efforts. The initial efforts of the NGSBC laid a foundation for DoD expansion of WGS in 2021 in response to novel SARS-CoV-2 VOCs, to aid in investigating outbreaks and in monitoring diagnostics and vaccine effectiveness.

This report describes SARS-CoV-2 genomic surveillance findings among DoD beneficiaries from 1 March 2020 through 31 December 2020 and highlights the utility of SARS-CoV-2 sequence data for providing a baseline for further characterization of emerging variants that could impact DoD beneficiaries and operations.

METHODS

In early 2020, GEIS and NGSBC representatives from U.S. Naval Medical Research Center (NMRC), U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Walter Reed Army Institute of Research (WRAIR), U.S. Air Force School of Aerospace Medicine (USAFSAM), U.S. Naval Health Research Center (NHRC), and overseas partner laboratories worked to rapidly evaluate protocols and establish best practices and guidance for SARS-CoV-2 WGS and standardize genomic and epidemiologic meta-data during early 2020.[16] These protocols were shared with DoD laboratories in the U.S. and abroad (https://carepoint.health.mil/sites/AFHSB/geis/programmatics/ngsbc/).

Sample collection and selection

Samples from SARS-CoV-2 positive specimens were obtained through clinical care, outbreak response, or participation in the DoD respiratory surveillance program[3] as part of the GEIS NGSBC efforts to provide advanced testing for SARS-CoV-2 (including viral isolation and WGS). Nasopharyngeal, oropharyngeal, nasal, and buccal swabs were collected and stored in universal or viral transport media. Generally, samples were collected, transported, and stored consistent with Centers for Disease Control and Prevention (CDC) interim guidance.[17] Samples were selected for sequencing from clinical specimens submitted from diverse geographic locations among MHS COVID-19 cases. Samples with higher viral loads, as approximated from real-time reverse transcription polymerase chain reaction (RT-PCR) cycle-threshold (Ct) values ≤30, were prioritized.

Consistent with 45 CFR 46 guidelines, sequencing sites obtained an Institutional Review Board determination of nonhuman subject research, or a determination that sequencing was intended as a public health surveillance activity.

Laboratory testing

Sequencing. After samples were collected and RNA was extracted, SARS-CoV-2 sequencing was performed using 2 different methods **(Figure 1)**. For the majority of samples, amplicon-based approaches were used, including the ARTIC Network and YouSeq protocols **(Figure 1)**.[18,19] Briefly, total ribonucleic acid (RNA) was extracted and reverse-transcribed into complementary deoxynucleic acid (cDNA), followed by the selective amplification of SARS-CoV-2-derived cDNA using specific PCR primers. Alternatively, in some instances, to enrich for SARS-CoV-2 cDNA, hybridization approaches were applied using the Illumina Respiratory Virus Oligos Panel **(Figure 1)**. Each sample was then barcoded and combined and sequenced in multiplexed reactions, primarily using Illumina sequencing platforms (MiSeq and NextSeq).

Analysis. As previously described, for quality control steps, low quality genome sequence reads and artifacts from sequence library preparation were removed.[20,21] Individual sequence reads were then aligned to the Wuhan-Hu-1 SARS-CoV-2 reference genome (NC_045512.2).[22] Consensus genomes were generated[23] and classified into lineages using the PANGO (Phylogenetic Assignment of Named Global Outbreak lineage) nomenclature [24,25] and clades using Nextstrain.[26,27] After clearance for public release, consensus genomes were deposited into public databases including GISAID or Genbank (https://www.ncbi.nlm.nih.gov/genbank/). Accompanying sample epidemiologic data were compiled and descriptive statistical analysis was performed using SAS/STAT software, version 9.4 (2014, SAS Institute, Cary, NC).

RESULTS

A total of 1,366 SARS-CoV-2 samples collected during 1 March to 31 December 2020 from 36 U.S. states or territories and 10 countries were sent for sequencing at NGSBC laboratories. These represented samples from individual MHS cases of COVID-19 illness and from MHS beneficiaries with preclinical/asymptomatic SARS-CoV-2 infections, collected from at least 80 military installations or military treatment facilities and 9 naval vessels within 5 Global Combatant Commands (GCC) (USEUCOM, USCENTCOM, USINDOPACOM, USNORTHCOM, and USSOUTHCOM). Most samples were collected in NORTHCOM (80.4%) while the remainder came from locations outside of the continental U.S. (14.0%) or naval vessels (5.6%) **(Table 1)**. In December 2020, the 223 samples that were sequenced represented the largest monthly count of the year **(Figure 2a)**. The second highest monthly count of samples sequenced was in August 2020 (n=214).

The primary reasons for submitting a sample for sequencing were routine surveillance (82.9%; n=1,132) followed by potential diagnostic anomalies (4.9%; n=67), and a suspected outbreak cluster (2.6%; n=35) **(Table 1, Figure 2b)**. The majority of routine surveillance samples were collected as part of previously existing DoD respiratory

surveillance programs or residual diagnostic and surveillance specimens. Furthermore, across all sample collection months, routine surveillance was cited as the primary reason for sequencing for the majority of samples **(Figure 2b)**. However, samples sent for sequencing due to suspected diagnostic anomalies, such as dropout of 1 or more RT-PCR targets, increased dramatically at the end of the year accounting for 28% (n=63) of samples collected in December 2020 (n=223) **(Figure 2b)**.[28] Most of the reported outbreak-associated samples came from public health investigations in the early half of the year; however, additional outbreak-associated clusters were identified after genomic analyses.

Sequencing results

Samples varied in terms of viral load and nucleic acid quality, and analysis of a subset of sequenced samples showed that lower RT-PCR Ct values correlated with a higher sequencing success rate. These data also showed that a Ct value of 30 or lower was a reasonable threshold for prioritizing samples for sequencing **(Figure 3)**. Of all sequenced samples, 1,159 (84.8%) had sufficient sequence quality (i.e., breadth and depth of coverage across the genome) to generate a PANGO lineage call. The most common SARS-CoV-2 lineages in 2020 were B.1.2 (16.7%), B.1 (14.1%), and B.1.1 (7.6%). Ten additional lineages were observed less frequently at nearly 1% each **(Table 2)**. No single lineage was dominant in 2020; in most months, the combination of other (<1% frequency) lineages accounted for over one-third of all sequenced samples **(Figure 4)**.

Outbreaks and suspected clusters

A subset of sequenced samples was collected from suspected outbreaks at overseas locations, on naval vessels, or at recruit training installations. Sequencing results were either used to complement more traditional epidemiological data to better describe transmission patterns or to retrospectively confirm outbreak clusters.[11] Several examples include: 1) a cluster of B.1.428.1 cases (n=28) identified in samples from Iraq collected in June 2020; 2) a cluster of B.1.588.1 cases (n=26) from Romania collected in November 2020; 3) a likely outbreak of B.1.177 cases (n=10) collected from 28 April through 13 May 2020 on a Navy ship; and 4) other potential outbreaks on naval vessels and at recruit training installations (e.g., MCRD Parris Island, SC and MCRD San Diego, CA) **(Table 2)**.

Early detection of the Epsilon variant in MHS

In December 2020, 8 Epsilon (a WHO named variant comprised of the B.1.427 and B.1.429 lineages) cases were identified in the MHS **(Table 2)**. Two cases were infections caused by the B.1.427 lineage, identified in CA (Port Hueneme) and in OH (Wright Patterson Air Force Base (AFB). Six cases caused by the B.1.429 lineage were identified in CA (Edwards AFB and Port Hueneme), ND (Minot AFB), and from a U.S. naval vessel. Epsilon samples contained the L452R amino acid substitution in the receptor-binding domain of the spike protein associated with immune evasion and increased infectivity.[29] No other WHO-named variant infections were detected among the MHS samples collected and sequenced in 2020.

