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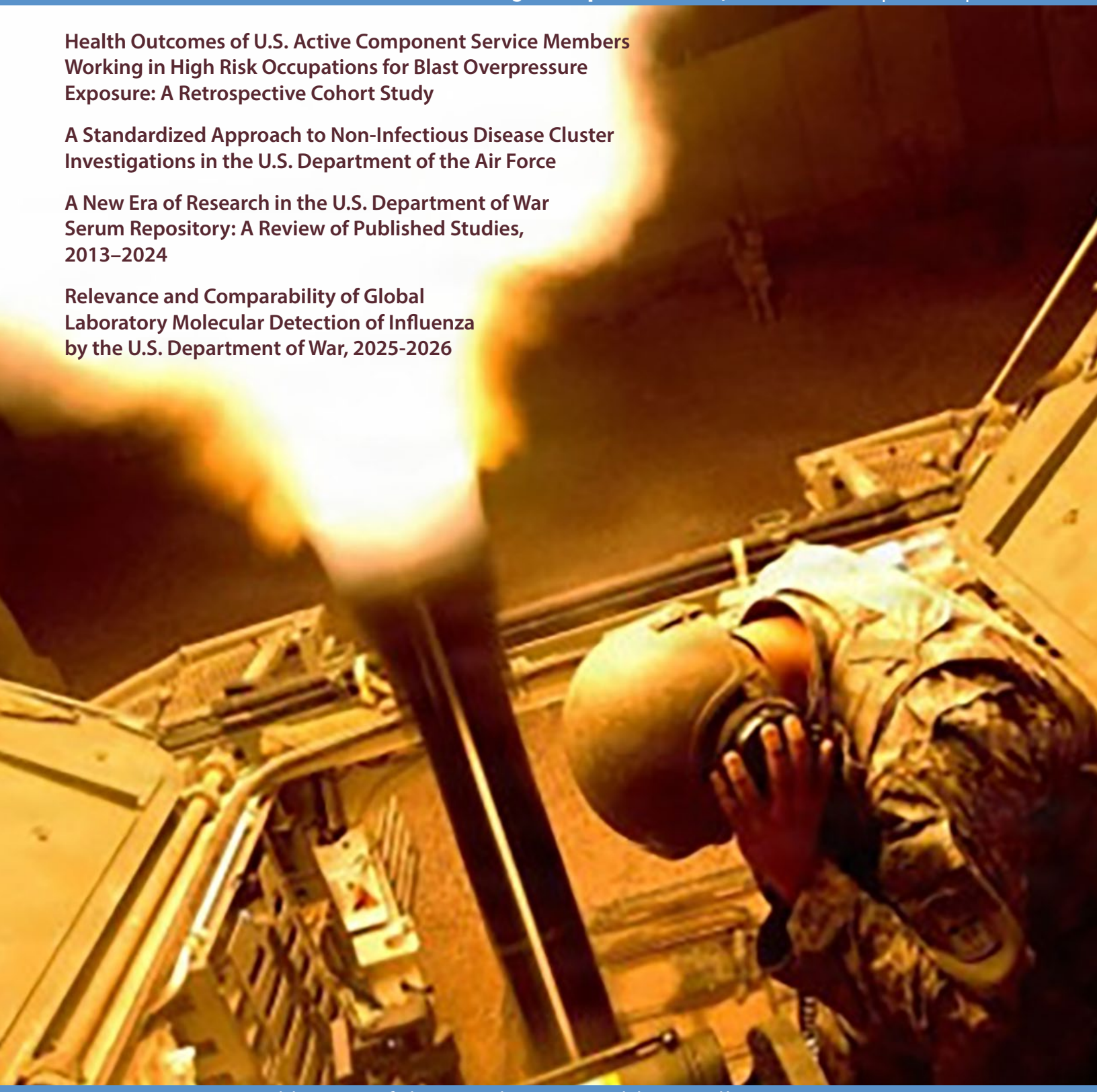

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Medical Surveillance for Military Readiness

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Health Outcomes of U.S. Active Component Service Members Working in High Risk Occupations for Blast Overpressure Exposure: A Retrospective Cohort Study

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Active component military service members are exposed to increased risk of occupational blast overpressure (BOP) exposure during deployment as well as training. This retrospective cohort study examined the incidence of first-time diagnoses of traumatic brain injury (TBI), insomnia, migraine headache, depressive or anxiety disorders, noise-induced hearing injury (NIHI), and essential hypertension among active component service members (ACSMs) in the U.S. Army, Air Force, and Marine Corps. Incidence rates were compared between ACSMs who served in occupations at high risk for BOP exposure (n=831,050) and those who never served in such occupations (n=2,229,594). Overall incidence of TBI was 243.8 per 10,000 person-years in the high-risk occupational cohort and 140.9 per 10,000 person-years in the low-risk occupational cohort. Incidence of NIHI was 342.7 and 218.1 per 10,000 person-years in the high- and low-risk cohorts, respectively. After adjusting for demographic and military characteristics, ACSMs in occupations with high risk of BOP experienced higher incidence rates of TBI (adjusted incidence rate ratio [aIRR] 1.43; 95% CI 1.42, 1.44) and NIHI (aIRR 1.39; 95% CI 1.38, 1.40). Increasing time since entering the cohort was associated with a greater increase in migraine headache incidence among ACSMs in high-risk BOP occupations compared with those in low-risk occupations. Despite these differences, the distribution of disease burden categories from 2024 health care encounters was similar among cohorts. These findings emphasize the importance of mitigating occupational blast hazards and strengthening surveillance efforts to protect the long-term health of ACSMs.

What are the new findings?

Adjusted incidence rates of traumatic brain injury (TBI) and noise-induced hearing injury (NIHI) were higher among service members in occupations at high risk for BOP exposure than among those who had never worked in such occupations. Increasing time in the cohort was associated with a greater increase in migraine headache incidence among service members in high-risk BOP occupations than among those in low-risk occupations.

What is the impact on readiness and force health protection?

This analysis aimed to characterize potential long-term health consequences associated with serving in military occupations at high risk for BOP exposure and inform force health protection efforts. Enhanced BOP exposure monitoring, occupational hazard mitigation, and targeted health surveillance may help identify and reduce adverse health outcomes among personnel serving in occupations with higher risk.

Blast injuries are a significant occupational hazard in the military as well as law enforcement, mining, construction, and chemical manufacturing environments.[1] During an explosive event, rapid release of energy generates a primary blast wave that compresses the surrounding air and produces a sudden increase in atmospheric pressure above ambient levels. The positive-pressure phase of the blast wave—termed blast overpressure (BOP)—produces an outward-propagating shock wave, followed by blast wind and a subsequent negative-pressure phase.[2]

Blast exposure varies by intensity and exposure pattern. Low-level blast exposure is commonly associated with routine weapons training, including firing of heavy-caliber weapons that generate "blast wind" and are often repetitive and cumulative in nature. In contrast, high-level blast exposure is typically associated with acute, high-energy events such as improvised explosive devices, rocket-propelled grenades, and landmines, which generate larger shockwaves and are more often singular or episodic. BOP exposure is therefore characterized not only by intensity (low vs. high) but also by exposure frequency (single vs. repetitive) and operational context (training-related vs. combat-related).

Active component service members (ACSMs) are at increased risk

of occupational BOP exposure during both garrison training and deployment. A retrospective cohort study conducted by the Department of Veterans Affairs found that more than 70% of veterans who served during operations Iraqi Freedom and Enduring Freedom reported histories of blast exposure, most of which involved high-level blast events.[3,4]

Since direct measures of cumulative blast exposure are often unavailable, military occupational specialty serves as a validated proxy, with demonstrated utility in identifying service members with a history of occupational blast exposure.[5] Primary military occupational specialties (PMOSs) at greatest risk include armor, artillery, gunnery, combat engineering, explosive ordnance disposal, infantry, medical personnel assigned to expeditionary units, military training instructors, and special operations forces.[6]

According to the U.S. Department of War Brain Injury Research Coordinating Office, acute BOP exposure exceeding 4 pounds per square inch (psi) may result in adverse health and cognitive effects and has served as the DOW's working exposure safety threshold since 2022.[7] Low- and high-level blast exposures can cause injury through 5 mechanisms of injury: primary blast injury (i.e., overpressure wave), secondary blast injury (i.e., debris), tertiary blast injury (i.e., body displacement), quaternary blast injury (i.e., heat and toxic exposures), and quinary blast injury (i.e., environmental contaminants).[8] Clinically, primary blast injury is often associated with symptoms such as poor concentration, dizziness, memory impairment, headache, tremor, noise sensitivity, and tinnitus.[9,10]

Physiologically, the overpressure wave generated during blast events is thought to induce neurovascular inflammation, oxidative stress, vascular injury, and systemic inflammatory responses that may propagate through interconnected biologic pathways.[11] Emerging literature further suggests that blast exposure may disrupt blood–brain barrier integrity and contribute to immune and gastrointestinal dysregulation.[12] The organ systems most susceptible to primary blast forces are those containing air- or fluid-filled structures, including the central nervous system (e.g., traumatic brain injury [TBI]),[13–16] auditory system (e.g., tympanic membrane rupture),[17,18] ocular system (e.g., globe rupture),[19] pulmonary system (e.g., "blast lung"),[20] and gastrointestinal system (e.g., hemorrhage, perforation).[21] Growing evidence indicates additional, less well-characterized health outcomes associated with BOP exposure, including hypertension,[11,22] insomnia,[23,24] noise-induced hearing injury (NIHI),[25] depressive symptoms,[26] and migraine headache.[27]

Due to logistical, safety, and ethical constraints in studying blast-related injuries, the evidence base regarding long-term health effects of BOP exposure remains limited. Clarifying these associations is important for active duty military personnel, given the implications for readiness, return-to-duty decisions, career longevity, and long-term health care burden within the Military Health System. Enhanced surveillance and early intervention of at-risk individuals may support force health protection efforts.

The aims of this analysis were to compare ACSMs who served in occupations at high risk for BOP exposure with those who never served in such occupations according to: 1) demographic and military service characteristics, 2) 2024 health care provision distribution by disease burden, 3) incidence of TBI, insomnia, migraine headache, depressive or anxiety disorders, NIHI, and essential hypertension, and 4) incidence of these conditions by cumulative time since entering the cohort or occupation.

Methods

Data source

This retrospective cohort study received a non-human subject research determination by the Defense Health Agency Component Office of Human Research Protections (protocol 25-22055). Medical encounter and demographic data were drawn from the Defense Medical Surveillance System (DMSS), the central repository of longitudinal medical surveillance data on U.S. military members. Medical record diagnoses of deployed service members were obtained from the Theater Medical Data Store (TMDS), which is integrated within DMSS. Complete inpatient encounter data were available from 1990 through 2024; outpatient encounter data were available from 1997 through 2024; TMDS data were available from 2008 through 2024; Army personnel data were available from 1985 through 2024; Air Force and Marine Corps personnel data were available from 1990 through 2024; and deployment data were available from 1990 through 2022.

Study population

The study population included ACSMs in the U.S. Army, Air Force, and Marine Corps who entered initial active component service from 2001 through 2024. Occupations at high risk for BOP exposure were identified using service-specific PMOS codes documented in the August 8, 2024 Deputy Secretary of Defense Memorandum.[28] ACSMs were assigned to the high-risk BOP cohort at the time they first entered 1 of these occupations on or before December 31, 2024. ACSMs assigned to all remaining occupational specialties defined the cohort not considered to be at high risk for occupational BOP exposure (referred to as "low-risk" occupational cohort). ACSMs in the Navy were excluded entirely due to incomplete occupational data in DMSS.

For the aim 2 burden analysis, medical encounters occurring in calendar year (CY) 2024 among individuals in the study population were summarized according to the primary (first-listed) diagnosis using International Classification of Diseases, 10th Revision (ICD-10) codes (A00–T88, Z37, U07.1, U09) and DOW unique personal history codes (DOD0101–DOD0105). This limited, cross-sectional sampling period was specifically chosen to appraise current force readiness and the contemporary health care burden on the Military Health System, rather than to provide a cumulative representation of the historical cohort's longitudinal morbidity. Diagnoses were classified into 25 major disease categories and 157 subcategories using the *MSMR* burden analysis methodology, a modified version of the World Health Organization Global Burden of Disease framework.[29,30]

Burden estimates included the number of encounters (limited to 1 encounter per person per category per day, with inpatient encounters prioritized over outpatient encounters) and hospital bed days derived from inpatient encounters.

For aims 3 and 4, the incidence of TBI, insomnia, migraine headache, depressive or anxiety disorders, and NIHI were assessed using all available records and ICD-9 and ICD-10 diagnosis codes defined by corresponding Armed Forces Health Surveillance Division case definitions.[31-36] For migraine headache, menstrual migraine diagnosis codes were excluded. Incident cases of essential hypertension were identified using ICD-9 (401*) and ICD-10 (I10.0, I16.0*) diagnosis codes (asterisks denote inclusion of all subsequent digits or characters within the specified code). For insomnia and depressive or anxiety disorders, a qualifying case required 2 or more inpatient, outpatient, or TMDS encounters containing a case-defining diagnosis code in any diagnostic position within a 90-day period, excluding encounters occurring on the same day. For the remaining conditions, a single inpatient, outpatient, or TMDS encounter with a case-defining diagnosis code was sufficient to qualify as an incident case.

Person-years (p-yrs) of follow-up accrued from the date an ACSM entered a high-risk BOP occupation (high-risk cohort) or entered active component service (low-risk cohort) and continued until the first incident diagnosis of the outcome of interest or the end of the surveillance period (December 31, 2024), whichever occurred first. For ACSMs in the high-risk BOP cohort, person-time accrued prior to entry into a high-risk occupation was excluded. Once an ACSM entered a high-risk occupation, all subsequent person-time was attributed to the high-risk cohort regardless of subsequent occupational changes. Time since entering the cohort was calculated as the number of years in military service following entrance into the high-risk occupational cohort, or as the number of years in military service following entrance into military service (for the low-risk occupational cohort). ACSMs who met the case definition for a given outcome before entering a high-risk occupation were excluded from analyses of that outcome. Unadjusted incidence rates (IRs) were calculated per 10,000 p-yrs of active component service. It should be emphasized that this analysis evaluated occupational assignment as a proxy for BOP exposure and did not incorporate individual measures of blast exposure intensity, frequency, or cumulative dose.

Statistical analysis

Statistical analysis for aims 1 and 2 included descriptive statistics. For aim 3, multivariable Poisson regression models were used to estimate adjusted incidence rate ratios (aIRRs) for each health condition among ACSMs in the high-risk BOP cohort compared with those who were never assigned to high-risk occupations. Models adjusted for sex, age, race and ethnicity, service branch, rank or grade, education, time since entering the cohort, and deployment history. For aim 4, person-time and incident case counts were summarized and aggregated by covariate strata, and multivariable Poisson regression models were applied to estimate aIRRs by time since entering the cohort, separately for the high-risk and low-risk cohorts. An offset for person-time was included to account for varying follow-up time within each stratum. Models adjusted for the same covariates listed earlier. All analyses were conducted using SAS Enterprise Guide (version 8.6).

Results

Aim 1: Demographic and military service characteristics of study population

The Army accounted for the largest proportion of ACSMs in both occupational cohorts, although it represented a larger share of the occupational cohort at high risk for BOP exposure than the low-risk occupational cohort (68.1% vs 43.6%) **(Table 1)**. Compared with the low-risk occupational cohort, the high-risk occupational cohort included a greater proportion of male (92.2% vs 79.9%) and non-Hispanic White (68.0% vs 58.0%) ACSMs. Additionally, fewer ACSMs in the high-risk occupational cohort had not deployed by the end of CY 2022 compared to the low-risk occupational cohort (55.4% vs 64.5%). In both cohorts, most ACSMs were enlisted (92.6% in high-risk cohort, 91.0% in low-risk cohort) and had served between 1 and less than 6 years (62.9% and 55.3%, respectively). Among ACSMs in high-risk occupations, 59.8% were in combat-related roles, most commonly infantryman (Army), rifleman (Marine Corps), and security forces journeyman (Air Force). In contrast, only 5.8% of ACSMs in the low-risk occupational cohort were in combat related occupations. The most common occupational categories were repair and engineering (28.9%) and communications and intelligence (26.0%).