EDITORIAL COMMENT

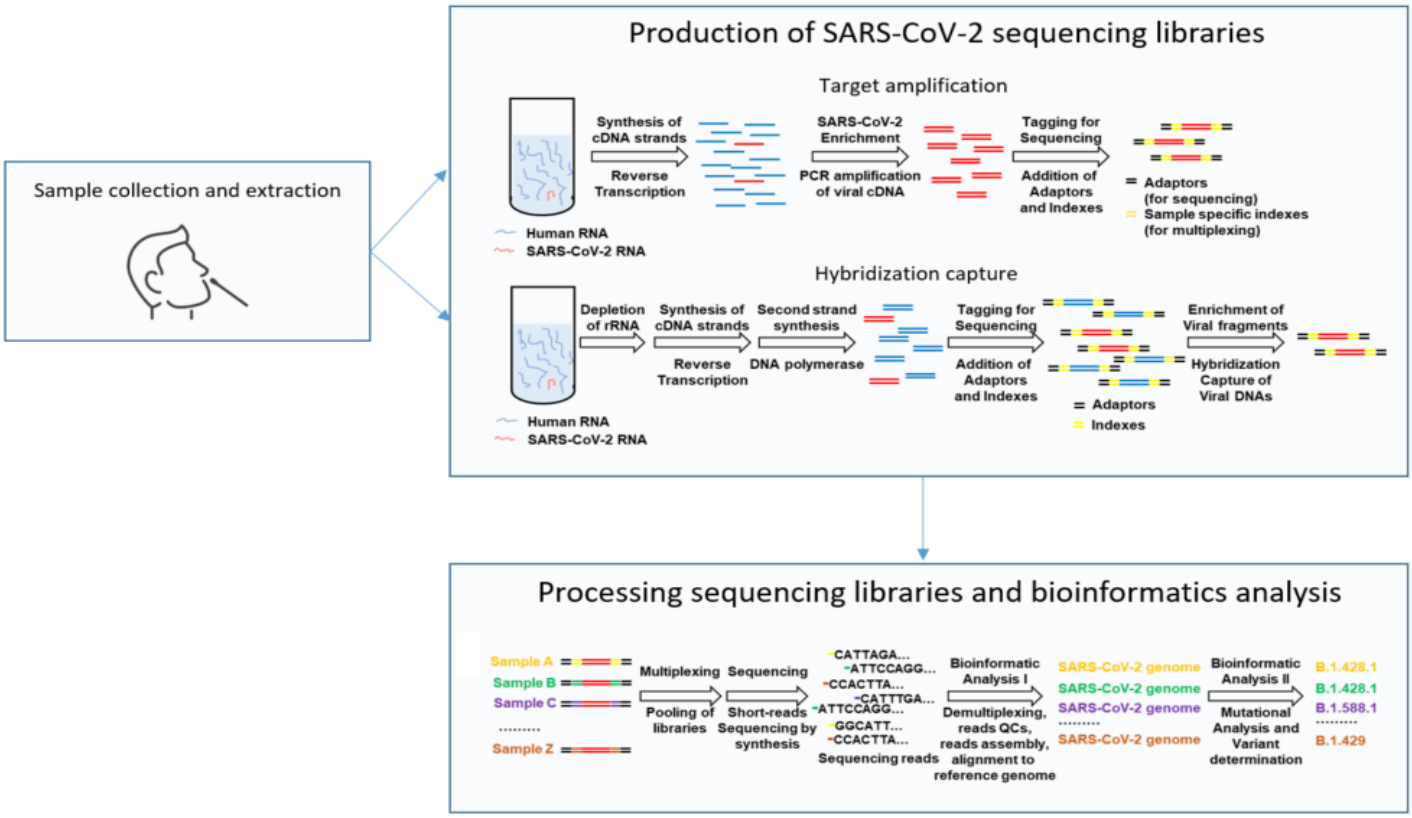
To respond to the emergence of SARS-CoV-2, the GEIS NGSBC and other DoD partners, using existing baseline funding and resources, rapidly established sequencing and genomic surveillance for SARS-CoV-2 within the MHS in early 2020. However, due to the lack of coordinated national response and DoD policy throughout 2020, less than 2% of COVID-19 cases reported within the MHS were sequenced by GEIS partners for surveillance purposes. While not all samples would have been eligible for sequencing, this demonstrates an untapped opportunity to leverage SARS-CoV-2 sequencing as an integral part of early DoD COVID-19 surveillance and response activities. In 2020, significant barriers limited the ability of GEIS partners to obtain and sequence samples, most notably lack of awareness and consensus about privacy and regulatory requirements

TABLE 1. Characteristics of SARS-CoV-2 samples (n=1,366) from the Military Health System submitted for sequencing, 1 March–31 December, 2020 (n=1,366)

	No.	%
Sequencing laboratory		
NHRC	161	11.8
NMRC	400	29.3
USAFSAM	805	58.9
Geographic combatant command		
USCENTCOM	31	2.3
USEUCOM	78	5.7
USINDOPACOM	81	5.9
USNORTHCOM	1,098	80.4
USSOUTHCOM	2	0.1
Ship/multi-GCC[a]	76	5.6
Country of sample collection		
U.S.	1,098	80.4
Ships/Multi-GCC	76	5.6
Guam[b]	64	4.7
Romania	40	2.9
Iraq	31	2.3
Germany	27	2.0
South Korea	14	1.0
England	6	0.4
Japan	3	0.2
Spain	3	0.2
Cuba	2	0.1
Italy	2	0.1
Primary reason for sample sequencing		
Routine surveillance	1,132	82.9
Case of interest: diagnostic anomaly	67	4.9
Cluster/outbreak	35	2.6
Recruit/trainee surveillance	16	1.2
Case of interest: other respiratory co-infection	5	0.4
Case of interest: unusual/ severe clinical presentation	1	0.1
Unknown	110	8.1

[a]Sample was collected in relation to an outbreak or exposure on a naval vessel.
[b]U.S Territory.
NHRC, Naval Health Research Center; NMRC, Naval Medical Research Center; USAFSAM, U.S. Air Force School of Aerospace Medicine; USCENTCOM, U.S. Central Command; USEUCOM, U.S. European Command; USINDOPACOM, U.S. Indo-Pacific Command; U.S. Northern Command; USSOUTHCOM, U.S. Southern Command; GCC, Geographic Combatant Command.

FIGURE 1. Schematic representation of sample preparation, sequencing, and bioinformatics methods



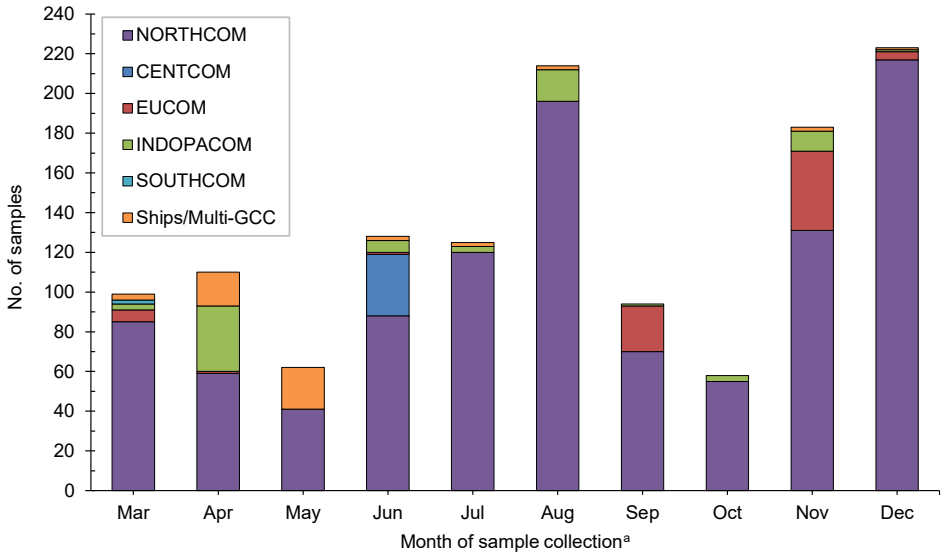
Note: After samples were collected and the RNA was extracted, the SARS-CoV-2 sequencing libraries were produced using 2 different methods--processing of RNA samples for production of sequencing libraries using target amplification methods (specifically, ARTIC and YouSeq libraries) and processing of RNA samples for production of sequencing libraries using viral hybridization capture (Illumina Respiratory Virus Oligos Panel). The second panel shows the step of processing DNA fragment libraries for multiplexing sequencing, Illumina short-reads sequencing and SARS-CoV-2 genomes assembly, and variant analysis using PANGO lineages and Nextstrain clades.

for sharing of samples and their associated epidemiological data during the pandemic. Similar to civilian public health settings, compliance regarding sample and data sharing across the DoD contributes to slow approval processes, delaying important analyses and reducing the timeliness of results.[30] Clarity on these regulations within the DoD during a public health emergency is critical to facilitate prompt genomic surveillance priorities. It was the emergence of the Alpha (B.1.1.7) variant in the U.K. in late 2020 and its eventual global spread that generated momentum within DoD to establish a policy to recognize WGS as a critical capability in pandemic response and to expand genomic sequencing surveillance across the MHS.[31]

Along with efforts to characterize the clinical and public health impacts of SARS-CoV-2, genomic surveillance helped guide intervention and mitigation strategies to protect U.S. service members and other MHS beneficiaries. The findings of this report, based on global genetic sequence data from MHS beneficiaries, are consistent with other reports of global and North American SARS-CoV-2 genetic diversity in 2020.[32] Sequencing data also indicated that early diagnostics and countermeasures, such as vaccines and monoclonal antibodies, against the original Wuhan-Hu-1 reference would have been effective against the variants of SARS-CoV-2 circulating in the MHS in 2020. These initial surveillance efforts also provided critical baseline information and scientific infrastructure for monitoring emerging VOCs (e.g., Alpha, Beta, Gamma, Delta, Epsilon, and Omicron) and COVID-19 vaccine effectiveness in 2021.

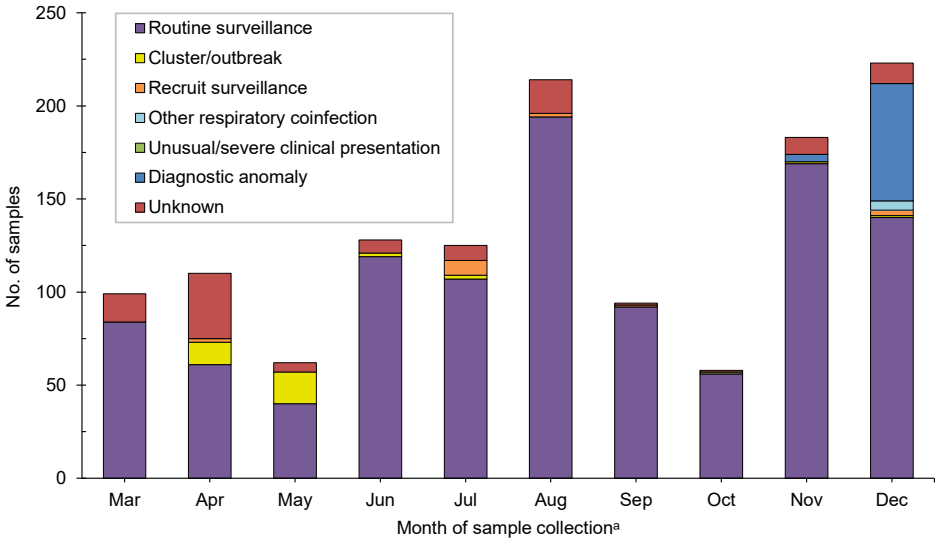
The flexibility and robustness of this genomic surveillance program was also evident in several ways. First, as information became available about the sequencing success rate in relation to diagnostic Ct values or specific sequencing protocols, recommendations were made for prioritization of samples for sequencing and adjustments to preferred protocols. Second, in late 2020, there was a dramatic increase in the number of samples being sent for sequencing that had suspected diagnostic anomalies. This increase was likely due to clinical and laboratory awareness of the need for enhanced national surveillance for Spike-gene target failures that could be indicative of B.1.1.7 (the variant first identified in the UK and later renamed to VOC Alpha). Finally, the geographic coverage of samples submitted from routine surveillance and outbreak response allowed for the detection of unique variants from several overseas locations in CENTCOM and EUCOM and the detection of Epsilon cases within the MHS in NORTHCOM in December 2020 **(Table 2)**. Epsilon, first detected in southern California, was ultimately elevated to its highest level, a VOC, by the U.S. SARS-CoV-2 Interagency Group from 19 March to 29 June 2021.

FIGURE 2a. Numbers of samples sequenced by collection month and geographic combatant command, 1 March–31 December 2020



[a]Month of sample collection was missing for 70 samples (NORTHCOM=36; Ships/Multi-GCC=26; INDOPACOM=5; EUCOM=3).

FIGURE 2b. Numbers of samples sequenced per month by collection month and reason for sampling, 1 March–31 December 2020



[a]Month of sample collection was missing for 70 samples (routine surveillance).

There are several important limitations to the DoD WGS approach. Samples sent to NGSBC laboratories for genomic surveillance were not explicitly selected to be representative of all COVID-19 cases within the MHS but were the result of either participation in existing DoD respiratory surveillance networks or the awareness and willingness of a provider, clinician, or public health authority to share samples. Sampling bias can complicate prevalence estimates and interpretation of sequence data and missing epidemiologic data can further limit insights from phylogenetic analysis.[33] Finally, there is a need for better methods to account for over, under, and biased sampling for both global and regional public genomic datasets and within local outbreaks. Notably, these efforts provided some of the only SARS-CoV-2 sequence data available from locations such as Cuba, Iraq, and Romania in 2020.

A second challenge was the misunderstanding of sequencing capabilities within DoD line, medical, and public health organizations. Officials from these institutions are often too heavily burdened with frontline activities (e.g., patient care, contact tracing) to engage in what might be perceived as research. Education about the importance of DoD sequencing capabilities and genomic surveillance in the context of public health is important and can facilitate earlier access to samples and associated epidemiologic data.

Several SARS-CoV-2 VOCs have emerged in 2021 that exhibited enhanced transmission, increased severity, reduced antiviral or immunotherapy efficacy, or evasion of molecular detection assays.[15] The capabilities established through this collaborative DoD effort will continue to provide critical information about SARS-CoV-2 transmission patterns and help monitor medical countermeasure effectiveness for 1.4 million active component and 331,000 reserve personnel and other beneficiaries of the MHS (e.g., family members, retirees, etc.). Sequence data are also relevant for understanding transmission patterns within the DoD since military personnel are highly mobile, share close-quarter accommodations during deployments, and operate globally. In an outbreak setting, sequence data can help determine if cases may result from infections acquired from local transmission while deployed or reflect transmission chains initiated prior to deployment.

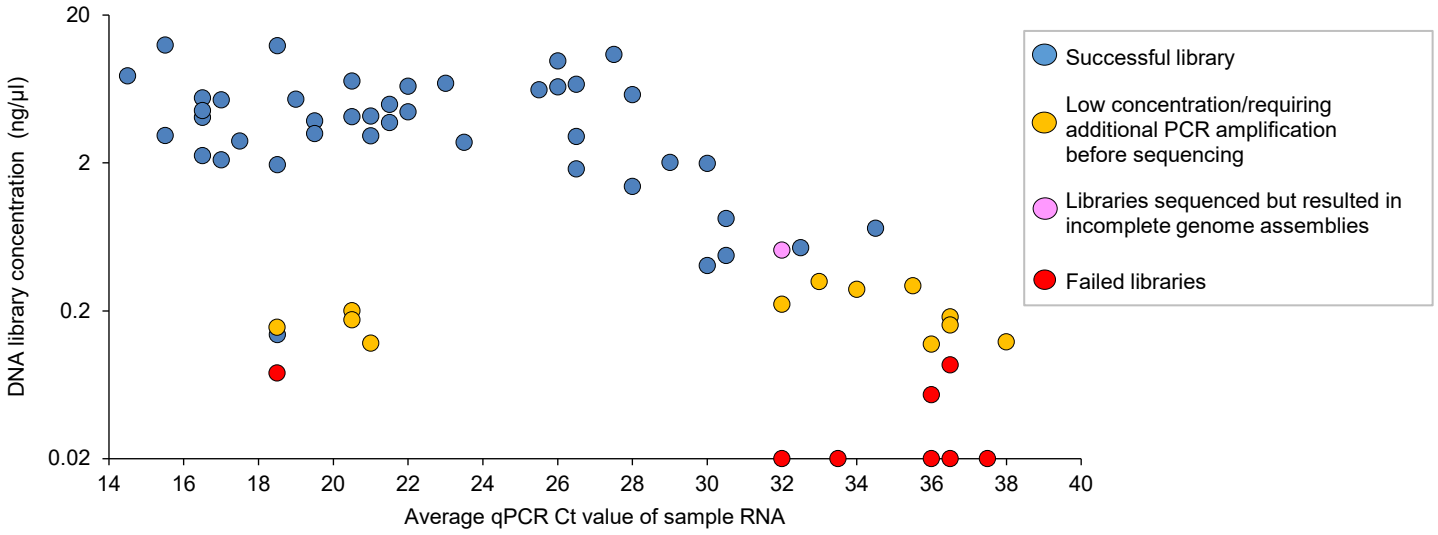
In early 2020, lack of sustained funding, limitations in public health laboratory and bioinformatics infrastructure, including limited trained personnel and lack of validated protocols, impeded rapid deployment of sequencing and bioinformatics analysis for global COVID-19 response and within the civilian sector in the U.S.[434] The percentage of COVID-19 cases sequenced was also far lower than several European countries with long-standing investments in genomic surveillance for infectious diseases of public health concern.[35, 36] Fortunately, in the years before 2020, the GEIS

TABLE 2. Distribution of SARS-CoV-2 lineages among Military Health System samples (n=1,366) collected, 1 March–31 December 2020

Lineage	Clade (no.)	WHO label	First detected in DoD	Last detected in DoD in 2020	Country (no.)	No.	%
B.1.427[a]	20C	Epsilon	Dec	Dec	U.S	2	0.2
B.1.429[a]	20C	Epsilon	Dec	Dec	U.S. (5), ship/multi (1)	6	0.4
B.1.2	20G (216), 20A (1), 20C (2)		Jul	Dec	U.S. (224), South Korea (2), ship/multi (2)	228	16.7
B.1	20C (101), 20A (68), 19A (11), 20B (7), 20G (2), 19B (1)		Mar	Dec	U.S. (174), Germany (10), England (4), Guam (1), South Korea (1), ship/multi (3)	193	14.1
B.1.1	20B (99), 20C (2), 20A (1)		Mar	Dec	U.S. (50), Guam (33), Germany (1), England (1), ship/multi (19)	104	7.6
B.1.451	20C		May	Sept	U.S.	44	3.2
B.1.240	20A		Jul	Dec	U.S.	37	2.7
B.1.243	20A		Jul	Dec	U.S. (15), Guam (13), ship/multi (1)	29	2.1
B.1.428.1	20C		Jun	Jun	Iraq	28	2.1
B.1.588.1	20C		Nov	Nov	Romania	26	1.9
B.1.596	20G		Jul	Dec	U.S.	22	1.6
B.1.369	20C		May	Dec	U.S.	19	1.4
B.1.234	20A		Aug	Dec	U.S. (16), Germany (1), South Korea (1)	18	1.3
B.1.595	20C		Mar	Dec	U.S.	16	1.2
B.1.177	20C		Apr	May	Ship/multi	15	1.1
Other[b]	Multiple clades		--	--	Multiple locations	333	24.4
None[c]	Multiple clades		--	--	Multiple locations	246	18.0