Aim 2: Comparison of health care provision distribution by cohort

During CY 2024, ACSMs in occupations at high risk for BOP exposure accounted for 22.2% of the 9,768,558 inpatient and outpatient medical encounters documented among the study population. The distribution of morbidity burden categories was generally similar between occupational cohorts. For both cohorts, the 5 most common major burden categories included injury and poisoning, musculoskeletal diseases, mental disorders, ill-defined signs and symptoms, and neurological conditions. Likewise, the most frequently represented subcategories were other back problems, knee injuries, arm and shoulder injuries, all other signs and symptoms, and organic sleep disorders **(Figure 1)**. A total of 270,135 hospital bed days were recorded for the study population during CY 2024, of which 24.4% occurred among ACSMs in high-risk occupations. Mental health conditions accounted for approximately 53% of hospital bed days in both cohorts **(Figure 2)**. Differences were noted in the secondary contributors to hospitalization burden. Among ACSMs in high-risk occupations, injury and poisoning (14.7%) accounted for a greater proportion of hospital bed days than maternal conditions (7.4%). In contrast, among ACSMs in low-risk occupations for BOP exposure, maternal conditions (15.4%) accounted

TABLE 1. Demographic and Military Service Characteristics of Occupations with High and Low Risks for Blast Overpressure Exposure, Active Component, U.S. Armed Forces Who Joined Service 2001–2024

Characteristic	High-Risk Occupation		Low-Risk Occupation	
	No.	%	No.	%
Total	831,050	27.2	2,229,594	72.8
Sex				
Male	765,876	92.2	1,781,893	79.9
Female	65,174	7.8	447,701	20.1
Age group at end of follow-up, *y*				
<20	56,202	6.8	217,992	9.8
20–24	399,202	48.0	945,956	42.4
25–29	223,878	26.9	583,130	26.2
30–34	86,430	10.4	260,477	11.7
35–39	41,523	5.0	139,825	6.3
≥40	23,815	2.9	82,214	3.7
Race and ethnicity				
White, non-Hispanic	564,877	68.0	1,293,590	58.0
Black, non-Hispanic	92,302	11.1	370,235	16.6
Hispanic	117,931	14.2	357,666	16.0
Other or unknown	55,940	6.7	208,103	9.3
Branch of service				
Army	565,847	68.1	971,648	43.6
Air Force	105,383	12.7	670,896	30.1
Marine Corps	159,820	19.2	587,050	26.3
Rank (grade) at end of follow-up				
Enlisted (E1-E9)	769,511	92.6	2,029,356	91.0
Commissioned officer (O1-O10)	57,059	6.9	184,852	8.3
Warrant officer (W)	4,480	0.5	15,386	0.7
Occupation				
Combat-related	497,109	59.8	128,483	5.8
Motor transport	1,650	0.2	95,502	4.3
Pilot, air crew	3,262	0.4	50,001	2.2
Repair, engineering	64,715	7.8	644,804	28.9
Communications, intelligence	81,365	9.8	578,907	26.0
Health care	4,386	0.5	190,613	8.6
Other	178,563	21.5	541,284	24.3
Cumulative time since entering the cohort, at end of follow-up, *y*				
<1	112,115	13.5	376,406	16.9
1 to <6	522,329	62.9	1,232,985	55.3
6 to <10	108,251	13.0	328,549	14.7
≥10	88,355	10.6	291,654	13.1
Deployment history at end of follow-up (through December 2022)				
Never deployed	460,181	55.4	1,437,738	64.5
1 prior deployment	209,142	25.2	433,661	19.5
≥2 prior deployments	161,727	19.5	358,195	16.1

Abbreviation: No., number; BOP, blast overpressure.

for a larger proportion of hospital bed days than injury and poisoning (10.1%). Overall, health care provision patterns were broadly similar between cohorts, although injury-related conditions contributed a larger share of hospitalization burden among ACSMs in high-risk occupations.

Aim 3: Incidence of medical conditions by cohort

The adjusted incidence of essential hypertension (aIRR 0.93; 95% CI 0.92, 0.94), depressive or anxiety disorders (aIRR 0.94; 95% CI 0.94, 0.95), and migraine headache (aIRR 0.94; 95% CI 0.93, 0.95) were slightly lower in the high-risk occupational cohort compared with the low-risk cohort **(Table 2)**. Incidence of insomnia was comparable between groups (aIRR 1.01; 95% CI 1.00, 1.02). In contrast, the high-risk BOP cohort demonstrated a 39% higher adjusted incidence of NIHI (aIRR 1.39; 95% CI 1.38, 1.40) and 43% higher adjusted incidence of TBI (aIRR 1.43; 95% CI 1.42, 1.44) compared with the low-risk cohort.

Aim 4: Incidence of medical conditions stratified by time since entering the cohort

Using less than 1 year time-in-service as the reference category for descriptive comparison of aIRRs within each occupational cohort, increased time-in-service was generally associated with increased incidence of all 6 health conditions **(Table 3)**. Within the 6-10 years and 10 years or greater time-in-service categories, aIRRs for migraine headache were higher in the high-risk occupational cohort than in the low-risk occupational cohort. Among individuals in the high-risk occupational cohort, those with 10 or more years of service had an 83% higher incidence of migraine headache compared to those with less than 1 year of service (aIRR 1.83; 95% CI 1.74, 1.93). In the low-risk cohort, the corresponding increase was 61% (aIRR 1.61; 95% CI 1.56, 1.65). In contrast, when compared descriptively, aIRRs for essential hypertension, insomnia, NIHI, TBI, and depressive or anxiety disorders were similar or lower in the high-risk occupational cohort compared with the low-risk cohort within the same time-in-service categories.

FIGURE 1. Percent Distribution of Medical Encounters by Disease Burden Subcategory in High-Risk Versus Low-Risk Blast Overpressure Occupational Cohorts, Active Component, U.S. Armed Forces, Calendar Year 2024

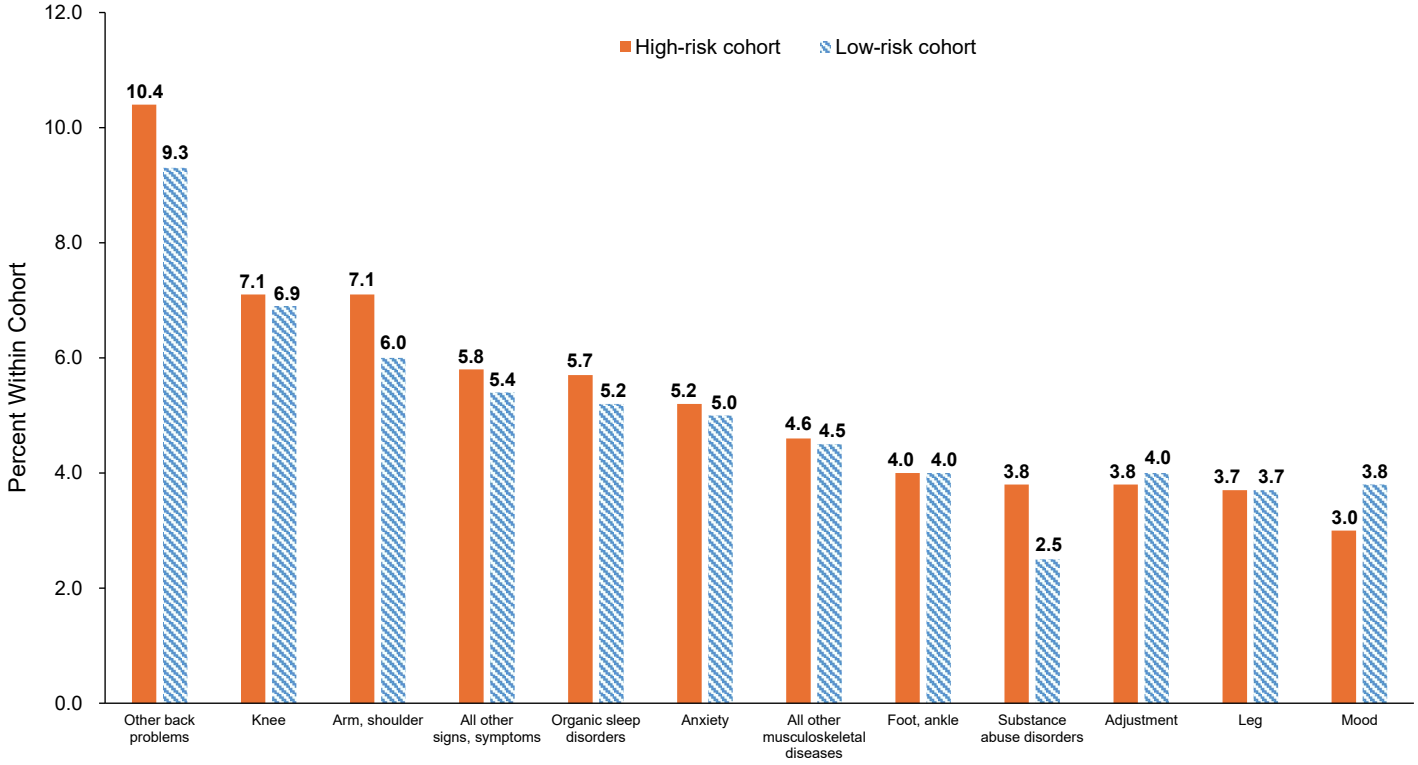

FIGURE 2. Percent Distribution of Hospital Bed Days by Major Disease Category in High-Risk Versus Low-Risk Blast Overpressure Occupational Cohorts, Active Component, U.S. Armed Forces, Calendar Year 2024

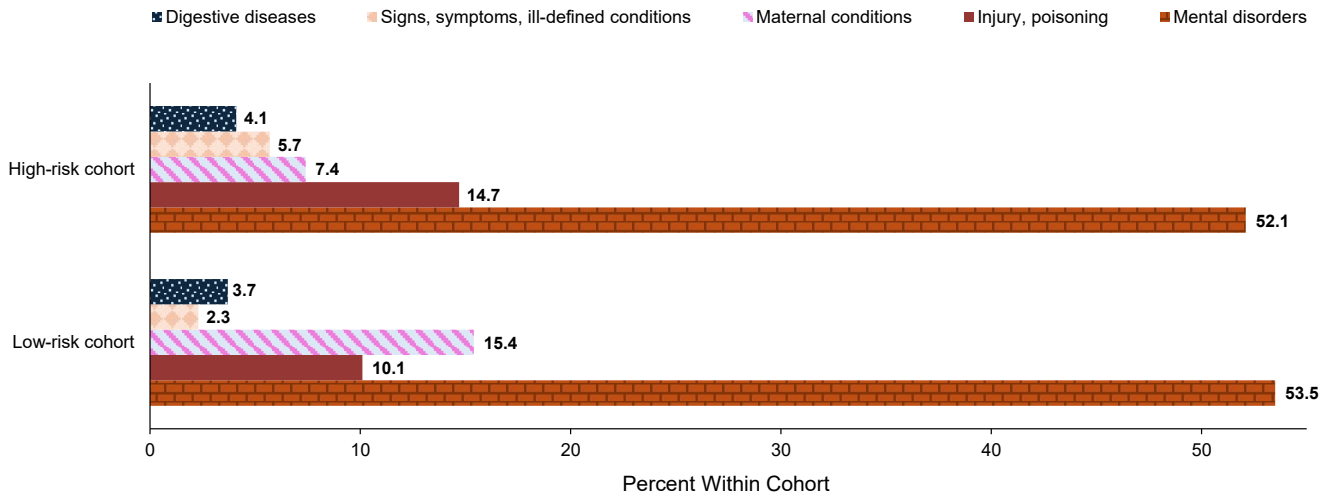

TABLE 2. Unadjusted and Adjusted Incidence Rate Ratios for Six Medical Conditions, High-Risk Versus Low-Risk Blast Overpressure Occupations, Active Component, U.S. Armed Forces, January 1990–December 2024

Medical Condition	High-Risk Occupation			Low-Risk Occupation			Adjusted IRR	Adjusted 95% CI
	Incident Case Count	Person-Years	Incidence Rate	Incident Case Count	Person-Years	Incidence Rate		
Traumatic brain injury	88,973	3,649,972.0	243.8	154,924	10,992,928.8	140.9	1.43	1.42–1.44
Insomnia	66,680	3,801,029.2	175.4	170,280	11,104,851.6	153.3	1.01	1.00–1.02
Migraine headache	50,342	3,816,278.4	131.9	182,547	10,967,160.2	166.5	0.94	0.93–0.95
Depressive or anxiety disorders	126,790	3,684,427.4	344.1	385,147	10,631,003.6	362.3	0.94	0.94–0.95
Noise-induced hearing injury	121,666	3,549,979.9	342.7	235,986	10,820,896.4	218.1	1.39	1.38–1.40
Essential hypertension	43,983	3,821,276.1	115.1	131,766	11,093,650.0	118.8	0.93	0.92–0.94

Abbreviations: IRR, incidence rate ratio; CI, confidence interval. Incidence rate per 10,000 person-years.

Because these comparisons are descriptive, no inference should be made regarding the differential effects of cumulative BOP exposure between cohorts.

TABLE 3. Unadjusted and Adjusted Incidence Rate Ratios for Six Conditions by Time in Service, High-Risk Versus Low-Risk Blast Overpressure Occupations, Active Component, U.S. Armed Forces, January 1990–December 2024

Medical Condition	Cumulative Time in Service	High-Risk Occupations		Low-Risk Occupations	
		Adjusted IRR	Adjusted 95% CI	Adjusted IRR	Adjusted 95% CI
Traumatic brain injury	<1 year	Ref	—	Ref	—
	1 to <6 years	1.19	1.16–1.21	1.37	1.35–1.40
	6 to <10 years	1.20	1.16–1.24	1.42	1.38–1.46
	≥10 years	1.30	1.25–1.36	1.42	1.37–1.47
Insomnia	<1 year	Reference	—	Reference	—
	1 to <6 years	2.28	2.20–2.35	2.42	2.37–2.47
	6 to <10 years	2.70	2.59–2.82	2.89	2.81–2.96
	≥10 years	2.59	2.47–2.72	2.90	2.82–2.99
Migraine headache	<1 year	Reference	—	Reference	—
	1 to <6 years	1.46	1.41–1.51	1.48	1.45–1.50
	6 to <10 years	1.72	1.65–1.80	1.62	1.58–1.65
	≥10 years	1.83	1.74–1.93	1.61	1.56–1.65
Depressive or anxiety disorders	<1 year	Reference	—	Reference	—
	1 to <6 years	1.25	1.23–1.27	1.43	1.41–1.44
	6 to <10 years	1.51	1.46–1.55	1.70	1.67–1.73
	≥10 years	1.45	1.40–1.50	1.75	1.72–1.79
Noise-induced hearing injury	<1 year	Reference	—	Reference	—
	1 to <6 years	1.74	1.70–1.78	1.79	1.77–1.82
	6 to <10 years	1.78	1.73–1.83	1.88	1.83–1.92
	≥10 years	1.80	1.74–1.87	1.99	1.94–2.04
Essential hypertension	<1 year	Reference	—	Reference	—
	1 to <6 years	1.53	1.48 - 1.59	1.49	1.45 - 1.52
	6 to <10 years	1.61	1.54 - 1.69	1.50	1.46 - 1.54
	≥10 years	1.55	1.46 - 1.63	1.45	1.41 - 1.50

Abbreviations: IRR, incidence rate ratio; CI, confidence interval.

Discussion

This large retrospective cohort study evaluated health outcomes among ACSMs in a high-risk occupational cohort for BOP exposure versus a low-risk cohort and identified several notable differences. Most prominently, ACSMs assigned to the high-risk cohort experienced significantly higher incidence of TBI and NIHI. These findings are consistent with the growing body of literature on occupational blast exposure risk to the central nervous and auditory systems,[37,38] including a 10-year service-wide cohort study of occupational low-level blast exposure risk.[39]

Although individual BOP exposure was not directly measured in this study, the observed associations between incidence of TBI and NIHI and assignment to occupations at high risk for BOP exposure support continued evaluation of occupational hazard mitigation strategies, including blast-attenuating helmets and dual-layer hearing protection. Together with prior evidence supporting the biological plausibility of blast-related neurological and auditory injury, these results reinforce the potential value of periodic neurocognitive and audiologic screening among personnel in high-risk occupational specialties, including infantry, artillery, and combat operations. Finally, the higher incidence of TBI and NIHI in the high-risk occupational cohort may be multifactorial and reflect additional characteristics of these occupations, including differences in physical demand, environmental exposures, training activities, and medical surveillance.

Future studies incorporating more detailed occupational and individual exposure data are needed to better clarify the contributions of these factors.

Conversely, adjusted analyses demonstrated similar or lower incidence of essential hypertension, migraine headache, depressive or anxiety disorders, and insomnia in the high-risk cohort compared with the low-risk cohort. This seemingly protective pattern may reflect the 'healthy warrior effect,' whereby individuals in combat-related occupations are generally healthier and more physically fit. These occupations also impose strict accession and retention standards, which may result in selection of healthier individuals for entry and medical attrition or reclassification of those who develop health conditions. Lower observed incidence of mental health disorders may also be influenced by under-diagnosis or under-reporting due to stigma and barriers to seeking care. Additionally, individuals with genetic predisposition for mental health and neurological conditions may exclude or remove themselves from physically demanding occupations that could accelerate or exacerbate symptoms. Residual confounding differences in health care provision between occupational cohorts may also have contributed to these findings. Given that several estimates were close to the null, the clinical significance of these differences should be interpreted cautiously.