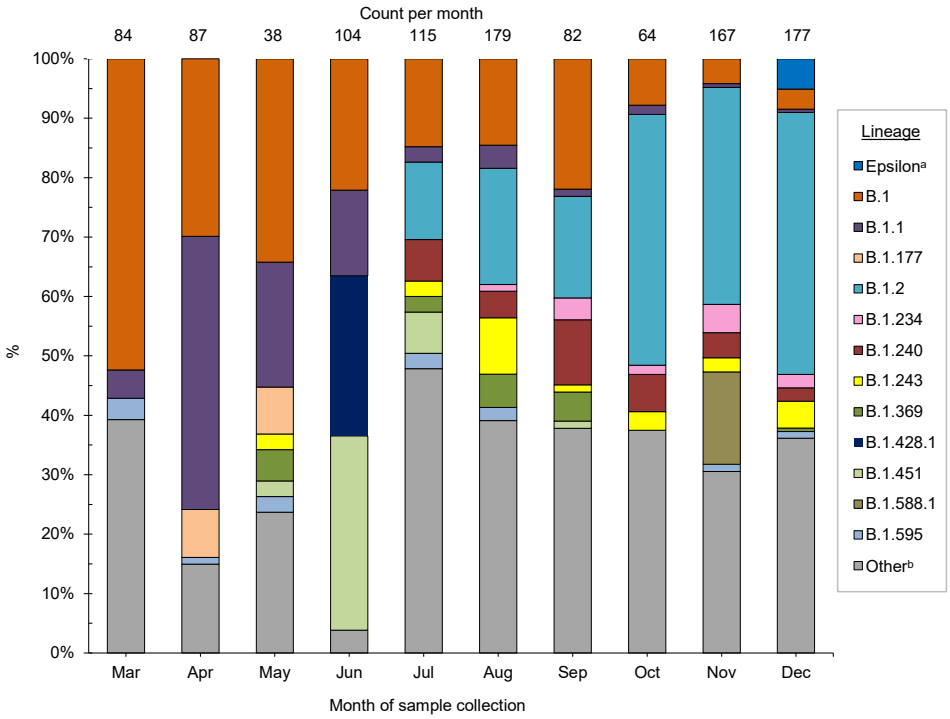
[a]Epsilon was elevated to its highest level, a variant of concern (VOC), on 19 March 2021. It was later downgraded to a variant of interest (VOI) on 29 June 2021 and then reclassified as a Variant Being Monitored (VBM) on 21 September 2021 by CDC/USG Interagency.
[b]Lineage <1% of overall samples and was not classified as a VOC, VOI, or identified as a lineage to monitor by WHO or CDC.
[c]Lineage assignment could not be made due to insufficient coverage or lineage was missing.
Lineage, Pango lineage; Clade, Nextstrain clade; No., number; DoD, Department of Defense; CDC, Centers for Disease Control and Prevention; USG, U.S. Government; WHO, World Health Organization; ship/multi, Naval ship/multiple locations including recruit training installations.

FIGURE 3. Correlation between the average SARS-CoV-2 RNA concentration in samples (n=63) with the end library DNA concentration and the sequencing success rate



qPCR, quantitative polymerase chain reaction; Ct, cycle threshold.

FIGURE 4. Distribution of SARS-CoV-2 lineages from Military Health System samples (n = 1,159) by sample collection month, 1 March–31 December, 2020



[a]Epsilon variant infections include both the B.1.427 and B.1.429 lineages.
[b]Low frequency lineages comprising less than 1% of all samples are denoted by "Other."

NGSBC recognized the need to coordinate and standardize prior investments by DoD in infectious disease surveillance and genomic sequencing which allowed for early contributions to DoD and the interagency response during the COVID-19 pandemic. Findings from this collaborative effort illustrate the importance of leveraging existing DoD sequencing assets and surveillance networks to rapidly respond to the COVID-19 pandemic and establish a robust global capacity to monitor SARS-CoV-2 evolution in support of DoD activities. DoD should prioritize expanding genomic surveillance systems and capabilities for future pandemic preparedness.

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REFERENCES

1. Malone JD. USS Theodore Roosevelt, COVID-19, and Ships: Lessons Learned. *JAMA Netw Open.* 2020;3(10):e2022095.
2. Payne DC, Smith-Jeffcoat SE, Nowak G, et al. SARS-CoV-2 Infections and Serologic Responses from a Sample of U.S. Navy Service Members - USS Theodore Roosevelt, April 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(23):714–721.
3. Chapleau RR, Christian M, Connors B, et al. Early Identification of SARS-CoV-2 Emergence in the Department of Defense via Retrospective Analysis of 2019-2020 Upper Respiratory Illness Samples. *MSMR.* 2021;28(6):2–5.
4. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol.* 2021;19(3):141–154.
5. Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. *Nature.* 2020;579(7798):265–269.
6. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med.* 2020;382(8):727–733.
7. Virological.org. Holmes EC. Novel 2019 coronavirus genome--SARS-CoV-2 coronavirus. 10 January 2020. Accessed 3 January 2022. https://virological.org/t/novel-2019-coronavirus-genome/319

8. Worobey M, Pekar J, Larsen BB, et al. The emergence of SARS-CoV-2 in Europe and North America. *Science.* 2020;370(6516):564-570.
9. MacCannell T, Batson J, Bonin B, et al. Genomic epidemiology and transmission dynamics of SARS-CoV-2 in congregate healthcare facilities in Santa Clara County, California. *Clin Infect Dis.* 2021.
10. Sekizuka T, Itokawa K, Kageyama T, et al. Haplotype networks of SARS-CoV-2 infections in the Diamond Princess cruise ship outbreak. *Proc Natl Acad Sci U S A.* 2020;117(33):20198–20201.
11. Letizia AG, Ramos I, Obla A, et al. SARS-CoV-2 Transmission among Marine Recruits during Quarantine. *N Engl J Med.* 2020;383(25):2407–2416.
12. Ballesteros N, Castaneda S, Munoz M, et al. Cluster characterization of SARS-CoV-2 in military personnel deployed to Egypt and subsequent introduction of B.1.1.7 and C.36 lineages to Colombia. *J Travel Med.* 2021;28(7):taab131.
13. Harvey WT, Carabelli AM, Jackson B, et al. SARS-CoV-2 variants, spike mutations and immune escape. *Nat Rev Microbiol.* 2021;19(7):409–424.
14. Lauring AS, Hodcroft EB. Genetic Variants of SARS-CoV-2-What Do They Mean? *JAMA.* 2021;325(6):529–531.
15. Lauring AS, Malani PN. Variants of SARS-CoV-2. *JAMA.* 2021;jama.2021.14181.
16. DoD Establishes Collaborative Virus Genetic Sequencing Capability for COVID-19. 2020.
17. CDC. Interim Guidelines for Collecting and Handling of Clinical Specimens for COVID-19 Testing.
18. Quick J. nCoV-2019 sequencing protocol v3. (LoCost) V.3; 25 August 2020. Accessed 3 January 2022. https://www.protocols.io/view/ncov-2019-sequencing-protocol-v3-locost-bh42j8ye
19. Larson D, Brodniak SL, Voegtly LJ, et al. A Case of Early Reinfection With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). *Clin Infect Dis.* 2021;73(9):e2827–e2828.
20. Bolger AM, Lohse M, Usadel B. Trimmomatic: a flexible trimmer for Illumina sequence data. *Bioinformatics.* 2014;30(15):2114–2120.
21. Smith DR, Singh C, Green J, et al. Genomic and Virological Characterization of SARS-CoV-2 Variants in a Subset of Unvaccinated and Vaccinated U.S. Military Personnel. *Front Med (Lausanne).* 2021;8:836658.
22. Bushnell B. BBMAP: A Fast, Accurate, Splice-Aware Aligner. Poster presented at: 9th Annual Genomics of Energy & Environment Meeting; 17–20 March 2014; Walnut Creek, CA.
23. Grubaugh ND, Gangavarapu K, Quick J, et al. An amplicon-based sequencing framework for accurately measuring intrahost virus diversity using PrimalSeq and iVar. *Genome Biol.* 2019;20(1):8.
24. Rambaut A, Holmes EC, O'Toole A, et al. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. *Nat Microbiol.* 2020;5(11):1403–1407.
25. Rambaut A, Holmes EC, O'Toole A, et al. Addendum: A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. *Nat Microbiol.* 2021;6(3):415.
26. I. A, C. R, E.B. H, R.A. N. Nextclade: clade assignment, mutation calling and quality control for viral genom. *Journal of Open Source Software.* 2021;6(65):3773.
27. Hadfield J, Megill C, Bell SM, et al. Nextstrain: real-time tracking of pathogen evolution. *Bioinformatics.* 2018;34(23):4121–4123.
28. Brown KA, Gubbay J, Hopkins J, et al. S-Gene Target Failure as a Marker of Variant B.1.1.7 Among SARS-CoV-2 Isolates in the Greater Toronto Area, December 2020 to March 2021. *JAMA.* 2021;325(20):2115–2116.
29. Motozono C, Toyoda M, Zahradnik J, et al. SARS-CoV-2 spike L452R variant evades cellular immunity and increases infectivity. *Cell Host Microbe.* 2021;29(7):1124–1136.
30. Black A, MacCannell DR, Sibley TR, Bedford T. Ten recommendations for supporting open pathogen genomic analysis in public health. *Nat Med.* 2020;26(6):832-841.
31. Galloway SE, Paul P, MacCannell DR, et al. Emergence of SARS-CoV-2 B.1.1.7 Lineage - United States, December 29, 2020-January 12, 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(3):95–99.
32. Chen Z, Azman AS, Chen X, et al. Global landscape of SARS-CoV-2 genomic surveillance and data sharing. *Nat Genet.* 2022;54(4):499–507.
33. Villabona-Arenas CJ, Hanage WP, Tully DC. Phylogenetic interpretation during outbreaks requires caution. *Nat Microbiol.* 2020;5(7):876–877.
34. National Academies of Sciences, Engineering, and Medicine; Division on Earth and Life Studies; Board on Life Sciences; Health and Medicine Division; Board on Health Sciences Policy; Committee on Data Needs to Monitor the Evolution of SARS-CoV-2. In: Genomic Epidemiology Data Infrastructure Needs for SARS-CoV-2: Modernizing Pandemic Response Strategies. Washington,DC: National Academies Press; 2020:chap 5.
35. ECDC. ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations, 2019–2021. Stockholm: ECDC; 2019.
36. Furuse Y. Genomic sequencing effort for SARS-CoV-2 by country during the pandemic. *Int J Infect Dis.* 2021;103:305–307.

Suicide Behavior Among Heterosexual, Lesbian/Gay, and Bisexual Active Component Service Members in the U.S. Armed Forces

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Lesbian, gay, and bisexual (LGB) individuals are at a particularly high risk for suicidal behavior in the general population of the United States. This study aims to determine if there are differences in the frequency of lifetime suicide ideation and suicide attempts between heterosexual, lesbian/gay, and bisexual service members in the active component of the U.S. Armed Forces. Self-reported data from the 2015 Department of Defense Health-Related Behaviors Survey were used in the analysis. Multivariable logistic regression demonstrated that lesbian/gay and bisexual service members were more likely to report past suicide ideation when compared to heterosexual service members (adjusted odds ratio [AOR] for lesbian/gay: 1.79; 95% CI: 1.14-2.82; AOR for bisexual: 2.33; 95% CI: 1.56-3.49). Similar results were observed for past suicide attempt for lesbian/gay (AOR: 2.29; 95% CI: 1.15-4.57) and bisexual SMs (AOR: 2.04; 95% CI: 1.24-3.38). Despite disparities in suicide ideation and attempt by sexual orientation, a majority of service members' behavioral health questionnaires do not assess sexual orientation. Clinical screenings of suicide risk in military settings should factor in sexual orientation to more comprehensively assess association between sexual orientation and suicidal behavior in this population.

WHAT ARE THE NEW FINDINGS?

This study found that lesbian/gay and bisexual service members had a 1.8 and 2.3-fold higher odds, respectively, of suicide ideation compared to heterosexual SMs. Furthermore, lesbian/gay and bisexual SMs had a 2.3 and 2.0-fold higher odds, respectively, of suicide attempt compared to heterosexual SMs.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Increased odds of suicide ideation and attempt among gay, lesbian, and bisexual service members indicate important disparities in mental health which may be associated with decreased readiness. Information about sexual orientation should be collected more routinely in order to determine if there are other mental and physical health disparities within this population.

The age-adjusted suicide rate in the U.S. increased 24% between 1999 and 2014.[1] Suicide is now the tenth leading cause of death in the US, with 47,173 cases reported in 2017.[2] Although suicide has steadily increased among the US general population, particular demographic groups are at a higher risk for suicidal ideation, attempt, and death by suicide.[3]

Lesbian, gay, and bisexual (LGB) populations suffer a disproportionate risk of suicidal behavior when compared to the US general population.[4,5] In a study of 123,289 suicide decedents reported to the US National Violent Death Reporting System, Lyons et al. reported that gay male decedents were more likely than non-gay male decedents to have had a documented mental health problem, depression at the time of death, recent treatment for mental health or substance abuse problems, a history of suicidal thoughts or plans, and/or relationship problems.[6] Similar risk factors were observed when comparing lesbian decedents and non-lesbian decedents.[6] In a study using data from the 2015–2016 Canadian Community Health Survey, LGB respondents were more likely to report suicide ideation across the lifespan.[7] A 2008 systematic review and meta-analysis of the prevalence of mental health disorders, substance misuse, suicide ideation, and suicide attempt reported that LGB individuals had an approximately 2.5-fold higher risk of lifetime suicide attempt when compared to heterosexual populations.[8] Numerous other studies among LGB youth and young adults have revealed similar disparities.[9-13]

Within LGB populations, those in certain occupations may be at an even higher risk of suicidal behavior. In 1994, the "Don't Ask, Don't Tell" policy was implemented which allowed LGB persons to serve in the military but prohibited LGB service members (SMs) from disclosing their sexuality. The "Don't Ask, Don't Tell" policy was removed in 2011, but the effects of the policy had negative mental health ramifications for LGB SMs, including suicide ideation and attempt.[14-16]

Adverse mental health outcomes are also reflected in LGB veteran populations. Analysis of the 2005–2010 Massachusetts Behavioral Risk Factor Surveillance Survey found that 11.5% of LGB veterans reported suicidal ideation in the past year, compared with only 3.5% of heterosexual veterans.[17]

Among veterans presenting for military sexual trauma (MST) consultation and treatment, Sexton and colleagues reported that 54% of LGB veterans reported a history of suicide attempt, compared with only 28% of non-LGB veterans.[18] A study using Veterans Health Administration electronic health records reported that suicide was the fifth leading cause of death for LGB veterans from October 2000 to September 2017, but only the tenth leading cause of death in the general population during this time frame.[19]

Despite evidence of elevated risk of suicide ideation and attempt among LGB veterans, there is a paucity of other studies examining suicidal behavior among active component military LGB populations.[20] At the time of this analysis, only 1 study had compared LGB service members' suicide behavior to that of heterosexual service members. While this study found an increased odds of suicide attempt among LGB SMs, the study did not analyze suicide ideation or control for demographic variables beyond age group.[21] As Matarazzo et al. opined, "Being a member of the US military, as well as identifying as [LGB], could potentially constitute a double-edged risk for suicide." Research on each of the aforementioned predisposing factors for suicidal behavior is essential to maintain military readiness.

The primary objective of this study was to use data from the 2015 Department of Defense (DoD) Health Related Behaviors Survey (HRBS) to determine if there are differences in the likelihood of past suicide ideation and attempts between active component heterosexual, gay or lesbian, and bisexual SMs, controlling for demographic variables.

METHODS

Study background

The HRBS is a DoD survey used to understand the health and well-being of service members across all 5 branches of military service.[22] The Defense Health Agency contracted with RAND Corporation to develop and administer the 2015 HRBS. Potential participants were eligible for the survey if they were: 1) active component U.S. military service members; 2) serving in the Air Force, Army, Marine Corps, Navy, or Coast Guard; 3) not deployed as of August 31, 2015, and 4) not enrolled as cadets in service academies, senior military colleges, or Reserve Officers' Training Corps programs.[22] Members of the National Guard and Reserve were excluded from the list of potential participants. Potential participants were stratified by service branch, pay grade, and birth sex; service members were randomly sampled from within each stratum. Invited participants were solicited via letter with follow-up postcard and email reminders and were provided with a universal resource locator (URL) to complete the survey. All survey responses were anonymous.

The outcomes for this analysis were lifetime suicide ideation and lifetime suicide attempt. Suicide ideation was measured using respondents' answers to the following question, "In your lifetime, did you ever seriously think about trying to kill yourself?" Suicide attempt was measured using respondents' answers to the following question: "In your lifetime, have you ever tried to kill yourself?"

Demographic predictors included birth sex, sexual orientation, age group, marital status, educational attainment, and racial/ethnic minority. Sexual orientation was measured with the following question, "Do you consider yourself to be…? Select one response" with three options: Heterosexual or straight; Gay or lesbian; Bisexual. Unlike other demographics questions, sexual orientation was placed near the end of the survey.

Statistical analyses

The HRBS oversamples service members in certain strata to produce estimates representative of the active component population. The oversampling is accounted for in post-stratification weights. Weighted frequencies with 95% confidence intervals were computed using these post-stratification weights.[22] Two multivariable logistic regression models were built to assess the association between lifetime suicide ideation and lifetime suicide attempt with selected demographics and sexual orientation disaggregated (lesbian/gay, bisexual, and heterosexual). Two additional multivariable logistic regression models were built to determine the effects of aggregating the last 2 categories of the sexual orientation variable (lesbian/gay and bisexual) on the suicide ideation and attempt outcomes. Only demographic variables were included in this analysis, since assessment of additional behavioral risk factors would introduce temporal ambiguity with respect to whether or not the risk factors preceded or followed lifetime suicidal behavior outcomes. Neither forward selection nor backward elimination were utilized. All analyses were completed using SAS software (i.e., PROC SURVEYFREQ for frequencies and PROC SURVEYLOGISTIC for multivariable models), version 9.4 (2014, SAS Institute, Cary, NC).

RESULTS

From a total of 195,220 eligible and contactable active component service members, a total of 16,699 usable surveys were obtained (8.6% overall response rate). There were 16,699 total respondents to the 2015 HRBS survey. Of the 13,871 respondents who answered the question on sexual orientation, 94.2% identified as heterosexual, 2.7% identified as gay or lesbian, and 3.1% identified as bisexual **(Table 1)**. In addition, a majority of respondents were between 25 and 44 years of age (64.4%), married (57.3%), had some college education or more (79.5%), and were not a racial or ethnic minority (58.3%).

Results of bivariate analyses indicated that 29.7% of lesbian/gay respondents and 35.4% of bisexual respondents reported that they had ever seriously thought about killing themselves, compared to 17.2% of heterosexual respondents **(Table 2)**. Among lesbian/gay respondents, 12.9% responded "yes" to the question, "In your lifetime, have you ever tried to kill yourself?" (hereafter referred to as suicide attempt), compared to 12.2% of bisexual respondents and 4.7% of heterosexual respondents.

Lesbian/gay and bisexual service members were more likely to report

lifetime suicide ideation compared to heterosexual service members (adjusted odds ratio [AOR]=1.79; 95% CI: 1.14–2.82 and AOR=2.33; 95% CI: 1.56–3.49, respectively) **(Table 3)**. In addition, compared to their respective counterparts, female service members, and those who were not a racial/ethnic minority (White) were more likely to report lifetime suicide ideation.