The time-in-service analysis identified differences in aIRRs among cumulative time-in-service categories within each occupational cohort. For most conditions, aIRRs were stable or increased with progressive time since entering the study for both cohorts, with the highest estimates observed among individuals with 10 or more years of service. For migraine headache, however, aIRRs were consistently higher among cumulative time-in-service categories in the high-risk occupational cohort compared to the low-risk occupational cohort. These findings are compatible with a cumulative exposure hypothesis but should be interpreted cautiously, as cumulative time-in-service is not a direct measure of cumulative BOP exposure. In contrast, aIRRs for TBI were consistently lower for the same time-in-service category in the high-risk occupational cohort compared to the low-risk occupational cohort. This finding was unexpected and warrants further investigation. Since this analysis focused on first-ever TBI diagnoses, results may differ if recurrent TBI or subclinical injuries were included. Future studies incorporating individual-level blast exposure metrics, including blast frequency, estimated overpressure, average and cumulative psi from dosimetry readings, and use of protective equipment, are needed to directly evaluate cumulative BOP exposure and better characterize exposure and outcome relationships.

The morbidity burden analysis demonstrated broadly similar patterns of health care provision among cohorts, despite differences in sex, race and ethnicity, service branch, occupational code, and deployment history. In both groups, health care provision was primarily driven by injuries, musculoskeletal conditions, mental health disorders, and neurological conditions. These patterns suggest that occupational BOP exposure may not substantially alter overall patterns of health care, although subtle differences in specific diagnostic categories were observed. Maternal conditions accounted for a higher proportion of hospital bed days in the low-risk occupational cohort compared to the high-risk cohort (15.4% vs. 7.4%, respectively), likely secondary to the higher proportion of women in this cohort. Interestingly, substance use disorders accounted for a greater proportion of outpatient encounters (3.8% vs. 2.5%) and hospital bed days (17% vs. 13.9%) in the high-risk cohort compared to the low-risk cohort. These findings emphasize the importance of continued evaluation of behavioral health outcomes in populations with potential occupational blast exposure.

There are several limitations to this study. First, ACSMs in the Navy, the second largest branch of the U.S. Armed Forces (n=337,800),[40] were excluded due to incomplete occupational data in DMSS, limiting generalizability for the total force.

Second, the absence of individual data on BOP exposure characteristics (e.g., frequency, intensity, protective equipment use) likely resulted in exposure misclassification. Our use of a static exposure classification—whereby individuals were permanently assigned to the high-risk cohort upon their first entry into a high-risk occupation—did not account for subsequent changes in occupational risk. For instance, a service member who spent only a few years in a high-risk occupation before transferring to a low-risk role was still attributed entirely to the high-risk cohort. This exposure misclassification dilutes the true effect of continuous exposure, biasing the incidence rate ratios toward the null. Consequently, the estimates reported in this study likely underestimate the true magnitude of differences in disease incidence between the high-risk and low-risk occupational groups.

Third, outcome detection bias may have occurred since ACSMs in high-risk occupations may undergo more frequent occupational health evaluations. Additionally, follow-up for the high-risk cohort began at the time of occupational entry rather than entry to service, resulting in a short period of military service prior to entering the cohort (median 30 days, mean 144 days). While this slight misalignment in follow-up start times could introduce a survivor effect, sensitivity testing adjusting for time since military entry demonstrated minimal impact on the aIRRs, indicating that the overall findings remain robust.

Fourth, this analysis did not perform exposure lag modeling to account for latency periods in conditions with delayed onset, such as essential hypertension and NIHI. Additionally, study outcomes were identified using medical encounter diagnosis codes and may not capture all underlying symptoms or diseases. Finally, behavioral and lifestyle factors (e.g., tobacco use, alcohol consumption, sleep, physical fitness) were not available and may confound or modify exposure and outcome relationships.

This analysis contributes to the growing evidence that links service in occupations at high risk for BOP with adverse health outcomes. Importantly, it complements, rather than replaces, direct individual exposure monitoring, which remains essential for accurately characterizing cumulative blast exposure. These findings support continued surveillance, targeted prevention efforts, and enhanced exposure

monitoring for personnel in high-risk occupations to better define the long-term health effects of blast exposure, inform force health protection strategies, and preserve military readiness.

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Disclaimers
The views expressed in this report reflect the results of research conducted by the authors and do not necessarily reflect official policy nor position of the Defense Health Agency, Department of War, or the U.S. Government.

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Public Health Practice

A Standardized Approach to Non-Infectious Disease Cluster Investigations in the U.S. Department of the Air Force

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The U.S. Air Force School of Aerospace Medicine (USAFSAM) developed a systematic, multi-phased process for receiving, evaluating, and responding to inquiries about potential non-infectious disease clusters, particularly cancer, within the Department of the Air Force. Created in response to a rise in cluster concerns, this process provides a validated, transparent, and objective evaluation framework with 4 distinct phases: 1) establishing lines of communication, 2) feasibility assessment, 3) epidemiological evaluation, and 4) epidemiological investigation. This framework allows a merit-based evaluation for determining if a full epidemiological study is warranted. The framework emphasizes robust risk communication and partnerships to manage expectations and address all concerns with scientific rigor. In 2023 and 2024 this process evinced savings of $6.25 million and 102 months of person-time for the USAFSAM team, ensuring responsible use of public health resources.

What is the impact on readiness and force health protection?

The process enables a timely, evidence-based response to potential health threats. It ensures public health resources are used responsibly, for scientifically valid investigations, and builds trust within the Air Force community to directly support the health, fitness, and readiness of U.S. Air Force service members.

Background and Operational Context

In recent years, the U.S. Department of the Air Force has received an increasing number of inquiries regarding perceived clusters of non-infectious diseases, particularly cancer. The U.S. Centers for Disease Control and Prevention (CDC) defines a disease cluster as "a greater than expected number of the same or etiologically related cases within a specific geography and time period."[1] While identifying a true cluster can inform public health policy, establishing a definitive link to an environmental cause is complicated due to numerous factors. These challenges include long latency periods between exposure and disease onset, population mobility, confounding lifestyle and genetic factors, and the statistical instability inherent in small case counts.[1]

Historically, investigations of suspected cancer clusters rarely confirm a cause. A 2012 review by Goodman et al. found that only 72 of 576 investigations of suspected cancer clusters were confirmed as having statistical excesses of cases, and just 1 had a definitive, established cause.[2] This finding highlights the need for a precise balance between receptiveness to concerns about non-infectious diseases and finite public health resources.

To address these challenges, the U.S. Air Force School of Aerospace Medicine (USAFSAM) established a standardized process, based on CDC guidelines, to objectively investigate potential non-infectious disease clusters.[1,3] This report describes the USAFSAM process and its demonstrated application and value for the Department of the Air Force, Public Health, and the Department of War.

Framework

The USAFSAM framework for evaluating suspected disease clusters is a 4-phased, collaborative process, aligned with the CDC's 4-step framework for cluster investigations.[1,3] The USAFSAM framework was formalized in 2023 and subsequently codified into a standard operating procedure (SOP).[4] The framework involves partnerships with major commands, leadership, as well as installation public health, bioenvironmental engineering, and aerospace medicine assets. The investigative approach is summarized in the **Figure**.

Phase 1: Establishing lines of communication

The initial phase begins when a concern about a potential non-infectious disease cluster is first reported. The primary goal is to gather as much information as possible from the individual or group raising the concern. Information gathered includes details about the types of illnesses, numbers of cases, geographic areas of concern, and periods when illnesses were observed. USAFSAM evaluates

the final merit of an inquiry based on the initial validity assessment provided by the installation's public health and medical assets.

During this phase, it is crucial to establish a trusting relationship with the community by listening empathetically to their concerns and providing clear, consistent communication. Responders also take this opportunity to educate the community about the nature of the disease in question, its known risk factors, and the process for investigating potential clusters. A key decision at the end of this phase is to determine if the reported situation warrants further investigation, based on whether the information provided could plausibly meet the definition of a disease cluster.

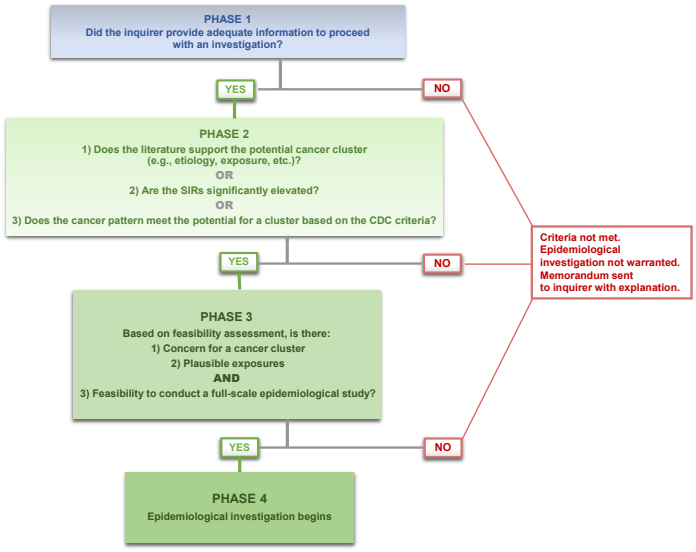
To facilitate the assessment, USAFSAM requests specific information from the inquiring unit, including: a roster or estimated size of the population at risk during the specified timeframe; a line list of affected individuals, including demographics and clinical information (e.g., disease type, date of diagnosis); any observed patterns in the timing of diagnoses or other notable trends, such as cases diagnosed at unusually young ages; and details on specific exposures of concern and known or suspected routes of exposure. A preliminary case definition is constructed to specify the non-infectious disease condition, affected population, location, and period of interest (i.e., "any cases of prostate cancer in active duty maintenance personnel located at building X at base X from 2005-2015").

To proceed with phase 2, the assessment requires either an adequate number of etiologically linked cases (verified by a power calculation assessment, generally 16 or more cases) or a determination that the number of cases is concerning given the population size. [5]

Phase 2: Feasibility assessment

Once it is determined that a concern warrants further attention, the next step is a feasibility assessment to determine if a statistically significant excess of cases exist. This is a preliminary statistical analysis that compares the numbers of reported cases in the community to the numbers of cases expected based on rates in a larger comparison population, such as the state.

FIGURE. Department of the Air Force Cancer and Non-Infectious Disease Cluster Response Process Phases



Abbreviations: SIRs, standardized incidence rates; CDC, Centers for Disease Control and Prevention.

During this phase, an SOP is employed that specifies which activities can legally be conducted by USAFSAM prior to an epidemiological investigation. As a public health authority operating under HIPAA (Health Insurance Portability and Accountability Act), USAFSAM is legally permitted to review the minimum necessary protected health information (PHI) solely to prepare research protocols, provided no PHI is removed or stored from its original source. These preparatory activities are strictly limited to data validation and feasibility assessments and must be concluded before a formal study begins, under institutional review board (IRB) approval. These preparatory activities are needed to determine the merit of further investigations and prioritize resources. The preparatory activities designation, in conjunction with a public health authority determination, allows USAFSAM to augment self-reported case counts from the inquiring unit by utilizing Air Force medical and personnel databases. These activities, in conjunction with the inquirers case ascertainment, provide appropriate estimates of case capture required for phase 2.

USAFSAM epidemiologists validate case numbers and calculate standardized incidence ratios (SIRs) or standardized mortality ratios (SMRs) by comparing the observed cases to the expected number in a similar reference population (e.g., state specific cancer registries). An SIR or SMR greater than 1.0 indicates that there are more cases or deaths than expected. This phase requires careful definition of the study population, geographic boundaries, and period for the analysis. The findings of this assessment help to determine if a more in-depth investigation is scientifically justified.

To proceed with phase 3 of the assessment, requirements for advancing from phase 1 to phase 2 must be met. Additionally, calculated SIRs or SMRs must provide evidence of elevated incidence or mortality in the study population.

Phase 3: Epidemiological evaluation

This phase serves as the critical decision point for determining if a full-scale epidemiological investigation is warranted and feasible. Using the data gathered in phase 2's feasibility assessment, USAFSAM conducts a merit-based evaluation to synthesize the findings and decide on the path forward. The primary goal is to assess whether a more resource-intensive study is scientifically justified, has a reasonable chance of success, and could contribute to public health knowledge or policy.

The evaluation considers several key factors. An investigation is typically merited if there is a statistically significant excess of a specific disease, a confirmed exposure to a known environmental or occupational hazard, and a large enough number of cases (generally 16 or more) to provide adequate statistical power.[5] The potential for the findings to affect Air Force policy or Department of Veterans Affairs (VA) benefits are also key considerations.

Conversely, a full investigation is generally not pursued if the number of cases is too small for a meaningful statistical analysis, if no statistically significant excess of disease is found, or if there is no probable or biologically plausible environmental exposure. Additionally, if the link between the exposure and the outcome of interest is already well established in scientific literature, a new study may not be undertaken. For instance, there is a well-established association between Parkinson's disease and military toxic exposures, a presumptive service connection recently expanded by the PACT Act (Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics Act) of 2022. This recognition has driven large-scale funding through Congressionally Directed Medical Research Programs and the VA, meaning foundational descriptive epidemiological studies by individual services are less important at this point.[6] The ultimate decision from this phase is to either proceed to a full epidemiological investigation (phase 4) or to conclude the inquiry and communicate the findings and rationale to concerned parties.

To proceed with phase 4 of the assessment, requirements for moving from all previous phases must be met. Additionally, a confirmed exposure to a known environmental or occupational hazard must exist for the non-infectious disease of interest. Furthermore, the disease cluster investigated must affect Air Force or Public Health policy or contribute to scientific knowledge. Lastly, the investigation must be novel, not duplicating previously established exposure and disease relationships, nor duplicating the work of others.

Phase 4: Epidemiological investigation

The final phase is the formal epidemiological investigation, which is a comprehensive scientific study designed to test the hypothesis developed in the previous phase. This is the most resource-intensive part of the process and is only undertaken when strong evidence suggests that the study will have merit, may affect policy, or contribute to scientific knowledge. This phase requires an IRB determination to access and utilize cancer registry data to include the Department of Defense Central Cancer Registry (DoDCCR), VA Central Cancer Registry (VACCR), or any state or territorial registries.

Throughout an investigation it is critical to communicate to the community that even a full-scale investigation may not identify a definite cause, due to the complexity of disease causation and the challenges of accurately assessing past exposures. Ultimately, all findings of an investigation are shared with all interested parties, to ensure transparency, address public health concerns, and promote healthy behaviors.

Operational Outcomes

By applying the multi-phased approach to incoming consultations, USAFSAM was able to triage which inquiries required full-scale epidemiological investigations versus those that could be addressed through other means, such as an initial email response, formal memorandum, or public meeting, because they did not meet the necessary criteria for a full study. From 2023-2024, the framework was applied to 8 representative consultations, to assess their need for full epidemiological investigation **(Table)**. Two consultations warranted full epidemiological studies, but the remainder did not warrant further investigation: 3 were resolved at phase 1, 2 were resolved at phase 2, and 1 was resolved at phase 3. The following 2 consultations are examples that did not warrant a full study.

TABLE. Descriptions of Consultations, with Costs and Durations for Completion, January 1, 2023–December 31, 2024

Description of Consultation	Resolution	Disposition	Estimated Cost	Estimated Time (mo.)	Cost Avoided	Time Saved (mo.)
Totals					$6,250,000	102
Non-cancer concern, base A	Resolved, phase 3	Conference call	$750,000	9	$562,500	9
Non-cancer concern, base B	Resolved, phase 1	Memorandum	$750,000	9	$562,500	9
Cancer concern, base C	Resolved, phase 1	Email response	$1,500,000	24	$1,500,000	24
Cancer concern, population D	Resolved, phase 2	Memorandum, talking points	$1,500,000	24	$1,500,000	24
Cancer concern, base E	Resolved, phase 2	Memorandum, public meeting	$1,500,000	18	$1,500,000	18
Cancer concern, base F[a]	Phase 4 study	Memorandum, Congressional briefing	$750,000	6	N/A	N/A
Cancer concern, population G[a]	Phase 4 study	Memorandum, public meetings	$1,500,000	24	N/A	N/A
Cancer concern, base H	Resolved, phase 1	Email response	$1,125,000	18	$1,125,000	18

[a]Consultation completed all 4 phases, resulting in a comprehensive epidemiological investigation.

In July 2023, an inquiry was received from an Air Force Reserve unit about a perceived elevated cancer risk among its personnel, located on a closed Air Force base designated as a Superfund site. The unit provided a list of 18 individuals diagnosed with different types of cancer over a 10-year period. USAFSAM proceeded to investigate the potential cluster using phases 1 and 2 of the new procedure. By calculating SIRs and comparing the unit's data to state-specific cancer rates, USAFSAM epidemiologists determined that the observed 18 cases were well below the expected number of approximately 50 cases for that population. Since the analysis did not show a greater than expected number of cancers, and the reported cancers were not etiologically related, a full epidemiological investigation was not warranted, and the consultation was resolved at phase 2. The results and rationale were formally communicated to unit leadership and subsequently shared with all personnel in a public meeting, evincing the process's effectiveness in providing a timely, data-driven, and transparent response.

In September 2023, USAFSAM received an inquiry regarding concerns of a potential amyotrophic lateral sclerosis (ALS) cluster associated with a specific residential area at an Air Force installation from 2004 through 2007. The initial investigation included collaboration with national environmental and disease experts, a review of historical environmental surveillance data, and an examination of individual medical records. Epidemiologists determined that the total number of ALS cases was too low to conduct a reliable statistical analysis or meet the threshold required to advance to phase 2. Additionally, because there are no known environmental triggers for ALS, and none of the individuals were diagnosed while stationed at the base, no scientifically supported correlations could be drawn. As a result, a full epidemiological investigation was not warranted, and the consultation was resolved at the end of phase 1. Findings were formally communicated to the unit, along with educational materials and guidance encouraging affected military families to participate in the national ALS registry.

The total cost avoidance of the 6 studies not warranting a full-scale investigation was $6,250,000 and yielded a time savings of 102 months. These figures were derived from the estimated duration of complex studies multiplied by the salaries of the required investigative team (e.g., physicians, epidemiologists, data managers). The analysis of these savings is detailed in the **Table**.

The standardized process was successfully disseminated after being presented to public health professionals at an Air Force conference in February 2025, and the SOP was published on an Air Force website in April 2025. In addition, the process was presented at the Military Health System Research Symposium in August 2025, generating international interest with a health protection delegation from a partner nation. The framework's practical value was again demonstrated in August 2025 when a Public Health officer independently applied the procedure to evaluate a potential testicular cancer cluster, an assessment later validated by USAFSAM. This successful field application underscores the procedure's effectiveness in providing timely, evidence-based, and objective evaluations at the installation level.

Public Health Implications

The successful implementation and evaluation of this standardized process provide the Air Force with a transparent, validated, and resource efficient framework. The results demonstrate that by systematically triaging inquiries, the Air Force can achieve significant cost and time savings, optimizing finite public health resources. This multi-team approach ensures that concerns are evaluated objectively and that full-scale investigations are directed toward inquiries with the greatest scientific merit and potential public health importance.

The challenges inherent in these investigations, as outlined by the CDC, cannot be overstated.[1,3] Proving causation is exceptionally difficult due to long latency periods, population mobility that complicates exposure assessments, absence of completed exposure pathway, and numerous confounding variables such as diet, heredity factors, and outside environmental exposures.[1,3] In Goodman et al.'s study, out of 576 cancer cluster investigations, only 1 had a clearly identified cause, underscoring the rarity of establishing a definitive link.[2]

The Air Force's process acknowledges these scientific hurdles by managing expectations early and focusing on statistical evaluation before committing to a costly and time intensive full-scale etiological investigation. The framework's emphasis on partnership and risk communication is critical. Cancer is a common and emotionally charged disease. By communicating the scientific process and results transparently, leadership can address concerns directly and build trust, even when a full investigation is not warranted. This validated framework ensures all concerns are evaluated equitably and scientifically, prioritizing the health and safety of the Air Force community while maintaining responsible resource stewardship.

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A New Era of Research in the U.S. Department of War Serum Repository: A Review of Published Studies, 2013–2024

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The Department of War Serum Repository (DOWSR, formerly DODSR[1]) was established in 1989 after the initiation in 1985 of the U.S. Department of War's universal mandatory human immunodeficiency virus (HIV) screening program. DOWSR, which is currently maintained by the Armed Forces Health Surveillance Division (AFHSD), preserves over 78 million serum specimens. Similar to a study that investigated research conducted from 1985 through 2012 utilizing the serum repository, this study evaluated DOWSR specimen availability, stratified by demographic variables, and conducted an analysis to determine total number and types of research studies performed using the DOWSR from 2013 through 2024. Two methods were employed: a structured PubMed search and an exhaustive online search based on records of requests for serum samples from AFHSD. Results show that the focus of DOWSR's research within the past decade has increased, especially in regulatory molecules, autoimmune indicators, and microRNA expression patterns, with increases in both the number of sponsored studies and variety of analytes investigated. Changes in the types of studies pursued by DOWSR research may reflect changing trends in funded research regarding health concerns for service members and veterans.

What are the new findings?

This review identified 112 published and 21 non-published studies that used DOWSR sera during the study period. Of the published 112 studies, 30 investigated infectious diseases, 25 investigated autoimmune disorders, 13 investigated neoplasms, and 11 investigated chronic metabolic outcomes. More studies using DOWSR specimens were published on environmental exposures and autoimmune disorders compared to prior years.

What is the impact on readiness and force health protection?

To inform risk assessments and validate force health protection measures, researchers and public health professionals use the DOWSR to retrospectively analyze emergent pathogens, exposures, and unrecognized health threats. This medical surveillance and research each enhances military readiness by improving understanding of debilitating conditions that affect service members, such as autoimmune and infectious diseases, neoplasms, and chronic metabolic conditions.

The U.S. Department of War Serum Repository (DOWSR) is an important biomedical resource, with millions of serological specimens collected from military personnel over multiple decades. The DOWSR is believed to be the largest bank of human serum in the world. The DOWSR was established in 1989 after the beginning of the Department of War (DOW)'s universal mandatory human immunodeficiency virus (HIV) screening program, initiated in 1985.[2-6] The DOWSR's initial purpose was to store residual serum samples to study and refine HIV testing, establish epidemiological risk factors, and investigate other infectious diseases.[2,3] Over time, its mission expanded significantly, to include collection and storage of operational deployment specimens in addition to those from all branches of service of the U.S. Armed Forces.[2,4,5] The policies for serum sample collection in the armed forces have not changed since the last DOWSR review study.[2]

The DOWSR is currently maintained by the Armed Forces Health Surveillance Division (AFHSD), preserving over 78 million serum specimens.[2,3] Approximately 1-2 million specimens are added annually.[5] One of the most important components of the DOWSR's utility is its direct link to the Defense Medical Surveillance System (DMSS), which allows researchers and public health investigators to link specific serum specimens to an individual's service history, deployments, and health outcomes.[7] This longitudinal data link makes the DOWSR an invaluable epidemiological surveillance tool, supporting force health protection, disease prevention, and public health policy.

Prior studies have investigated the origination, utility, and description of the DOWSR.[2,3,7,8] The main objective of this study is to update and compare 2013-2024 data and results to the previously published description, utility, and review of published studies using the DOWSR from 1985 through 2012.[2] This report presents the total number and types of research studies performed using the DOWSR from 2013 through 2024, with an update on the number of specimens currently available.

Methods

Data on serum specimens through the end of 2024 were obtained from DMSS. Serum availability was stratified by sex, age, and branch of service. Serum samples were not accessed; only data on the availability of specimens were utilized.

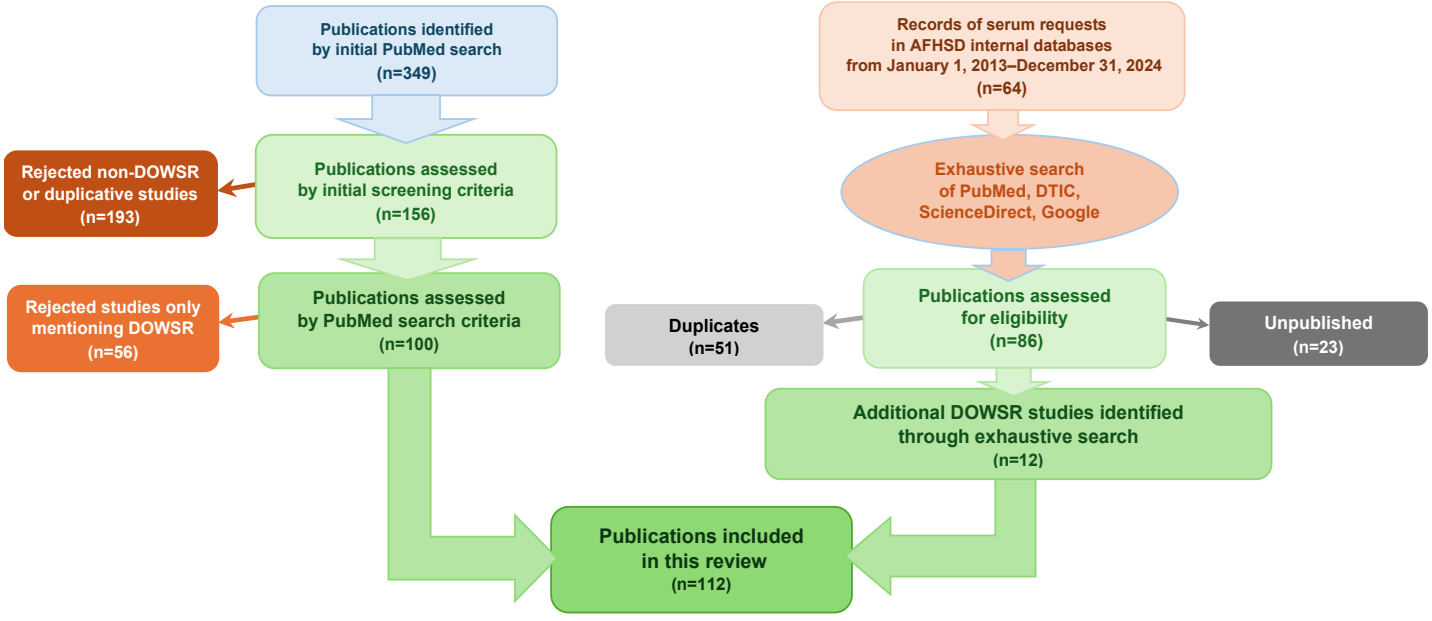
To determine the total number of publications using DOWSR serum samples, the authors conducted a review of internal, controlled-access AFHSD records, and of external public records. First, external publicly accessible scientific literature in the PubMed database was queried using the following text string: "department of defense biorepository", "dod biorepository", "DoDSR", "dodsr", "dod serum repository", "dod sr", "Department of Defense Serum Repository (DoDSR)", "Armed Forces Health Surveillance Center" (and "Branch" and "Division"), "Department of Defense Serum Repository", "military", "dod", "defense" and "biorepository*", "repositor*", " stored", "storage", "bank", and "frozen"—in English. There were 349 publications initially identified, which the researchers then restricted by the additional criteria: research studies conducted by or for the U.S. military as identified by known authors, sponsors, and institutions, confirmed use of DOWSR samples in the paper's methodology, and publication status within the study period, 2013-2024. 100 of the 349 externally identified studies met all inclusion criteria **(Figure 1)**.

The second part of the analysis was an internal search utilizing a list of serum-based studies queried at AFHSD that were supported from 2013 through 2024. The DOWSR management database tool and research protocol review tracker are record management systems implemented to manage and track all research and serum studies supported by AFHSD. According to their records, 164 unique serum requests were completed and provided to their requesters during the study period.

Additionally, for each DOWSR request, the names of the investigators and health condition(s) under study were searched first in PubMed, then if not found, in Google, then, finally, in the Defense Technical Information Center (DTIC); DTIC is an organization within the U.S. Department of War (DOW) that serves as a central repository for scientific and technical records, including reports and both published and unpublished research. In each search, the full title, list of authors, then combination of partial title and author list were queried, with results reviewed for a match with internal records. This exhaustive search method identified an additional 12 articles that used DOWSR specimens and were published from 2013 through 2024.

These record searches resulted in a combined total of 112 published studies. A systematic literature review then determined the analyte(s) and health condition(s) investigated, methodology, and significance of findings. Neither a meta-analysis nor any other statistical analyses were performed, nor were there any *a priori* decisions for inclusion based on study design.

FIGURE 1. Department of War Serum Repository Results in Literature Search Using Both Algorithmic and Intense Methods



Abbreviations: n, number; AFHSD, Armed Forces Health Surveillance Division; DOWSR, Department of War Serum Repository; DTIC, Defense Technical Information Center.

When possible, health outcomes were categorized based on the groupings defined in the previous study,[2] for ease of comparison, as was the case for 8 categories. Otherwise, categories were classified by the authors (for cases of burn pit exposure, osteoporosis, cardiovascular disease, tobacco use, deployment exposures; **Table 4**). This classification was based on the main outcome or, for studies without clear outcomes, exposure investigated. This approach was necessary chiefly to account for the emergence of exposure-focused studies, without defined outcomes, that did not conform to the previously established categories.

TABLE 1. Summary Statistics for Ages of Individuals at Serum Collections and Timings of Specimen Collections for Department of War Serum Repository[a]

	Minimum	Maximum	Mean	Standard Deviation	Median
Age at date of collection, *y*	17	70	27.71	8.64	25
Specimens per person, *n*	1	35	5.52	4.74	4
Duration between specimens, *y*	0	34	1.40	1.32	1
Duration between first and last specimens, *y*	0	37	6.32	6.79	4

Abbreviation: *y*, years; *n*, number.
[a] Analysis restricted to samples with ages 17-70 years at collection.

Results

Contents of the DOWSR

At the end of this study's surveillance period, December 31, 2024, the DOWSR contained just under a total of 78.6 million samples. The exclusion of unavailable samples and those without identifiable or demographic information resulted in 61.9 million samples from 11.4 million distinct service members. After the exclusion of samples with erroneous or outlier information (e.g., missing age, younger than age 17 years or older than age 70 years at collection, outlier SSNs with the top 0.01% serum sample counts, n=1,112), 61.3 million (78.1%) of the serum samples were available for researchers, from 11.1 million members, with an average age of 27.7 years (standard deviation [SD] 8.64, median 25) at time of serum collection. There was a mean of 5.5 samples per person (SD 4.75, median 4), with a mean of 1.4 years between sample collections (SD 1.32, median 1), and a mean range from first to last sample per person of 6.3 years (SD 6.79, median 4) **(Table 1)**.

Among the 61.3 million samples that met the inclusion criteria, contributors were mostly male (77.9%) and served in the Army (41.0)% (data not shown). The annual number of serum samples provided to the DOWSR steadily increased from 1985 to its peak in 2003 (n=2.3 million), then remained relatively stable until 2010, after which it slowly started to decrease to 1.3 million samples at the end of 2024 **(Figure 2)**.

Figure 3 shows the distribution of age at time of serum collection for service members ages 17-70 years. 21-year-olds contributed the highest number of serum samples (n=4.1 million, 6.8%). From 21 years of age, serum contribution decreased with increasing age **(Figure 3)**. Service members who were younger than age 30 years contributed 68.6% of all serum specimens during the surveillance period, while those older than age 50 years contributed only 1.7% of serum samples **(Figure 3)**. The majority (69.3%) of service members provided 3 or more specimens to the DOWSR, with over one-third (36.1%) contributing 6 or more specimens **(Table 2)**.

FIGURE 2. Distribution of Total Department of War Serum Repository Specimens, by Year

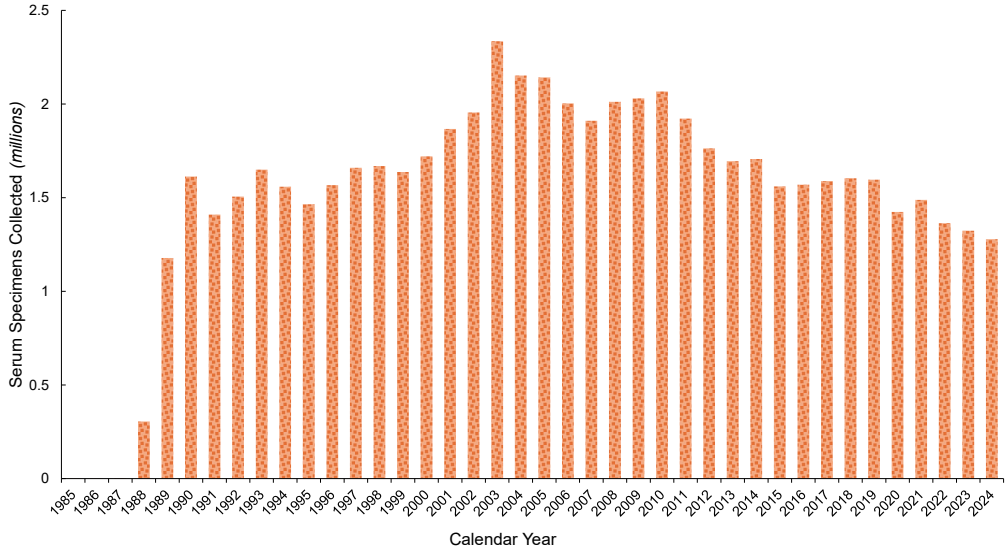
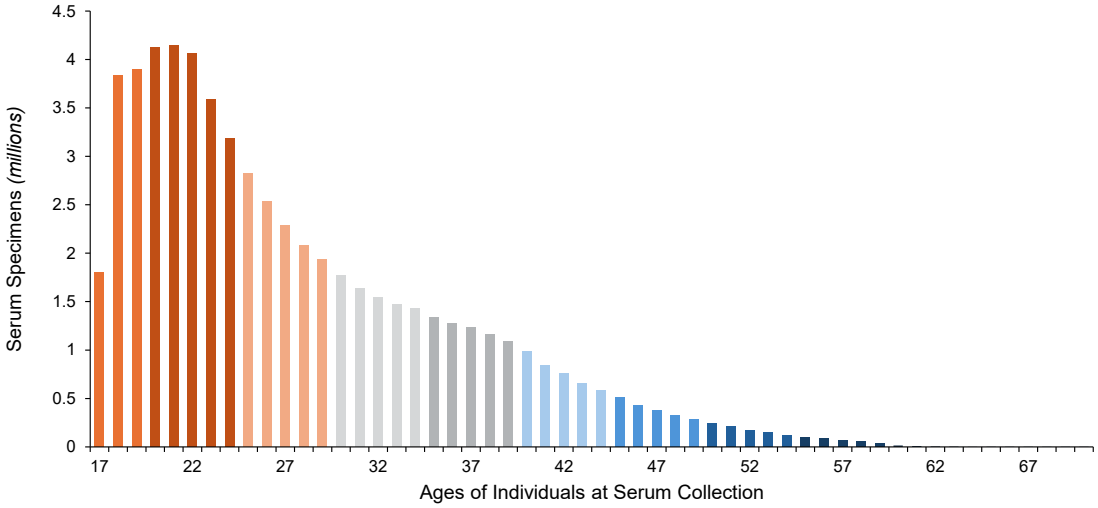


FIGURE 3. Distribution of Ages at Serum Collections for Department of War Serum Repository[a]



*Excluded are samples without date of birth, younger than 17, or older than 70 years of age at collection.