Similar results were observed for past suicide attempt for lesbian/gay service members and bisexual service members compared to heterosexual service members (AOR=2.29; 95% CI: 1.15–4.57 and AOR=2.04; 95% CI: 1.24–3.38, respectively) **(Table 4)**. In addition, compared to their respective counterparts, female service members and those who were not married were more likely to report lifetime suicide attempt.

The last 2 models used the aggregated version of the sexual orientation variable with gay, lesbian, and bisexual SMs collapsed into 1 category. The same patterns held for both lifetime suicide ideation and lifetime suicide attempt. The aggregated groups of lesbian, gay or bisexual service members were more likely to report lifetime suicide ideation and lifetime suicide attempt compared to heterosexual service members (adjusted odds ratio [AOR]=2.07; 95% CI: 1.51-2.83 and AOR=2.16; 95% CI: 1.38–3.38, respectively) **(data not shown)**.

TABLE 1. Weighted demographics and past suicide behavior of respondents to the Department of Defense Health-Related Behaviors Survey, 2015 (n=16,699)

	No.	%	95% CI
Sex			
Male	14,099	84.4	(83.7–85.1)
Female	2,600	15.6	(14.9–16.3)
Sexual orientation[a] (n=13,871)			
Heterosexual or straight	13,068	94.2	(93.4–95)
Gay or lesbian	373	2.7	(2.2–3.2)
Bisexual	430	3.1	(2.5–3.7)
Age group (years)			
17–24	4,795	28.7	(27.1–30.4)
25–34	6,991	41.9	(40.3–43.5)
35–44	3,759	22.5	(21.4–23.7)
45+	1,141	6.8	(6.3–7.4)
Racial/ethnic minority			
Not a racial/ethnic minority	9,740	58.3	(56.8–60.0)
Racial/ethnic minority	6,936	41.5	(40.0–43.2)
Highest level of education			
High school or less	3,413	20.4	(19.0–21.9)
Some college/associate degree	8,104	48.5	(46.9–50.2)
Bachelor's or above	5,181	31.0	(29.7–32.4)
Marital status			
Married	9,565	57.3	(55.7–58.9)
Not married	7,129	42.7	(41.1–44.3)
Ever seriously thought about killing oneself			
No	11,641	81.9	(80.6–83.3)
Yes	2,570	18.1	(16.7–19.4)
Seriously thought about killing oneself (past 12 months)			
No	1,672	65.2	(61.0–69.4)
Yes	892	34.8	(30.6–39.0)
Ever tried to kill oneself			
No	13,473	94.9	(94.1–95.7)
Yes	724	5.1	(4.3–5.9)
Tried to kill oneself (past 12 months)			
No	527	72.8	(65.0–80.6)
Yes	197	27.2	(19.4–35.0)

[a]The sexual orientation question had a higher proportion of missing responses compared to the other demographic variables due to survey placement (question 127 out of 133 questions).
No., number; CI, confidence interval.

EDITORIAL COMMENT

The present study found that LGB service members (SMs) had a higher odds of reporting both lifetime suicide ideation and attempt compared to heterosexual SMs. In addition, all models resulted in weighted estimates indicating elevated risk for suicide behavior among female SMs. These suicide behavior trends in an active-component sample largely mirror the disparities reported in civilian samples.[13]

This study has several limitations. First, although the 2015 HRBS employed a random, stratified sampling design, the response rate was 8.6%.[22] Therefore, it is unclear how generalizable these findings are to the entire active component population. However, the overall findings in the 2015 HRBS are similar to the findings in the 2011 HRBS, which had a response rate of 22%.[23] Second, 13.7% of respondents had missing data for the sexual orientation question. This degree of item-level missing data (i.e., missingness) may be due to the placement of the sexual orientation question at the end of the survey (question 127 of 133 questions). To determine if the level of missingness on this item was likely due to not reaching the question (survey fatigue) or purposefully omitting a response (social desirability bias), the proportion of missing data on the sexual orientation item was compared to the missingness on a sleep measure which appeared even later in the survey (question 129). The sleep and sexual orientation questions had a similar proportion of missing responses (14% for sexual orientation vs. 14% for sleep), and only 13 respondents answered the sleep question without answering the sexual orientation question. Therefore, it was concluded that missingness on the sexual orientation item was likely due to survey

TABLE 2. Weighted demographic and past suicide behavior differences by sexual orientation with Rao-Scott chi-square differences, Department of Defense Health-Related Behaviors Survey, 2015 (n=14,405)

	Heterosexual (94.2%)		Gay/lesbian (2.7%)		Bisexual (3.1%)	
	Weighted %	95% CI	Weighted %	95% CI	Weighted %	95% CI
Sex						p<.001
Male	86.4	(85.7–87.1)	60.4	(51.8–69.0)	55.1	(46.6–63.7)
Female	13.6	(12.9–14.3)	39.6	(31.0–48.2)	44.9	(36.3–53.4)
Age group (years)						p<.001
17–24	27.0	(25.2–28.8)	36.5	(26.3–46.8)	49.4	(40.1–58.7)
25–34	41.6	(39.8–43.4)	48.2	(38.1–58.2)	39.3	(30.6–48.0)
35–44	23.9	(22.5–25.2)	11.6	(6.4–16.9)	8.7	(5.7–11.6)
45+	7.5	(6.9–8.2)	3.7	(2.0–5.4)	2.7	(1.1–4.2)
Racial/ethnic minority						p=.144
Not a racial/ethnic minority	60.1	(58.3–62.0)	59.4	(49.7–69.0)	50.9	(41.6–60.2)
Racial/ethnic minority	39.9	(38.0–41.7)	40.6	(31.0–50.3)	49.1	(39.8–58.4)
Highest level of education						p<.001
High school or less	19.5	(17.9–21.2)	12.6	(5.8–19.3)	29.2	(19.3–39.0)
Some college/associate degree	47.2	(45.4–49.1)	62.2	(52.9–71.5)	52.8	(43.5–62.2)
Bachelor's degree or above	33.2	(31.7–34.8)	25.2	(17.6–32.9)	18.0	(11.6–24.4)
Marital status						p<.001
Married	60.0	(58.1–61.8)	27.7	(19.2–36.1)	35.7	(27.8–43.6)
Not married	40.0	(38.2–41.9)	72.3	(63.9–80.8)	64.3	(56.4–72.2)
Ever seriously thought about killing oneself						p<.001
No	82.8	(81.4–84.2)	70.3	(61.3–79.3)	64.6	(56.0–73.2)
Yes	17.2	(15.8–18.6)	29.7	(20.7–38.7)	35.4	(26.8–44.0)
Seriously thought about killing oneself (past 12 months)						p=.137
No	66.1	(61.6–70.6)	55.1	(37.1–73.0)	53.5	(38.6–68.3)
Yes	33.9	(29.4–38.4)	44.9	(27.0–62.9)	46.5	(31.7–61.4)
Ever tried to kill oneself						p<.001
No	95.3	(94.5–96.2)	87.1	(79.8–94.4)	87.8	(83.0–92.7)
Yes	4.7	(3.8–5.5)	12.9	(5.6–20.2)	12.2	(7.3–17.0)
Tried to kill oneself (past 12 months)						p=.797
No	73.3	(64.7–82.0)	64.6	(35.3–94.0)	70.3	(48.6–92.0)
Yes	26.7	(18.0–35.3)	35.4	(6.0–64.7)	29.7	(8.0–51.4)

CI, confidence interval.

fatigue as opposed to social desirability bias. Third, suicidal behavior is often stigmatized and may be underreported by respondents due to fears about disclosure to commanders and subsequent career consequences. However, the HRBS was self-administered online and all responses were anonymous. These safeguards may have reduced the impact of social desirability bias. Lastly, the population in the present study may not be directly comparable to convenience samples of veteran populations. Comparisons between active component and veteran populations were made due to a relative lack of current literature regarding sexual orientation and suicide behaviors among active component populations.

LGB populations experience a disparate rate of suicide behavior when compared to heterosexual populations in both military and civilian settings; however, the magnitude of the disparity is unclear due to incomplete data reporting. Healthy People 2020 is the U.S. Federal Government's effort to identify and address the most significant threats to the public's health. For LGB individuals, Healthy People 2020 seeks to address systematic underreporting of sexual orientation data in an attempt to "increase the number of population-based data systems... that include in their core a standardized set of questions that identify lesbian, gay, bisexual, and transgender populations."[24]

At the time of this study, a waiver is needed to ask questions on sexual

orientation in the military.[25] This requirement has resulted in a small number of studies that included survey questions that ask about sexual orientation. Although disparities in suicide behavior exist by sexual orientation, the lack of systematic data collection on sexual orientation means that the full extent of the disparities is not evident. The lack of data on sexual orientation in military settings is further compounded by the concern that reporting behaviors associated with suicidal behavior could jeopardize a service member's career, resulting in a substantial reporting bias.[26]

Despite these difficulties, military clinical assessments of suicidal behavior should include collecting information on sexual orientation to more comprehensively assess its association with suicidal behavior. Furthermore, SMs should be encouraged to report their true mental health symptoms without fear of reprisal or career consequences. By more comprehensively assessing SM demographics and decreasing mental health stigma, military commanders and military healthcare providers will be able to more accurately assess SMs who are at risk for suicidal behavior, ensuring the health of their installation and maximizing the readiness of the Force.