Publication of studies using DOWSR specimens, 2013–2024

Combining external and internal search methods **(Figure 1)**, a total of 112 published studies that utilized specimen from the DOWSR were identified; this study determined that 21 of the supported studies resulted in non-peer reviewed reports. Among the 112 studies, 137 analytes were investigated, with some studies investigating more than 1 analyte **(Table 3, Table 4)**. Four of the most common analytes studied were regulatory molecules (22 studies), microRNA expression patterns (9 studies), rheumatoid arthritis biomarkers (8 studies), and 25-hydroxyvitamin D (6 studies) **(Table 3)**.

The studies investigating regulatory molecules, which included metabolites, hormones, chemokines, and cytokines, were varied and included studies on numerous cancers, multiple sclerosis, traumatic brain injury, effects of burn pit exposure, lupus, and many more (data not shown). As an example of research conducted using regulatory analytes, 1 study evaluated the association between pentraxin 3 (PTX3) and schizophrenia and bipolar disorder and found that low serum levels of PTX 3 were predictive of schizophrenia.[9]

Of the 9 studies that analyzed microRNA expression patterns, 5 investigated burn pit deployment outcomes and non-specific environmental exposures. These deployment studies showed that miRNAs were a valid measure for environmental exposures and polycyclic aromatic hydrocarbons (PAH) exposures were elevated post-deployment.[10,11] The other studies investigating microRNA expression patterns comprised 2 feasibility or pilot studies, 1 methods validation study, and 1 study of miRNA dysregulation due to post-traumatic stress disorder (PTSD).[12] Also investigating environmental exposures, studies evaluating persistent organic pollutants known to be endocrine disruptors, such as polybrominated diphenyl ethers (PBDEs), polybrominated biphenyls (PBBs) and polychlorinated biphenyls (PCBs), and per- and polyfluoroalkyl substances (PFAS) showed evidence to suggest that being an Air Force firefighter was a major predictor of measurable PFAS, which was directly linked to higher risk of testicular germ cell tumors **(Table 3)**.[23]

Of the 8 rheumatoid arthritis studies, 5 investigated anti-cyclic citrullinated peptides (ACCPs) and found evidence both that ACCPs were good predictors of future rheumatoid arthritis diagnoses and were associated with more rapid progression from pre-clinical to clinical rheumatoid arthritis.[13-17]

Studies investigating 25-hydroxyvitamin D (25[OH]D) included a study that showed subjects in the lowest octile of 25(OH)D had the highest risk of suicide.[18] An influenza vaccine response study showed no evidence of association between 25(OH)D levels and post-vaccination antibody titers to influenza vaccine.[19] The remaining 3 studies, which investigated type 1 diabetes mellitus, Crohn's disease, and osteoporosis, found a higher risk of type 1 diabetes mellitus among individuals whose 25(OH)D levels were in the lowest 20% of those measured,[20] and no significant associations between 25(OH)D levels and Crohn's disease or osteoporosis, respectively.[21,22]

The most common investigational health outcomes were infectious diseases (30 studies) and autoimmune disorders (25 studies) **(Table 4)**. Neoplasms were the focus

TABLE 2. Counts of Individuals Who Provided Specimens to the Department of War Serum Depository and Numbers of Specimens per Individual

No.	No.	%
1	1,728,781	15.55
2	1,685,535	15.16
3	1,389,424	12.50
4	1,260,634	11.34
5	1,040,951	9.36
>5	4,011,106	36.08

Abbreviation: No., number.

TABLE 3. Analytes from Published Studies Utilizing Department of War Serum Depository Samples and Counts of Articles in Which Each Analyte Appears

Articles No.	Analytes Investigated
22	Regulatory molecules (cytokines, chemokines, hormones)
9	microRNA (miRNA) expression patterns
8	Rheumatoid arthritis factor; anti-cyclic citrullinated peptides, anti-bacterial serum antibodies
7	Cotinine levels
6	25-hydroxyvitamin D
5	Polycyclic aromatic hydrocarbons (PAHs)
4	Influenza A antibodies, C-reactive proteins
3	Multiple sclerosis (whole proteome autoantibodies, IgG systemic sclerosis autoantibodies); leishmaniasis; lupus nephritis anti-double stranded DNA antibodies; polybrominated biphenyls (PBBs); polychlorinated biphenyls (PCBs); human DNA
2	Crohn's disease antibodies; SARS-CoV-2; irritable bowel disease; meningitis vaccine; tick-borne rickettsia; IgG for leptospirosis; polybrominated diphenyl ethers (PBDEs); Epstein-Barr virus (EBV) peptides; human papillomavirus (HPV); dengue virus; mumps virus; yellow fever; organochlorine pesticides; collagen, aggrecan synthesis biomarkers; bone turn-over biomarkers; adenovirus 36 antibody
1	Japanese encephalitis antibodies; granulomatosis with polyangiitis; IgG for *Neisseria gonorrhoeae*; hemagglutinin pseudovirus antibodies; M-type phospholipase A2 receptor; herpes, syphilis antibodies; thrombospondin type-1 domain 7A (THSD7A); nutritional metabolites; immunoglobulin light chain amyloidosis; coccidioides IgG or IgM; *Amblyomma americanum* (lone star tick);, tick-borne ehrlichia; thyroid peroxidase (TPO) antibodies; B-cell follicular lymphoma (FL); diffuse large B-cell lymphoma (DLBCL); per-, polyfluoro-alkyl substances (PFAS); protein biomarkers; inflammation-related candidate biomarkers: TNF receptor 2 (TNFR2), IL17A, VEGFR3, and resistin; lupus erythematosus interferon alpha; β-trace protein (BTP), β2-microglobulin (B2M); metanephrine (MN); normetanephrine (NMN); *Porphyromonas gingivalis* antibody; anti-salmonella, anti-norovirus antibodies; smallpox vaccine; IgG for *Borrelia burgdorferi*; bacterial translocation biomarkers; soluble CD14 (sCD14); Ross River virus antibodies; hepatitis B antibody; hepatitis C antibody; monoclonal protein; free light chains; polychlorinated dibenzo-p-dioxins (PCDDs); polychlorinated dibenzofurans (PCDFs)

Abbreviations: miRNA, micro-ribonucleic acid; PAHs, Polycyclic aromatic hydrocarbons; IgG, immunoglobulin G; DNA, deoxyribonucleic acid; PBBs, polybrominated biphenyls; PCBs, polychlorinated biphenyls; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; PBDEs, polybrominated diphenyl ethers; EBV, Epstein-Barr virus; HPV, human papillomavirus; THSD7A, thrombospondin type-1 domain 7A; IgM, immunoglobulin M; TPO, thyroid peroxidase; FL, follicular lymphoma; DLBCL, diffuse large B-cell lymphoma; PFAS, per-, polyfluoro-alkyl substances; TNF, tumor necrosis factor; TNFR2, tumor necrosis factor receptor 2; IL17A, interleukin-17A; VEGFR3, vascular endothelial growth factor receptor 3; BTP, β-trace protein; B2M, β2-microglobulin; MN, metanephrine; NMN, normetanephrine; sCD14, soluble CD14; polychlorinated dibenzo-p-dioxins; PCDFs, polychlorinated dibenzofurans.

TABLE 4. Publication Counts from Studies Utilizing the Department of War Serum Repository, by Health Outcome and Analyte Investigated, 2013–2024

Health Exposure or Outcome	Antibodies	Regulatory Molecules, Biomarkers	Chemical Compounds	Human DNA	Nutrient	Total Analytes	Total Unique Studies
	No.	No.	No.	No.	No.	No.	No.
Infectious diseases	28	3		1		32	30
Neoplasms	3	9	3			15	13
Chronic metabolic	6	5	4		2	17	11
Autoimmune disorders	18	11	1	1	2	33	25
Non-specific	1	2	1			4	4
Vaccine-induced immunity	4				1	5	4
Physical injury[a]		6			1	7	7
Mental illness		2	1			3	3
Burn pit exposure	1	6	4			11	8
Osteoporosis		2			2	4	3
Cardiovascular disease				1		1	1
Tobacco use		1				1	1
Deployment exposures[b]		2	2			4	2
Total	61	49	16	3	8	137	112

Abbreviations: DNA, deoxyribonucleic acid; No., number.
[a] Includes studies on suicide.
[b] Non-specific deployment exposures.

of 13 studies, chronic metabolic disorders were the focus of 11 studies, physical injuries were the focus of 7 studies, and burn pit exposures were the focus of 8 studies **(Table 4)**. Four studies were classified as nonspecific: 3 were on general environmental exposures, 1 was for the creation of a biorepository for future study **(Table 4)**.

For comparison of both health exposure and outcome with analytes measured, certain types of analytes were grouped **(Table 4)**: cytokines, chemokines, and hormone-like molecules were grouped generally as regulatory molecules. Studies conducting human DNA sequencing were similarly grouped, and antibodies for specific outcomes were grouped by outcome to simplify the analysis. After analytes were grouped into major categories, 61 studies investigated antibodies, mostly in the infectious disease (n=28) and autoimmune disorder (n=18) categories. Forty-nine studies investigated regulatory molecules and biomarkers, chiefly autoimmune disorders (n=11). Sixteen studies investigated chemical compounds, mostly within the burn pit exposures (n=4) and chronic metabolic (n=4) categories. The 8 studies of nutrients were arrayed among a variety of categories including chronic metabolic (n=2), autoimmune (n=2), and osteoporosis (n=2) studies, and the 3 of human DNA were within infectious disease, autoimmune, and cardiovascular categories **(Table 4)**.

Discussion

In 1997, the DOWSR began expanding from being chiefly an instrument of the DOW HIV program to support a wider mission of broader health surveillance and identifying, preventing, and controlling service-linked illnesses.[28,30] It is no surprise that the variety of study topics has continued to increase since inception. The total number of studies and analytes investigated increased from 57 distinct analytes within 76 studies from 1985 to 2012[2] to 65 analytes within 112 studies from 2013 to 2024.

This study noted several differences in the types of analytes and health exposures or outcomes assessed by investigators since the last review of DOWSR-supported publications in 2015.[2] In particular, the number of studies analyzing regulatory molecules, miRNAs, and autoantibodies increased. Although the leading investigational outcomes (e.g., infectious disease, autoimmune disorders, neoplasms) were the same in both periods, this study indicates that in the past decade attention within those outcome categories shifted. In addition, studies investigating chronic metabolic conditions, physical injuries, and deployment-related exposures increased.

Reflecting the initial goal of the DOWSR, sexually transmitted infections (including HIV and herpes) had previously been the most popular infectious disease study topic.[2] In 2013-2024, focus of infectious disease research shifted to respiratory infections (including influenza and SARS-CoV2) and to a wide array of vector-borne diseases including leishmaniasis and rickettsia **(Table 3)**. Increasingly prevalent studies on arboviruses and vector-borne pathogens may reflect changes in operational deployments in areas with higher risk and spread of vector-borne diseases within the U.S. and abroad.

There was a slight increase in the number of studies published on autoimmune disorders compared to the prior review, with rheumatoid arthritis biomarkers representing a large proportion of these studies (n=3 previously, increased to n=8).[2] The DOW Peer Reviewed Medical Research Program has funded arthritis research since 2009, and the Fiscal Year 2024 National Defense Authorization Act established a standalone Arthritis Research Program under the Congressionally Directed Medical Research Programs (CDMRP), which will likely continue to increase the number of these DOWSR-supported biomarker studies.[32]

As the world's largest serum repository, and with a chronology exceeding 20 years for many individuals, the DOWSR contains pre-diagnostic data for many individuals who have developed rare cancers. This is a well-suited resource to the risk factor analyses increasingly performed for cancer studies. Increased neoplasm research has likely been fueled by the cancer "moonshot" initiatives of 2016 and 2022, which sought to engage private and public resources and expertise to accelerate development of cancer treatments, diagnostics, and prevention.[33] Research projects led by the Murtha Cancer Center[26] helped advocate for increased cancer research related to military exposures through the Framingham and Project for Military Exposures and Toxin History Evaluation in US service members (PROMETHEUS) initiatives. The trends seen in this review—an increase from the original review's 11 studies targeting neoplasms within 27 years to 13 studies within 11 years—correlate with the broader priorities of those initiatives and emphasize the growing utilization of the DOWSR for oncological research.

Studies on burn pit and other environmental or deployment-related exposures became more common following the 2016 publication of the *Journal of Occupational and Environmental Medicine*,[29] which highlighted deployment exposures, biomarkers, and health outcomes studies utilizing specimens from the DOWSR; there was only a single burn pit study from 1985 to 2012, compared to 8 from 2013 to 2024.[2] Many environmental exposure studies are linked to concerns about exposures at specific bases, such as radioactive, heavy metal, pesticide, and PFAS. These studies have become more common following passage of the Sergeant First Class Heath Robinson Honoring Our Promise to Address Comprehensive Toxics (PACT) Act of 2022, which mandated that the Department of Veterans Affairs (VA) and other federal agencies conduct new health and exposure research studies.[24] The PACT Act also helped establish the VA 'presumption of exposure' policy, which assumes that veterans who served in specific locations during certain periods of time were exposed to the harmful chemicals used (with Agent Orange an explicit example); this reduces the burden of proof for veterans seeking care.[24] Further, the CDMRP has expanded over the past decade, funding research into numerous conditions affecting service members including toxic exposures.[25] Research using the presumptive exposure model may become more common in DOWSR studies, with increased veterans' advocacy to understand exposure associations with health outcomes, and as laboratory methods for metabolomic and genomic studies improve.

The primary limitation of this study is that investigators were not systemically contacted, which means it was possible for some studies to have been missed in this review, particularly studies with 'negative' or inconclusive findings, as those are less likely to be published. In addition, abstracts were not included in this review. Because AFHSD tracks all requests for serum as part of its record management systems, it is unlikely that a significant number of published studies are missing from this review, however.

Findings from this review of studies published from 2013 through 2024 indicate that DOW researchers and public health professionals have continued to utilize the DOWSR to enhance military readiness by contributing to the etiological understanding of debilitating conditions, as well as providing important information to improve our understanding of the spread of infectious diseases. The DOWSR is a crucial resource for maintaining a healthy and deployable force. Its importance lies in its ability for researchers and public health personnel to efficiently and retrospectively analyze emergent pathogens, novel exposures, and previously unrecognized health threats to inform risk assessments and validate force health protection measures.

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Disclaimers
The views expressed in this report reflect the results of research conducted by the authors and do not necessarily reflect official policy nor position of the Defense Health Agency, Department of War, or the U.S. Government.

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SUPPLEMENTARY TABLE. Studies Included in Analyses Utilizing Department of War Serum Repository Samples, with Categories Assigned, 2013–2024

Title	Journal, Book or Database	Publication Year	Category
Performance of Anti-Cyclic Citrullinated Peptide Assays Differs in Subjects at Increased Risk of Rheumatoid Arthritis and Subjects with Established Disease	*Arthritis & Rheumatology*	2013	Auto-immune disorder or disease
Low Vitamin D Status and Suicide: A Case-Control Study of Active Duty Military Service Members	*PLoS One*	2013	Physical injury
Preclinical Serum 25-Hydroxyvitamin D Levels and Risk of Type 1 Diabetes in a Cohort of US Military Personnel	*American Journal of Epidemiology*	2013	Chronic metabolic
Elevated Subclinical Double-Stranded DNA Antibodies and Future Proliferative Lupus Nephritis	*Clinical Journal of the American Society of Nephrology*	2013	Auto-immune disorder or disease
Relation Between Asymptomatic Proteinase 3 Antibodies and Future Granulomatosis with Polyangiitis	*Clinical Journal of the American Society of Nephrology*	2013	Auto-immune disorder or disease
HPV Seroprevalence Among Servicemembers Entering Military Service During 2011-2012	*MSMR*	2013	Infectious diseases
Increased Serum Free Light Chains Precede the Presentation of Immunoglobulin Light Chain Amyloidosis	*Journal of Clinical Oncology*	2014	Chronic metabolic
Adenovirus 36 Antibodies Associated with Clinical Diagnosis of Overweight/Obesity But Not BMI Gain: A Military Cohort Study	*Journal of Clinical Endocrinology and Metabolism*	2014	Chronic metabolic
Serum Proteomic Analysis of a Pre-Symptomatic Multiple Sclerosis Cohort	*European Journal of Neurology*	2015	Auto-immune disorder or disease
Effects of Traumatic Amputation on β-Trace Protein and β2-Microglobulin Concentrations in Male Soldiers	*American Journal of Nephrology*	2015	Physical injury
Anti-Carbamylated Protein Antibodies Are Present Prior to Rheumatoid Arthritis and Are Associated with its Future Diagnosis	*Journal of Rheumatology*	2015	Auto-immune disorder or disease
Seroconversion to Japanese Encephalitis Virus Among U.S. Infantry Forces in Korea	*American Journal of Tropical Medicine and Hygiene*	2015	Infectious diseases
Seroprevalence and Seroincidence of Herpes simplex Virus (2006-2010), Syphilis (2006-2010), and Vaccine-Preventable Human Papillomavirus Subtypes (2000-2010) Among US Military Personnel	*Sexually Transmitted Diseases*	2015	Infectious diseases
Seroprotective Antibodies to 2011 Variant Influenza A(H3N2v) and Seasonal Influenza A(H3N2) Among Three Age Groups of US Department of Defense Service Members	*PLoS One*	2015	Infectious diseases
Pilot Metabolome-wide Association Study of Benzo(a)pyrene in Serum From Military Personnel	*Journal of Occupational and Environmental Medicine*	2016	Burn pit
Detection of Serum microRNAs from Department of Defense Serum Repository: Correlation With Cotinine, Cytokine, and Polycyclic Aromatic Hydrocarbon Levels	*Journal of Occupational and Environmental Medicine*	2016	Chronic metabolic
High-Resolution Metabolomics for Nutrition and Health Assessment of Armed Forces Personnel	*Journal of Occupational and Environmental Medicine*	2016	Chronic metabolic
High-Resolution Metabolomics Assessment of Military Personnel: Evaluating Analytical Strategies for Chemical Detection	*Journal of Occupational and Environmental Medicine*	2016	Chronic metabolic
Longitudinal Plasma Metanephrines Preceding Pheochromocytoma Diagnosis: A Retrospective Case-Control Serum Repository Study	*European Journal of Endocrinology*	2016	Neoplasm
The Association Between Serum Biomarkers of Collagen Turnover and Subsequent Anterior Cruciate Ligament Rupture	*American Journal of Sports Medicine*	2016	Physical injury
MicroRNA Expression Profiling of the Armed Forces Health Surveillance Branch Cohort for Identification of "Enviro-miRs" Associated with Deployment-Based Environmental Exposure	*Journal of Occupational and Environmental Medicine*	2016	Burn pit
Metabolic Pathways and Networks Associated with Tobacco Use in Military Personnel	*Journal of Occupational and Environmental Medicine*	2016	Tobacco use
Serologic Microbial Associated Markers Can Predict Crohn's Disease Behaviour Years Before Disease Diagnosis	*Alimentary Pharmacology & Therapeutics*	2016	Auto-immune disorder or disease
Altered Type II Interferon Precedes Autoantibody Accrual and Elevated Type I Interferon Activity Prior to Systemic Lupus Erythematosus Classification	*Annals of the Rheumatic Diseases*	2016	Auto-immune disorder or disease
Identification of Extracellular miRNA in Archived Serum Samples by Next-Generation Sequencing from RNA Extracted Using Multiple Methods	*Molecular Biology Reports*	2016	Chronic metabolic

SUPPLEMENTARY TABLE. Studies Included in Analyses Utilizing Department of War Serum Repository Samples, with Categories Assigned, 2013–2024

Title	Journal, Book or Database	Publication Year	Category
Introduction to Department of Defense Research on Burn Pits, Biomarkers, and Health Outcomes Related to Deployment in Iraq and Afghanistan	*Journal of Occupational and Environmental Medicine*	2016	Burn pit
Immune Responses in U.S. Military Personnel Who Received Meningococcal Conjugate Vaccine (MenACWY) Concomitantly with Other Vaccines Were Higher than in Personnel Who Received MenACWY Alone	*Clinical and Vaccine Immunology*	2016	Vaccine-induced immunity
Anti-Myeloperoxidase Antibodies Associate with Future Proliferative Lupus Nephritis	*Autoimmune Diseases*	2017	Auto-immune disorder or disease
Elevated Serum Levels of sCD30 and IL6 and Detectable IL10 Precede Classical Hodgkin Lymphoma Diagnosis	*Cancer Epidemiology, Biomarkers & Prevention*	2017	Neoplasm
Dengue Virus Exposures Among Deployed U.S. Military Personnel	*American Journal of Tropical Medicine and Hygiene*	2017	Infectious diseases
Thyroid-Stimulating Hormone, Thyroid Hormones, and Risk of Papillary Thyroid Cancer: A Nested Case-Control Study	*Cancer Epidemiology, Biomarkers & Prevention*	2017	Neoplasm
Serially Measured Pre-Diagnostic Levels of Serum Cytokines and Risk of Brain Cancer in Active Component Military Personnel	*British Journal of Cancer*	2018	Neoplasm
Combination of Anti-Citrullinated Protein Antibodies and Rheumatoid Factor Is Associated with Increased Systemic Inflammatory Mediators and More Rapid Progression from Preclinical to Clinical Rheumatoid Arthritis	*Clinical Immunology (Orlando)*	2018	Auto-immune disorder or disease
25-Hydroxyvitamin D, Influenza Vaccine Response and Healthcare Encounters Among a Young Adult Population	*PLoS One*	2018	Vaccine-induced immunity
Asymptomatic Visceral *Leishmania infantum* Infection in US Soldiers Deployed to Iraq	*Clinical Infectious Diseases*	2018	Infectious diseases
Metabolome-wide Association Study of Deployment to Balad, Iraq or Bagram, Afghanistan	*Journal of Occupational and Environmental Medicine*	2019	Deployment exposures
Use of Biomarkers to Assess Environmental Exposures and Health Outcomes in Deployed Troops	*Journal of Occupational and Environmental Medicine*	2019	Burn pit
Mumps Outbreak and MMR IgG Surveillance as a Predictor for Immunity in Military Trainees	*Vaccine*	2019	Infectious diseases
Autoantibodies are Present Before the Clinical Diagnosis of Systemic Sclerosis	*PLoS One*	2019	Auto-immune disorder or disease
Cohort Profile of the Proteomic Evaluation and Discovery in an IBD Cohort of Tri-Service Subjects (PREDICTS) Study: Rationale, Organization, Design, and Baseline Characteristics	*Contemporary Clinical Trials Communications*	2019	Non-specific
Machine Learning Approach for Predicting Past Environmental Exposures From Molecular Profiling of Post-Exposure Human Serum Samples	*Journal of Occupational and Environmental Medicine*	2019	Non-specific
Integrative Network Analysis Linking Clinical Outcomes with Environmental Exposures and Molecular Variations in Service Personnel Deployed to Balad and Bagram	*Journal of Occupational and Environmental Medicine*	2019	Non-specific
Neutralizing and Neuraminidase Antibodies Correlate with Protection Against Influenza During a Late Season A/H3N2 Outbreak Among Unvaccinated Military Recruits	*Clinical Infectious Diseases*	2019	Vaccine-induced immunity
Detection of Head and Neck Cancer Based on Longitudinal Changes in Serum Protein Abundance	*Cancer Epidemiology, Biomarkers & Prevention*	2020	Neoplasm
Timing of Elevations of Autoantibody Isotypes Prior to Diagnosis of Rheumatoid Arthritis	*Arthritis & Rheumatology*	2020	Auto-immune disorder or disease
Detection of PLA2R Autoantibodies Before the Diagnosis of Membranous Nephropathy	*Journal of the American Society of Nephrology*	2020	Auto-immune disorder or disease
Serum Neurofilament Light Chain Levels in Patients with Presymptomatic Multiple Sclerosis	*JAMA Neurology*	2020	Auto-immune disorder or disease
Polybrominated Diphenyl Ethers, Polybrominated Biphenyls, and Risk of Papillary Thyroid Cancer: A Nested Case-Control Study	*American Journal of Epidemiology*	2020	Neoplasm
Blast Traumatic Brain Injury and Serum Inflammatory Cytokines: A Repeated Measures Case-Control Study Among U.S. Military Service Members	*Journal of Neuroinflammation*	2020	Physical Injury

SUPPLEMENTARY TABLE. Studies Included in Analyses Utilizing Department of War Serum Repository Samples, with Categories Assigned, 2013–2024

Title	Journal, Book or Database	Publication Year	Category
The Serogroup B Meningococcal Outer Membrane Vesicle-based Vaccine 4CMenB Induces Cross-Species Protection Against *Neisseria gonorrhoeae*	*PLoS Pathogens*	2020	Infectious diseases
Duration of Seropositivity Following Yellow Fever Vaccination in U.S. Military Service Members	*Vaccine*	2020	Infectious diseases
Cohort Profile of a US Military Population for Evaluating Pre-Disease and Disease Serological Biomarkers in Rheumatoid and Reactive Arthritis: Rationale, Organization, Design, and Baseline Characteristics	*Contemporary Clinical Trials Communications*	2020	Auto-immune disorder or disease
Serum Biomarkers Identify Patients Who Will Develop Inflammatory Bowel Diseases up to 5 Years Before Diagnosis	*Gastroenterology*	2020	Chronic metabolic
Leptospirosis Seroconversion Surveillance Among US Marines Assigned to Japan, 2011–2015	*Military Medicine*	2020	Infectious diseases
Levels of Vitamin D Are Low After Crohn's Disease Is Established But Not Before	*Clinical Gastroenterology and Hepatology*	2020	Auto-immune disorder or disease
Circulating Blood Metabolite Trajectories and Risk of Rheumatoid Arthritis Among Military Personnel in the Department of Defense Biorepository	*Annals of the Rheumatic Diseases*	2021	Auto-immune disorder or disease
Combinations of Anticyclic Citrullinated Protein Antibody, Rheumatoid Factor, and Serum Calprotectin Positivity Are Associated with the Diagnosis of Rheumatoid Arthritis Within 3 Years	*ACR Open Rheumatology*	2021	Auto-immune disorder or disease
Serum Fatty Acid Latent Classes Are Associated with Suicide in a Large Military Personnel Sample	*Journal of Clinical Psychiatry*	2021	Physical Injury
Cohort Profile: A Migratory Cohort Study of US Marines Who Train in Australia	*BMJ Open*	2021	Infectious diseases
The Human Immune Response to Saliva of *Phlebotomus alexandri*, the Vector of Visceral Leishmaniasis in Iraq, and Its Relationship to Sand Fly Exposure and Infection	*PLoS Neglected Tropical Diseases*	2021	Infectious diseases
Antibodies to Citrullinated Protein Antigens, Rheumatoid Factor Isotypes and the Shared Epitope and the Near-Term Development of Clinically-Apparent Rheumatoid Arthritis	*Frontiers in Immunology*	2022	Auto-immune disorder or disease
The Seroepidemiology of Dengue in a US Military Population Based in Puerto Rico During the Early Phase of the Zika Pandemic	*PLoS Neglected Tropical Diseases*	2022	Infectious diseases
Immune Interference Revisited: Impact of Live-Attenuated Influenza Vaccine Prior to Yellow Fever Vaccination	*Vaccine*	2022	Vaccine-induced immunity
Coccidioidomycosis Seroincidence and Risk Among Military Personnel, Naval Air Station Lemoore, San Joaquin Valley, California, USA	*Emerging Infectious Diseases*	2022	Infectious diseases
Pre-Existing Thyroid Autoimmunity and Risk of Papillary Thyroid Cancer: A Nested Case-Control Study of US Active-Duty Personnel	*Journal of Clinical Oncology*	2022	Neoplasm
Antibody Responses to *Phlebotomus papatasi* Saliva in American Soldiers with Cutaneous Leishmaniasis Versus Controls	*Frontiers in Tropical Diseases*	2022	Infectious diseases
Prediagnostic Appearance of Thrombospondin Type-1 Domain 7A Autoantibodies in Membranous Nephropathy	*Kidney360*	2023	Auto-immune disorder or disease
A Predictive Autoantibody Signature in Multiple Sclerosis	*medRxiv.org*	2023	Auto-immune disorder or disease
Use of Longitudinal Serum Analysis and Machine Learning to Develop a Classifier for Cancer Early Detection	*Methods in Molecular Biology*	2023	Neoplasm
Serum Antibodies to Periodontal Pathogens Prior to Rheumatoid Arthritis Diagnosis: A Case-Control Study	*Seminars in Arthritis and Rheumatism*	2023	Auto-immune disorder or disease
Seroprevalence as an Indicator of Undercounting of COVID-19 Cases in a Large Well-Described Cohort	*AJPM Focus*	2023	Infectious diseases
Longitudinal Changes in Immune Activation Serum Biomarkers Prior to Diagnosis and Risk of B-Cell NHL Subtypes	*Cancer Epidemiology, Biomarkers & Prevention*	2023	Neoplasm
A Nested Case-Control Study of Serum Per- and Polyfluoroalkyl Substances and Testicular Germ Cell Tumors among U.S. Air Force Servicemen	*Environmental Health Perspectives*	2023	Neoplasm
Serologic Response to the Epstein-Barr Virus Peptidome and the Risk for Multiple Sclerosis	*JAMA Neurology*	2024	Auto-immune disorder or disease

SUPPLEMENTARY TABLE. Studies Included in Analyses Utilizing Department of War Serum Repository Samples, with Categories Assigned, 2013–2024

Title	Journal, Book or Database	Publication Year	Category
Organochlorine Pesticides and Risk of Papillary Thyroid Cancer in U.S. Military Personnel: A Nested Case-Control Study	*Environmental Health*	2024	Neoplasm
Multi-Autoantibody Testing Identifies Expansion of Reactivity to Targeted Antigens Before a Diagnosis of Rheumatoid Arthritis	*ACR Open Rheumatology*	2024	Auto-immune disorder or disease
Incidence of Alpha-Gal IgE Sensitization in 3000 Military Personnel, Assessing Sex, Race, Installation, and Occupational Impacts	*Journal of Clinical Medicine*	2024	Infectious diseases
Smoking and Multiple Sclerosis Risk in Black People: A Nested Case-Control Study	*Multiple Sclerosis and Related Disorders*	2024	Auto-immune disorder or disease
Changes in the Seroprevalence of Tick-Borne Rickettsia and Ehrlichia Among Soldiers: Fort Liberty, North Carolina, 1991–2019	*Journal of Infectious Diseases*	2024	Infectious diseases
Identifying a Level of Neutralizing Antibody that Correlates with Protection from Clinical Mumps Disease During a 2017 Mumps Outbreak Among Military Service Members	*Open Forum Infectious Diseases*	2024	Infectious diseases
Development of Automated Microfluidic Immunoassays for the Detection of SARS-CoV-2 Antibodies and Antigen	*Journal of Immunological Methods*	2024	Infectious diseases
Serum Concentrations of Persistent Endocrine-Disrupting Chemicals in U.S. Military Personnel: A Comparison by Race/Ethnicity and Sex	*International Journal of Hygiene and Environmental Health*	2025	Chronic metabolic
Serum Proteomic Signatures Before the Diagnosis of Rheumatoid Arthritis: Evolving Biologic Pathways and Specific Periods of Disease Development	*Arthritis & Rheumatology*	2025	Auto-immune disorder or disease
Circulating Inflammation Biomarkers and the Risk of Esophageal Adenocarcinoma: A Nested Case-Control Study in the Department of Defense Serum Repository	*Cancer Epidemiology, Biomarkers & Prevention*	2025	Neoplasm
Long-Term miRNA Changes Predicting Resiliency Factors of Post-Traumatic Stress Disorder in a Large Military Cohort–Millennium Cohort Study	*International Journal of Molecular Sciences*	2025	Mental illness
Post-Vaccination Serum Cytokines Levels Correlate with Breakthrough Influenza Infections	*Scientific Reports*	2023	Infectious diseases
Leptospirosis and Rickettsial Diseases Sero-Conversion Surveillance Among U.S. Military Personnel in Honduras	*Military Medicine*	2022	Infectious diseases
Changes in Serum Biomarkers of Cartilage Turnover After Anterior Cruciate Ligament Injury	*American Journal of Sports Medicine*	2013	Physical injury
Early Screening and Diagnosis for Low Bone Mineral Density Utilizing Opportunistic Screening, Serum Biomarkers, and Advanced Modeling	DTIC	2023	Osteoporosis
Integrative Cardiac Health Project	DTIC	2019	Cardiovascular disease
Vitamin D Supplementation for Prevention of Post-Traumatic Osteoarthritis: Evaluation in Animal and Clinical Models	DTIC	2019	Osteoporosis
Persistence of Serogroup C Antibody Responses Following Quadrivalent Meningococcal Conjugate Vaccination in United States Military Personnel	*Vaccine*	2014	Infectious diseases
Blast Concussion mTBI, Hypopituitarism, and Psychological Health in OIF/OEFVeterans	DTIC	2014	Physical injury
Infectious Related Triggers of Crohn's Disease in Susceptible Military Personnel		2015	Chronic metabolic
GlycomePREDICTS: IgG Glycome as a Predictor of Inflammatory Bowel Disease Development	DTIC	2019	Chronic metabolic
Humoral Immunity to Primary Smallpox Vaccination: Impact of Childhood Versus Adult Immunization on Vaccinia Vector Vaccine Development in Military Populations.		2017	Vaccine-induced immunity
Predictors of the Onset of Schizophrenia in US Military Personnel	*Journal of Nervous and Mental Disease*	2015	Mental illness
Assessment of Lyme Seroconversion Among US Military Personnel in Honduras	*Military Medicine*	2025	Infectious diseases
Hepatitis B Seroprevalence in the U.S. Military and Its Impact on Potential Screening Strategies	*Military Medicine*	2020	Infectious diseases
Different Repeat Annual Influenza Vaccinations Improve the Antibody Response to Drifted Influenza Strains	*Scientific Reports*	2017	Vaccine-induced immunity
Costs and Consequences: Hepatitis C Seroprevalence in the Military and Its Impact on Potential Screening Strategies	*Hepatology*	2016	Infectious diseases