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TABLE 3. Multivariable logistic regression of demographics on lifetime suicidal ideation among respondents to the Department of Defense Health Related Behaviors Survey, 2015 (n=14,366)

	Estimate	SE	p value	AOR	95% CI
Sex					
Male	ref	—	—	—	—
Female	0.31	0.08	<.001	1.37	(1.16–1.61)
Sexual orientation					p<.001
Heterosexual or straight	ref	—	—	—	—
Gay or lesbian	0.58	0.23	.012	1.79	(1.14–2.82)
Bisexual	0.85	0.20	<.001	2.33	(1.56–3.49)
Age group (years)					p=.045
17–24	0.14	0.19	.473	1.15	(0.79–1.69)
25–34	0.04	0.15	.803	1.04	(0.77–1.40)
35–44	0.32	0.15	.034	1.37	(1.02–1.84)
45+	ref	—	—	—	—
Racial/ethnic minority					
Not a racial/ethnic minority	ref	—	—	—	—
Racial/ethnic minority	-0.36	0.10	<.001	0.70	(0.58–0.85)
Highest level of education					p=.119
High school or less	0.24	0.16	.142	1.27	(0.92–1.75)
Some college/associate degree	0.20	0.10	.054	1.22	(1.00–1.50)
Bachelor's degree or above	ref	—	—	—	—
Marital status					
Married	ref	—	—	—	—
Not married	0.21	0.11	.053	1.24	(1.00–1.54)

Ref, reference group; SE, standard error; AOR, adjusted odds ratio; CI, confidence interval.

TABLE 4. Multivariable logistic regression of demographics on lifetime suicide attempt among respondents to the Department of Defense Health Related Behaviors Survey, 2015 (n=14,366)

	Estimate	SE	p value	AOR	95% CI
Sex					
Male	ref	—	—	—	—
Female	0.49	0.16	.002	1.63	(1.21–2.21)
Sexual orientation					p=.003
Heterosexual or straight	ref	—	—	—	—
Gay or lesbian	0.83	0.35	.019	2.29	(1.15–4.57)
Bisexual	0.72	0.26	.005	2.04	(1.24–3.38)
Age group (years)					p=.636
17–24	0.33	0.36	.360	1.39	(0.69–2.78)
25–34	0.18	0.33	.575	1.20	(0.63–2.27)
35–44	0.36	0.32	.261	1.43	(0.77–2.66)
45+	ref	—	—	—	—
Racial/ethnic minority					
Not a racial/ethnic minority	ref	—	—	—	—
Racial/ethnic minority	0.06	0.18	.739	1.06	(0.75–1.50)
Highest level of education					p=.342
High school or less	0.34	0.32	.292	1.40	(0.75–2.64)
Some college/associate degree	0.33	0.23	.147	1.39	(0.89–2.16)
Bachelor's degree or above	ref	—	—	—	—
Marital status					
Married	ref	—	—	—	—
Not married	0.44	0.21	.037	1.55	(1.03–2.33)

Ref, reference group; SE, standard error; OR, odds ratio; CI, confidence interval.

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REFERENCES

1. National Center for Health Statistics. Increase in Suicide in the United States, 1999–2014. 2016; Accessed 28 March 2022. https://www.cdc.gov/nchs/products/databriefs/db241.htm
2. Heron M. *Deaths: Leading causes for 2017.* Hyattsville, MD: National Center for Health Statistics;2019.
3. Stone DM, Simon TR, Fowler KA, et al. Vital Signs: Trends in State Suicide Rates - United States, 1999-2016 and Circumstances Contributing to Suicide - 27 States, 2015. *MMWR Morb Mortal Wkly Rep.* 2018;67(22):617–624.
4. Haas AP, Eliason M, Mays VM, et al. Suicide and suicide risk in lesbian, gay, bisexual, and transgender populations: review and recommendations. *J Homosex.* 2011;58(1):10–51.
5. Tucker RP. Suicide in Transgender Veterans: Prevalence, Prevention, and Implications of Current Policy. *Perspect Psychol Sci.* 2019;14(3):452–468.
6. Lyons BH, Walters ML, Jack SPD, Petrosky E, Blair JM, Ivey-Stephenson AZ. Suicides Among Lesbian and Gay Male Individuals: Findings From the National Violent Death Reporting System. *Am J Prev Med.* 2019;56(4):512–521.
7. Stinchcombe A, Hammond NG. Sexual orientation as a social determinant of suicidal ideation: A study of the adult life span. *Suicide Life Threat Behav.* 2021;51(5):864–871.
8. King M, Semlyen J, Tai SS, et al. A systematic review of mental disorder, suicide, and deliberate self harm in lesbian, gay and bisexual people. *BMC Psychiatry.* 2008;18(8):70.
9. Mustanski BS, Garofalo R, Emerson EM. Mental health disorders, psychological distress, and suicidality in a diverse sample of lesbian, gay, bisexual, and transgender youths. *Am J Public Health.* 2010;100(12):2426–2432.
10. Liu RT, Mustanski B. Suicidal ideation and self-harm in lesbian, gay, bisexual, and transgender youth. *Am J Prev Med.* 2012;42(3):221–228.
11. Mustanski B, Liu RT. A longitudinal study of predictors of suicide attempts among lesbian, gay, bisexual, and transgender youth. *Arch Sex Behav.* 2013;42(3):437–448.
12. Ream GL. What's Unique About Lesbian, Gay, Bisexual, and Transgender (LGBT) Youth and Young Adult Suicides? Findings From the National Violent Death Reporting System. *J Adolesc Health.* 2019;64(5):602–607.
13. Liu RT, Walsh RFL, Sheehan AE, Cheek SM, Carter SM. Suicidal Ideation and Behavior Among Sexual Minority and Heterosexual Youth: 1995-2017. *Pediatrics.* 2020;145(3):e20192221.
14. Barber ME. Mental health effects of don't ask don't tell. *J Gay Lesbian Ment Health.* 2012;16(4):346–352.
15. Bodon N. An Iraq Veteran's Story. *Journal of Gay & Lesbian Mental Health.* 2012;16(4):334–337.
16. Cianni V. Gays in the Military: How America Thanked Me. *J Gay Lesbian Ment Health.* 2012;16(4):322–333.
17. Blosnich JR, Bossarte RM, Silenzio VM. Suicidal ideation among sexual minority veterans: results from the 2005-2010 Massachusetts Behavioral Risk Factor Surveillance Survey. *Am J Public Health.* 2012;102 Suppl 1:S44–47.
18. Sexton MB, Davis MT, Anderson RE, Bennett DC, Sparapani E, Porter KE. Relation between sexual and gender minority status and suicide attempts among veterans seeking treatment for military sexual trauma. *Psychol Serv.* 2018;15(3):357–362.
19. Lynch KE, Gatsby E, Viernes B, et al. Evaluation of Suicide Mortality Among Sexual Minority US Veterans From 2000 to 2017. *JAMA Netw Open.* 2020;3(12):e2031357.
20. Matarazzo BB, Barnes SM, Pease JL, et al. Suicide risk among lesbian, gay, bisexual, and transgender military personnel and veterans: what does the literature tell us? *Suicide Life Threat Behav.* 2014;44(2):200–217.
21. Jeffery DD, Beymer MR, Mattiko MJ, Shell D. Health Behavior Differences Between Male and Female U.S. Military Personnel by Sexual Orientation: The Importance of Disaggregating Lesbian, Gay, and Bisexual Groups. *Mil Med.* 2021;186(5-6):556–564.
22. Meadows SO, Engel CC, Collins RL, et al. 2015 Department of Defense Health Related Behaviors Survey (HRBS). *Rand Health Q.* 2018;8(2):5.
23. Department of Defense. 2011 Department of Defense Health Related Behaviors Survey of Active Duty Military Personnel. 2011; Accessed 30 March 2022. https://www.health.mil/Reference-Center/Reports/2013/02/01/2011-Health-Related-Behaviors-Active-Duty-Executive-Summary
24. HealthyPeople.gov. Lesbian, Gay, Bisexual, and Transgender Health. 2020; Accessed 18 August 2021. https://www.healthypeople.gov/2020/topics-objectives/topic/lesbian-gay-bisexual-and-transgender-health/objectives
25. Under Secretary of Defense. Certification of the Repeal of "Don't Ask, Don't Tell.". 2011; Accessed 30 March 2022. https://www.iimef.marines.mil/Portals/1/documents/IG/Certification%20of%20Repeal%20of%20Don't%20Ask%20Don't%20Tell%20Jul%202011.pdf
26. Kazman JB, Gutierrez IA, Schuler ER, et al. Who sees the chaplain? Characteristics and correlates of behavioral health care-seeking in the military. *J Health Care Chaplain.* 2020:1–12.

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The Department of Defense (DoD) takes the issue of suicide very seriously and is actively working to reduce the number of suicides. To learn more about suicide and how to prevent it take a look at the resources available to you.

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The Defense Suicide Prevention Office oversees all strategic development, implementation, centralization, standardization, communication and evaluation of DoD suicide and risk reduction programs, policies and surveillance activities.