SUPPLEMENTARY TABLE. Studies Included in Analyses Utilizing Department of War Serum Repository Samples, with Categories Assigned, 2013–2024

Title	Journal, Book or Database	Publication Year	Category
Low Risk for Ross River Virus Infection in Expeditionary Forces Training in Australia Demonstrated by a Serological Survey of Marine Rotational Force-Darwin, 2012–2018	*MSMR*	2023	Infectious diseases
Monocyte Activation Detected Prior to a Diagnosis of Schizophrenia in the US Military New Onset Psychosis Project (MNOPP)	*Journal of Schizophrenia Research*	2018	Mental illness
The Deepwater Horizon Oil Spill Coast Guard Cohort Study	*Occupational and Environmental Medicine*	2018	Non-specific
Increased Risk of Monoclonal Gammopathy of Undetermined Significance in US Military Service Members: A Case-Control Study of 1,068 Service Members Deployed to Either Europe or Iraq, with or Without Reported Burn Pit and Toxic Smoke Exposure	*Blood*	2023	Non-specific
Longitudinal Analysis of Circulating Markers of Bone Turnover Across Multiple Decades in Osteoporotic Women	*Journal of Hand Surgery (American Vol.)*	2022	Osteoporosis
Live Oral Adenovirus Type 4 and Type 7 Vaccine Induces Durable Antibody Response	*Vaccines (Basel)*	2020	Infectious diseases
Analysis of Postdeployment Serum Samples Identifies Potential Biomarkers of Exposure to Burn Pits and Other Environmental Hazards	*Journal of Occupational and Environmental Medicine*	2019	Non-specific
A Nested Case-Control Study of Serum Polychlorinated Biphenyls and Papillary Thyroid Cancer Risk Among U.S. Military Service Members	*Environmental Research*	2022	Neoplasm
Assessing Health Outcomes After Environmental Exposures Associated with Open Pit Burning in Deployed US Service Members	*Journal of Occupational and Environmental Medicine*	2016	Non-specific
MicroRNAs as Novel Biomarkers of Deployment Status and Exposure to Polychlorinated Dibenzo-p-Dioxins/Dibenzofurans	*Journal of Occupational and Environmental Medicine*	2016	Deployment exposures
Polycyclic Aromatic Hydrocarbons and Polychlorinated Dibenzo-p-Dioxins/Dibenzofurans in Microliter Samples of Human Serum as Exposure Indicators	*Journal of Occupational and Environmental Medicine*	2016	Non-specific

Relevance and Comparability of Global Laboratory Molecular Detection of Influenza by the U.S. Department of War, 2025-2026

Dara A. Russell, MPH; Marissa K. Hetrich, MHS; Kathleen E. Creppage, DrPH; M. Shayne Gallaway, PhD

The U.S. Department of War's Global Emerging Infections Surveillance (GEIS) program conducts influenza surveillance within all geographic combatant commands to enhance U.S. force health protection and military readiness. This report compares laboratory-confirmed influenza data from the GEIS network with the World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS) from late 2025 through early 2026. Findings from the most recent 2025-2026 respiratory season show that while influenza trends were largely similar, with influenza A/H3N2 predominating, significant differences in percent positivity or subtype ratios emerged in Asia, East Africa, and South America. These discrepancies highlight the unique value of GEIS data, which fills critical surveillance gaps in strategic regions. This targeted surveillance provides crucial insights for mitigating infection risk to U.S. service members, informs annual vaccine strain selection, and ensures an early warning capability for emerging respiratory threats, directly supporting the readiness of the force.

What are the new findings?

During the 2025-2026 influenza season, subtype A/H3N2 was the most prevalent globally. While U.S. Department of War surveillance data largely concurred with the World Health Organization's surveillance data, there were notable differences in positivity rates and subtype ratios identified by Department of War surveillance in Asia, East Africa, and South America that revealed unique regional trends.

What is the impact on readiness and force health protection?

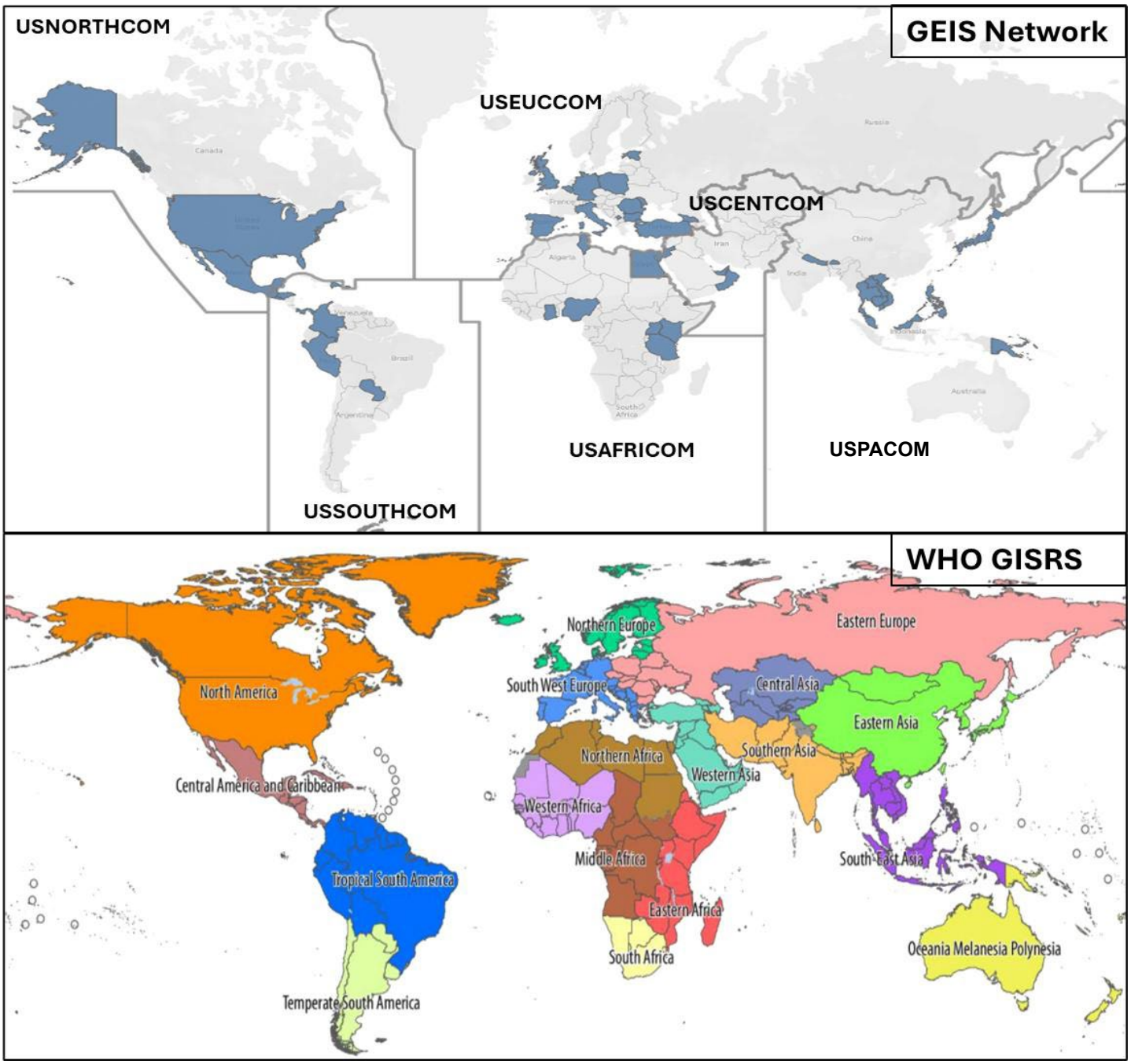
Global influenza surveillance provides vital data for mitigating risk of infection in military service members. This surveillance informs not only effective vaccine development but targeted prevention as well, directly enhancing force health protection and ensuring military readiness through the prevention of influenza outbreaks.

Historically, respiratory pathogens have caused high morbidity rates for the U.S. military and, as a result, undermined military readiness.[1] Training and deployment environments are well suited for the spread of pathogens for several reasons, including the close proximity of personnel within these settings.[2] Monitoring influenza among service members and surrounding populations is crucial for force health protection due to its potential to cause severe illness and spread rapidly. To further support force health protection and maintain battle space awareness for the armed forces, the U.S. Department of War (DOW) supports influenza laboratory and epidemiological surveillance through military, local government, and academic partners at approximately 400 locations in over 40 countries.

Laboratory capabilities and personnel expertise are the foundations for effective responses to any infectious disease threat, and the DOW's Global Emerging Infections Surveillance (GEIS) Branch of the Armed Forces Health Surveillance Division funds year-round surveillance, for both routine monitoring and possible outbreak investigations, of infectious diseases including influenza. The global network of DOW GEIS-supported laboratories generates critical data for force health protection and mitigation of infection risk to U.S. service members in all geographic Combatant Commands (CCMDs) **(Figure 1).** GEIS laboratory surveillance extends extensive DOW epidemiological surveillance utilizing Military Health System (MHS) patient health care encounter data; and complements other existing global efforts. This continual surveillance occurs at both military hospitals and clinics (CONUS and OCONUS) and foreign military and civilian sites. Surveillance efforts prioritize active duty U.S. service members and high-risk groups such as recruits and deployed personnel, but other populations (e.g., beneficiaries, foreign military, foreign civilians) are also surveilled in priority locations to increase understanding and early warning for virulent strains associated with influenza-like-illness and severe acute respiratory infections, particularly in severe or hospitalized cases.

This is achieved through extensive molecular detection and advanced genetic characterization capabilities to monitor how the influenza virus is circulating and potentially evolving. Across the GEIS Network (GEIS-N), molecular assays, including reverse transcription-polymerase chain reaction (RT-PCR), are used to identify influenza A and B and differentiate between influenza A subtypes (A/H1N1, A/H3N2).[3] The findings are shared with U.S. governmental interagency partners including the U.S. Centers for Disease Control and Prevention (CDC), in addition to the World Health Organization (WHO), with genomic data routinely uploaded to widely used public repositories including GenBank, GISAID, and the WHO Global Influenza Surveillance and Response System (GISRS).

FIGURE 1. Geographic Coverage of Influenza Surveillance by DOW GEIS-funded Laboratory Network and WHO GISRS, 2025



Abbreviations: GEIS, Global Emerging Infections Surveillance; WHO GISRS, World Health Organization, Global Influenza Surveillance and Response System; USAFRICOM, U.S. Africa Command; USCENTCOM, U.S. Central Command; USEUCOM, U.S. European Command; USPACOM, U.S. Pacific Command; USNORTHCOM, U.S. Northern Command; USSOUTHCOM, U.S. Southern Command.
Sources: Top, GEIS-created using Tableau; Bottom, WHO GISRS source image (https://www.who.int/initiatives/global-influenza-surveillance-and-response-system)

In many cases, these surveillance findings are uniquely informative: GEIS partner laboratories may be the only U.S. entity conducting infectious disease surveillance in regions where data would otherwise not exist, such as Djibouti.

Laboratory-confirmed influenza findings are disseminated routinely (immediately or monthly depending on risk threat) and are also aggregated and analyzed seasonally to contribute to greater scientific decision-making for seasonal influenza strain selection for the Northern Hemisphere influenza vaccine. Prior to the Vaccines and Related Biological Products Advisory Committee (VRBPAC)[4] meetings for the Northern Hemisphere and U.S influenza strain recommendations, the GEIS Program Office conducts a comparative analysis of circulating influenza subtype ratios between DOW GEIS partner laboratories and WHO GISRS.[5] This study assessed regional differences by analyzing and comparing laboratory confirmed influenza subtypes from the most recent 2025-2026 respiratory season between GEIS-N and WHO GISRS.

Methods

Data sources

The GEIS Program Office developed a procedure and initiated monthly standardized RT-PCR respiratory surveillance data collection in early 2020, anticipating a need for readily available information in response to the emerging COVID-19 pandemic. A standardized data collection form was developed to capture respiratory pathogens represented on widely used RT-PCR panels (updated again prior to the 2024-2025 respiratory season). As of 2026, RT-PCR respiratory testing results (including influenza by subtype) are collected from 10 GEIS-funded partner laboratories executing 30 different surveillance projects of varying scopes in 37 countries across all CCMDs. These include U.S. Northern Command (NORTHCOM), at the Department of Defense Global Respiratory Pathogen Surveillance Program and Naval Health Research Center; U.S. Southern Command (SOUTHCOM), at the Naval Medical Research Unit (NAMRU) South; U.S. European Command (EUCOM), at Landstuhl Regional Medical Center, Germany and Walter Reed Army Institute of Research (WRAIR) Europe Middle East; U.S. Africa Command (AFRICOM), at WRAIR Africa and NAMRU EURAFCENT, Ghana; U.S. Central Command (CENTCOM), at NAMRU EURAFCENT, Cairo, Egypt; and U.S. Pacific Command (PACOM), at NAMRU Indo-Pacific, WRAIR Armed Forces Research Institute of Medical Sciences (AFRIMS), and Public Health Command Pacific at Camp Zama, Japan; Tripler Army Medical Center, Honolulu, Hawai'i, and Joint Base Lewis McChord, Tacoma, Washington.

Routine reporting results are aggregated by CCMD to assess the frequency and distribution of viral subtypes over time. These routine respiratory surveillance data are used to: 1) develop or inform routine products for GEIS audience members, 2) inform *ad hoc* inquiries from CCMDs and other key stakeholders, and 3) provide context for the operational environment as needed, whether during times of conflict, military engagement, or public health emergency.

Among 135 WHO member states, WHO GISRS[5,6] serves as a global network that monitors influenza transmission and facilitates data sharing. Surveillance data generated through WHO GISRS include FluNet,[7] FluID,[8] and RespiMart.[9] FluNet is a global web-based data platform established in 1997 that is updated weekly to compile laboratory-confirmed influenza surveillance data[10]; the GEIS Program Office downloads these data once annually for comparison with GEIS laboratory-confirmed influenza surveillance data across CCMDs.

WHO transmission zones and CCMD areas of responsibility (AORs) serve different purposes and, as a result, do not mirror each other. WHO transmission zones were established to coordinate international public health efforts and disease surveillance, whereas CCMDs are U.S. Armed Forces-defined regions designed to organize and implement military operations and security cooperation activities.

As a DOW combat support agency, for this analysis GEIS realigned the WHO transmission zones to match DOW CCMD AORs to ensure maximum applicability for military service members. Some WHO regions were combined into broader groupings: 1) data from Northern Europe, Eastern Europe, South West Europe, and Western Asia (not including Israel) were combined to form 'Europe', 2) data from Central America and the Caribbean, Temperate South America, and Tropical South America were combined to form 'South America', 3) data from Northern Africa, Western Asia (Israel), Southern Asia (Afghanistan, Iran) were combined to form 'Middle East', 4) data from Eastern Asia, Southern Asia (not including Afghanistan, Iran), and South East Asia were combined to form 'Asia', while 5) data from North America, East Africa, and West Africa were unchanged and remained aligned to their regions.

Analysis

Epidemic curves or epicurves (i.e., a histogram or bar chart) were created to display the distribution of positive specimens over time associated with influenza. Time intervals are displayed on the x-axis (horizontal axis) with specimen counts displayed on the y-axis (vertical axis). These provide information on the counts, patterns of spread, time trends, and periods of increased positivity.

Influenza RT-PCR data generated from GEIS-funded surveillance activities were standardized to WHO regions by country of sample collection. Counts of influenza B Victoria and B/not-subtyped specimens were summed to create a single measure of influenza B positives for comparison to the equivalent influenza B sum in the WHO GISRS dataset. Counts for total specimens tested, specimens positive for influenza A subtypes (H1N1, H3N2, A/not-subtyped), all influenza B, and A/B co-infections were summed by WHO region and epi week.[11] Influenza percent positivity was calculated for each WHO region and epidemiological week by summing the number of H1N1, H3N2, A/not-subtyped, all influenza B, and A/B co-infection positive specimens divided by the total number of specimens tested. Co-infections were included in percent positive calculations (but not graphically represented) because co-infections were not separately defined in the WHO GISRS dataset.