Service Branch Programs

- http://www.af.mil/suicideprevention.aspx **(U.S. Air Force)**
- http://www.armyg1.army.mil/hr/suicide/default.asp **(U.S. Army)**
- http://www.nationalguard.mil/features/suicide_prevention/ **(U.S. National Guard)**
- http://www.usmc-mccs.org/services/support/suicide-prevention/ **(U.S. Marine Corps)**
- http://www.public.navy.mil/bupers-npc/support/21st_century_sailor/suicide_prevention/Pages/default.aspx **(U.S. Navy)**
- https://www.dcms.uscg.mil/Our-Organization/Assistant-Commandant-for-Human-Resources-CG-1/Health-Safety-and-Work-Life-CG-11/Office-of-Work-Life-CG-111/Suicide-Prevention-Program/ **(U.S. Coast Guard)**
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Brief Report: Phase I Results Using the Virtual Pooled Registry Cancer Linkage System (VPR-CLS) for Military Cancer Surveillance

Shauna L. Stahlman, PhD, MPH; Castine M. Clerkin, MS; Betsy Kohler, MPH; Will R. Howe Jr, BS; Kathy A. Cronin, PhD; Natalie Y. Wells, MD, MPH

The Armed Forces Health Surveillance Division, as part of its surveillance mission, periodically conducts studies of cancer incidence among U.S. military service members. However, service members are likely lost to follow-up from the Department of Defense cancer registry and Military Health System data sets after leaving service and during periods of time not on active duty. Therefore, an ongoing cancer surveillance study sought linkage with civilian state cancer registries through the Virtual Pooled Registry Cancer Linkage System (VPR-CLS) supported by the North American Association of Central Cancer Registries (NAACCR) and funded by the National Cancer Institute. These civilian state registries require the inclusion of all malignant or in situ neoplasms classified by the International Classification of Diseases for Oncology, Third Edition (ICD-O-3), with the exception of carcinoma in situ of the cervix and squamous/basal cell carcinomas of the skin. Since 2004, non-malignant benign/borderline primary tumors of the brain and central nervous system (CNS) have also been included as reportable cancers.[1] The VPR-CLS performs a Phase I and Phase II linkage process to identify members of the study population who have been diagnosed with a reportable cancer. In Phase I, an aggregate total of matched cancer cases are provided by each state cancer registry after performing the linkage behind their respective firewalls. In Phase II, after approval of additional applications and data use agreements, line-level data on each of the cancer cases can be provided. This report describes the Phase I linkage results.

METHODS

A roster of over 10.9 million current and former service members was provided to the VPR-CLS to facilitate the Phase I linkage after Defense Health Agency (DHA) Institutional Review Board (IRB) study approval as a public health surveillance activity. The roster included current and former members of the Army, Navy, Air Force, and Marine Corps who had a duty military occupation specialty code contained in the Defense Medical Surveillance System. This included active, reserve, and guard component members serving at any period through 2017, beginning in 1985 for Army members and 1990 for members of all other services. Individuals who joined service after 2017 were not included. Cancer case counts were quantified as high quality matches defined by a probabilistic linkage algorithm to identify matched pairs above a certain threshold when matched according to various combinations of SSN, name, sex, and date of birth. The case counts provided by the Phase I match results include all reportable cancers, as defined by the respective civilian state registry standards.[1] Furthermore, individuals with multiple primary cancers are counted for each primary cancer and for each state of residence at diagnosis, according to tumor inclusion and reportability standards.[1]

RESULTS

At the time of this report, Phase I match results were available for 44 out of 46 states in the VPR-CLS. Cases were identified as early as 1973 for some state cancer registries, and up through the most recently available data (2020 for most states). A total of 539,983 cases were identified among current and former military service members **(Table)**. Not surprisingly, the highest numbers of cases were identified in the some of the most highly populated states, including Texas, Florida, and California **(Table, Figure)**.

EDITORIAL COMMENT

Most previous military cancer surveillance studies have relied on data from the DoD cancer registry, the VA central cancer registry, TRICARE medical billing data, or a combination of these sources.[2–5] Similar to the DoD cancer registry, the VPR-CLS contains information about tumor staging, patient demographics, treatment, and vital status. The primary advantages of VPR-CLS for military cancer surveillance are its potential for enabling more complete surveillance among personnel who are diagnosed and treated in civilian facilities and that it is more likely to include former service members no longer on active duty. In addition, all state registries are certified annually by NAACCR for compliance with quality standards of completeness, timeliness, and accuracy.[6] Phase I counts allow investigators to determine the number of cancers identified in each state prior to completing the more intensive application and review processes for Phase II.

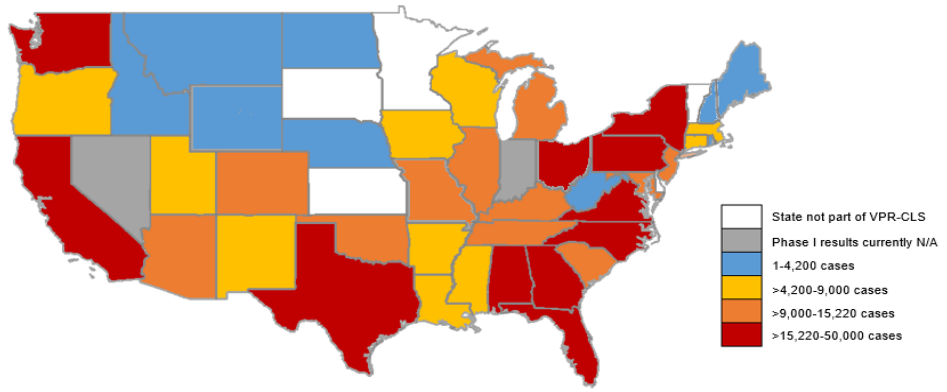
Limitations to the VPR-CLS include a lag in data availability, as cancer registries generally make their data available 24 months after the close of a diagnosis year in order to provide the most complete and consolidated data. In addition, although the VPR-CLS provides a systematic process for linkage with multiple civilian state cancer registries, 8 states in the VPR-CLS currently require separate applications and 20 require separate data use agreements for Phase II. Finally, it should be noted that the numbers presented in this report may not include cancers diagnosed

TABLE. Current and former U.S. military service member cancer cases identified from the Phase I VPR-CLS linkage for AFHSD surveillance study.

State	Total	%
Texas	48,786	9.03
Florida	43,154	7.99
California	38,107	7.06
Virginia	27,344	5.06
Georgia	27,038	5.01
North Carolina	25,271	4.68
Pennsylvania	21,465	3.98
New York	20,466	3.79
Ohio	16,289	3.02
Alabama	16,247	3.01
Seattle SEER Registry	15,234	2.82
Tennessee	15,204	2.82
South Carolina	14,785	2.74
Illinois	13,900	2.57
Maryland	13,066	2.42
Michigan	12,449	2.31
Colorado	12,434	2.30
Missouri	12,001	2.22
Arizona	11,322	2.10
New Jersey	9,962	1.84
Kentucky	9,764	1.81
Oklahoma	9,259	1.71
Wisconsin	8,995	1.67
Louisiana	8,825	1.63
Mississippi	8,313	1.54
Arkansas	8,243	1.53
Massachusetts	7,319	1.36
Oregon	6,304	1.17
Iowa	5,941	1.10
Utah	5,761	1.07
Hawaii	5,305	0.98
Connecticut	4,407	0.82
New Mexico	4,346	0.80
Nebraska	4,163	0.77
Idaho	4,028	0.75
West Virginia	3,922	0.73
Maine	3,593	0.67
Puerto Rico	3,364	0.62
Montana	3,218	0.60
New Hampshire	2,779	0.51
Alaska	2,607	0.48
Rhode Island	1,881	0.35
North Dakota	1,648	0.31
Wyoming	1,474	0.27
Total	539,983	100.00

VPR-CLS, Virtual Pooled Registry Cancer Linkage System; AFHSD, Armed Forces Health Surveillance Division.

FIGURE. Current and former U.S. military service member cancer cases identified from the Phase I VPR-CLS linkage for AFHSD surveillance study



Note: Alaska, Hawaii, and Puerto Rico are not shown

VPR-CLS, Virtual Pooled Registry Cancer Linkage System; AFHSD, Armed Forces Health Surveillance Division; N/A, not available.

Note: Alaska, Hawaii, and Puerto Rico are not shown.
VPR-CLS, Virtual Pooled Registry Cancer Linkage System; AFHSD, Armed Forces Health Surveillance Division; N/A, not available.

in individuals who are receiving care exclusively at military treatment facilities. At the time of this report, only 4 states had completed the requirements and agreements for DoD cancer registry data sharing. Given the large number of high-quality matches identified via the Phase I linkage process, this system serves as a promising tool for future military cancer studies. More information about the VPR-CLS can be found at: https://www.naaccr.org/about-vpr-cls/.

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REFERENCES

1. North American Association of Central Cancer Registries (NAACCR). Chapter III: Standards for Tumor Inclusion and Reportability. Accessed June 17, 2022. Accessed 24 June 2022. http://datadictionary.naaccr.org/default.aspx?c=3&Version=22
2. Zhu K, Devesa SS, Wu H, et al. Cancer incidence in the U.S. military population: comparison with rates from the SEER program. *Cancer Epidemiol Biomarkers Prev*. 2009;18(6):1740–1745.
3. Robbins AS, Pathak SR, Webber BJ, et al. Malignancy in U.S. Air Force fighter pilots and other officers, 1986-2017: A retrospective cohort study. *PLoS One*. 2020;15(9):e0239437.
4. Webber BJ, Tacke CD, Wolff GG, et al. Cancer Incidence and Mortality Among Fighter Aviators in the United States Air Force. *J Occup Environ Med*. 2022;64(1):71–78.
5. Lee T, Williams VF, Clark LL. Incident diagnoses of cancers in the active component and cancer-related deaths in the active and reserve components, U.S. Armed Forces, 2005–2014. *MSMR*. 2016;23(7):23–31.
6. North American Association of Central Cancer Registries (NAACCR). Certification Criteria. Accessed 24 June 2022. https://www.naaccr.org/certification-criteria/

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