WHO GISRS is based primarily on hemagglutinin (HI) RT-PCR, thus data counts for influenza A 'H1' and 'H1N12009' were combined into a single influenza A/H1N1 measure. WHO influenza A 'H3' was considered the equivalent of GEIS influenza A/H3N2. Similar to the GEIS calculations, counts for total specimens tested, specimens positive for influenza A subtypes, and influenza B were summed by WHO region and epidemiological week; and influenza percent positivity was calculated for each WHO region and epidemiological week by summing the number of H1N1, H3N2, A/not-subtyped, and influenza B positive specimens divided by the total number of specimens tested. The date of week start was converted to the date of the week end by adding 5 days to harmonize date ranges across GEIS and WHO data for data plotting.

To establish baseline seasonal patterns and directly compare the most recent respiratory seasonal findings, data from the last 2 respiratory seasons and the most current respiratory seasons were included

in the analysis (weeks ending October 7, 2023 through January 31, 2026). Counts of positive specimens by epidemiological week were graphed for each WHO region and percent positivity calculations were overlaid for each corresponding time-point. Weighted Dynamic Time Warping (wDTW)[12,13] analysis was then used to assess the similarity between the 2 trends of percent positivity (GEIS and WHO GISRS) for the most current respiratory season (September 2025–January 2026). A non-parametric permutation test was employed to allow for the statistical calculation of a *p*-value indicating the likelihood that the distance between temporal trends occurred by random chance. Given the low statistical power, a *p*-value of less than 0.20 was used as a threshold for significance. Data were processed and graphed using R Statistical Software (version 4.5.1).[14]

Results

Laboratory-confirmed influenza percent positivity temporal trends from late 2023 through early 2026 were generally similar between GEIS-N and WHO GISRS **(Figure 2)**. Prior GEIS-N and WHO GISRS respiratory season data (2023-2025) provide context for baseline observations and evolving trends and subtypes. Overall percent positivity ranged 0–38% for GEIS-N and 0–25% for WHO GISRS for all regions combined. The highest percent positivity consistently reported by GEIS was in Asia.

During the most recent respiratory season (2025-2026, **Table 1**), the percent positivity observed between GEIS-N and WHO GISRS regions was statistically different in North America ($p<0.01$), Europe ($p<0.01$), West Africa ($p<0.01$), and the Middle East ($p<0.05$), and statistically similar in South America ($p=0.33$), East Africa ($p=0.95$), and Asia ($p=0.99$). Notable differences in subtype-specific percent positivity were detected between GEIS-N and WHO GISRS regions: GEIS reported a higher percent positivity than WHO for influenza A/H3N2 in Europe (13.3% vs. 4.4%), South America (11.9% vs. 3.6%), and North America (10.4% vs. 2.5%), whereas WHO reported a higher percent positivity than GEIS for influenza A/H3N2 in Asia (20.0% vs. 11.3%); in East Africa and Asia, GEIS detected a higher percent positivity than WHO for influenza B.

Subtype ratios varied some between the GEIS-N and WHO GISRS from late 2023 through early 2026, with a greater ratio of WHO specimens being classified as influenza A (A/not-subtyped), likely a facet of laboratory testing processes by GEIS partner laboratories contributing to some WHO regions (e.g., West Africa,

TABLE. Influenza Percent Positivity by Geographic Region of GEIS-funded Laboratory Specimens and WHO GISRS, September 28, 2025–February 7, 2026

Geographic Region	GEIS[a]	GISRS	*p*-value[b]
North America	13.6	15.5	<0.01
A/not-subtyped	0.0	11.7	
A/H1N1	0.9	0.4	
A/H3N2	10.4	2.5	
B	1.1	0.9	
South America	19.4	10.4	0.33
A/not-subtyped	0.4	3.6	
A/H1N1	1.7	1.7	
A/H3N2	11.9	3.6	
B	1.6	1.5	
West Africa	16.1	19.2	<0.01
A/not-subtyped	0.2	3.6	
A/H1N1	1.8	3.8	
A/H3N2	13.2	11.0	
B	0.8	0.8	
East Africa	17.0	13.1	0.95
A/not-subtyped	7.3	0.8	
A/H1N1	1.7	4.1	
A/H3N2	2.9	7.0	
B	5.1	1.3	
Europe	18.2	24.3	<0.01
A/not-subtyped	2.9	18.5	
A/H1N1	1.7	1.3	
A/H3N2	13.3	4.4	
B	0.0	0.2	
Middle East	29.3	20.5	<0.05
A/not-subtyped	0.0	4.0	
A/H1N1	1.3	2.0	
A/H3N2	17.3	13.3	
B	0.5	1.2	
Asia	30.4	21.2	0.99
A/not-subtyped	10.4	0.1	
A/H1N1	1.1	0.3	
A/H3N2	11.3	20.0	
B	7.3	0.7	

Abbreviations: GEIS, Global Emerging Infections Surveillance; WHO, World Health Organization; GISRS, Global Influenza Surveillance and Response System; DOW, Department of War.
[a] Influenza A, B co-infections included in calculation of overall percent positivity by region for DOW GEIS surveillance.
[b] *p*-value corresponding to trend comparisons using dynamic time warping analysis

North America, South America, Europe, Middle East). During the most recent respiratory season (2025-2026), the subtype ratios observed between GEIS and WHO regions were generally similar in Asia, East Africa, Europe, North America, and South America, while dissimilar in the Middle East and West Africa. In the Middle East there are notable differences in the ratio of influenza A/H1N1 (33% and 21%) and A/not-subtyped (33% and 43%) specimens detected by GEIS and WHO, respectively, while influenza A/H3N2 accounts for about one third of all GEIS (33%) and WHO (36%) specimens in both systems. In West Africa, there are also notable differences in the ratio of influenza A/H1N1 (10% and 22%) and A/not-subtyped (59% and 43%) specimens detected by GEIS and WHO, respectively.

Discussion

Data collected from the GEIS-N are similar to what is seen in WHO GISRS during the most recent respiratory season (October 2025–January 2026). In some cases, GEIS-PL surveillance contributions are included in submissions by GEIS laboratories are closely aligned/partnered with (e.g., Ghana, Malaysia, Uganda, Vietnam) and in at least 1 instance make up a large proportion of the WHO GISRS data (NAMRU EURAFCENT Ghana influenza surveillance executed alongside CDC surveillance efforts). Differences between DOW GEIS surveillance and WHO GISRS highlight the importance of using the GEIS-N to identify and prioritize key samples for sequencing and advanced characterization. GEIS-N surveillance captures influenza circulating in over 30 countries, including several locations that border other countries, to maximize influenza specimens of viral genetic diversity. GEIS-N also includes a large service member population that is highly vaccinated (for influenza),[15] healthy, and has broad access to health care.

During each global influenza season approximately 1 billion cases occur, resulting in 3–5 million cases of severe illness and 290,000–500,000 deaths.[16] During the most recent season (October 2025–January 2026), percent positivity varied by geographic region, with highest GEIS-N-reported positivity in Asia and the Middle East and highest WHO GISRS-reported positivity in Asia and Europe.[17] Overall, in both systems, influenza A viruses predominated, with low levels of influenza B detected. Among influenza A viruses with a confirmed subtype, influenza A/H3N2 was the most prevalent in most regions.

The RT-PCR findings from GEIS-N are further enhanced and contextualized by GEIS-funded next-generation sequencing and bioinformatics (within an evolving and modernized data infrastructure). These program initiatives are a set of linked activities that support and enhance the effects and relevance of DOW influenza surveillance. Routine surveillance is important for establishing baseline trends so anomalies can be detected more rapidly. GEIS partner laboratories (with critical infectious disease surveillance capabilities) are strategically positioned in countries and regions vital to DOW operations for early, accurate detection of emerging infections. GEIS-N can also be leveraged to detect and characterize novel influenza or other emerging respiratory infections; for example, the next generation sequencing and bioinformatics capabilities that already existed were scaled up to monitor SARS-CoV-2 variants during the COVID-19 pandemic as the virus evolved and spread.[18]

Maintaining awareness of influenza activity and reinforcing preventive measures aligned with existing respiratory illness protocols are crucial for disease control. U.S. service member and beneficiary populations are the GEIS-N target populations of interest, and these findings aid in establishing a clear link to force health protection to ultimately improve health through the prevention, mitigation, and control of influenza virus transmission. Compliance with immunization requirements should be monitored to prevent transmission of influenza and other respiratory pathogens.[19]

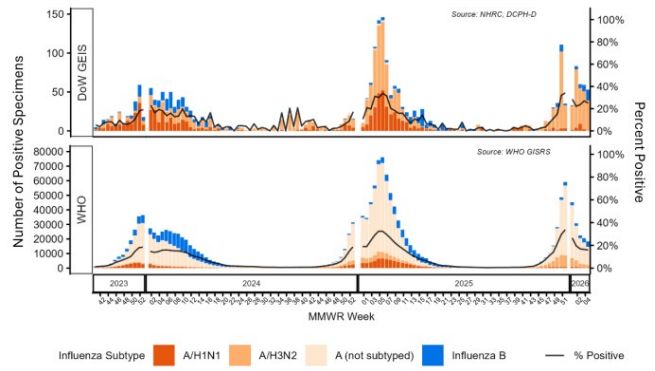
These findings should be considered alongside the following limitations. Both GEIS and WHO GISRS provide broad overviews across global regions, however the differences highlight the importance of understanding local laboratory surveillance practices. While the majority of GEIS partner laboratories currently use a respiratory viral panel (or a panel in combination with single pathogen testing), they are not formally required to test for all respiratory pathogens.[3] Likewise, sample collection and RT-PCR testing varies across GEIS surveillance projects (e.g., site collection and transport, reagent kits, shipping necessity), whereas WHO GISRS collects samples in transport media that allows specimens to be shipped to reference laboratories where they can be used for reagent production, virologic characterization, vaccine components, and other uses.

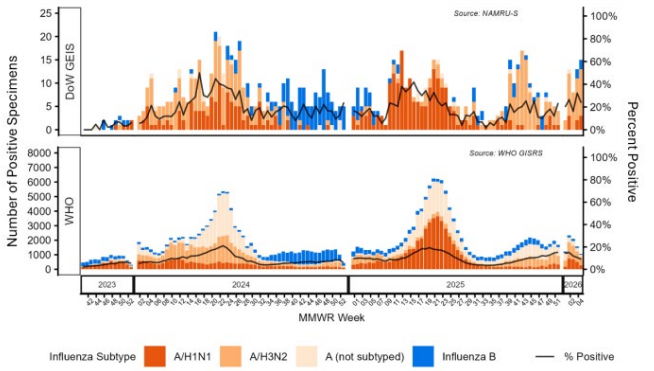
These results reflect surveillance data only reported directly to the GEIS program office by funded GEIS partner laboratories, thus it likely is an under-estimate of the true incidence and may not be representative of all respiratory infections among all DOW active component personnel globally or across the MHS. They are, however, indicative of subtypes circulating in the specified geographic populations and surveillance sites.

The GEIS and WHO GISRS target population characteristics and geographies are notably different, and we were unable to adjust for all possible confounders in this analysis that may have influenced the results. Regrouping of WHO GISRS transmission zone surveillance data into DOW CCMD AORs rather than using the established WHO GISRS transmission zones (representing well-defined seasonality patterns) may have obscured some localized transmission patterns and limit direct comparability of the 2 surveillance systems. In future analyses, we will explore how regrouping GEIS data to match WHO GISRS transmission zones will change the observed results. Finally, the DOW does not conduct influenza surveillance in every WHO member country, thus some variability is expected across regions depending on the degree of overlap between CCMDs and WHO influenza transmission zones.

Closely monitoring influenza infections can inform vaccine decision-making with broad global implications. DOW GEIS surveillance findings are unique because they include laboratory-confirmed data on a variety of populations in locations where there may be gaps in U.S. data.

FIGURE 2. Influenza Specimen Detection Numbers and Percent Positivity by GEIS-funded Laboratories and WHO GISRS, October 14, 2023–February 7, 2026





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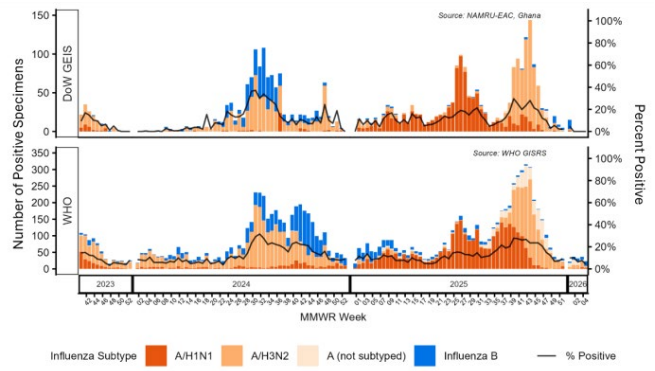
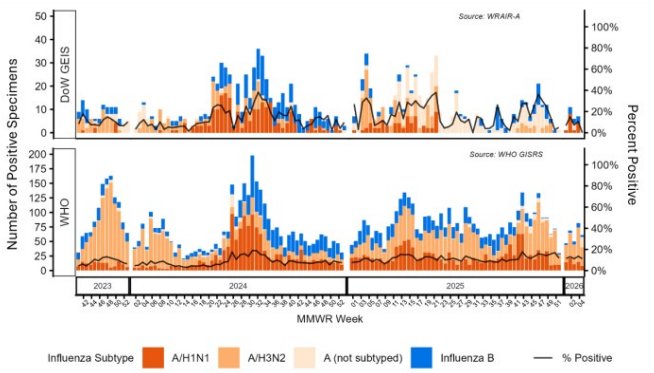
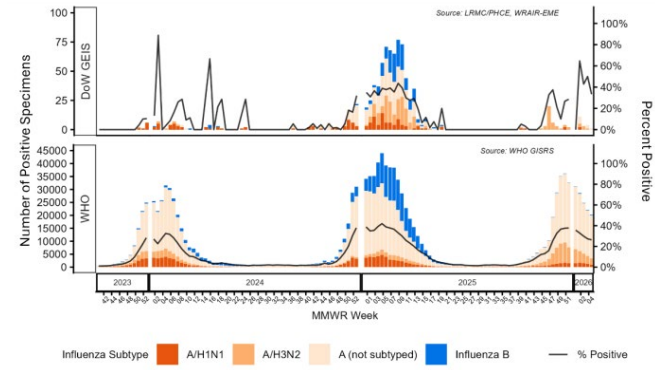


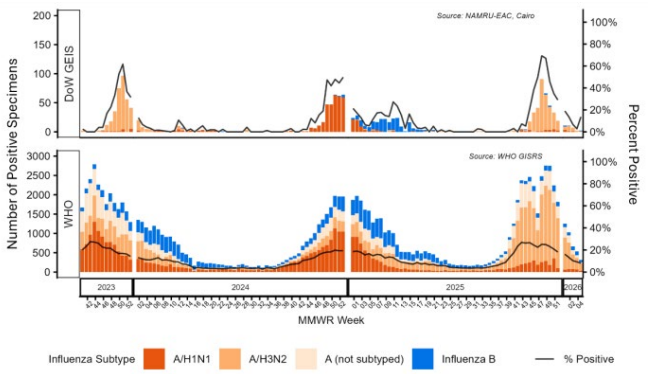
East Africa



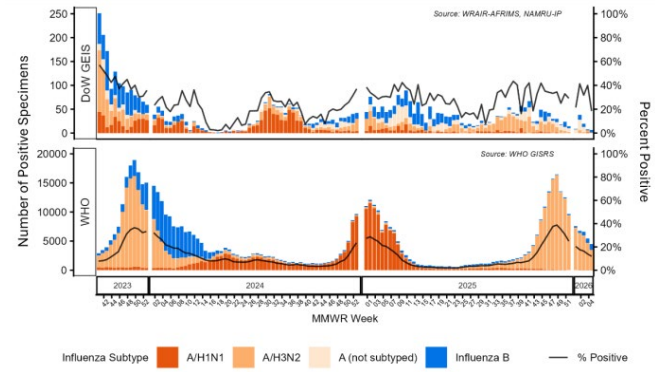
Europe



Middle East



Asia



Abbreviations: GEIS, Global Emerging Infections Surveillance; WHO, World Health Organization; GISRS, Global Influenza Surveillance and Response System; NAMRU-S, Naval Medical Research Unit SOUTH; NAMRU-EAC, Naval Medical Research Unit EURAFCENT; LRMC, Landstuhl Regional Medical Center; WRAIR-EME, Walter Reed Army Institute of Research Europe-Middle East; NHRC, Naval Health Research Center; DCPH-D, Defense Center for Public Health Dayton; WRAIR-A, Walter Reed Army Institute of Research Africa; WRAIR-AFRIMS, Walter Reed Army Institute of Research Armed Forces Research Institute of Medical Sciences; NAMRU-IP, Naval Medical Research Unit INDOPACIFIC.

GEIS-N also contributes to broader public health security objectives by establishing enduring, reliable partnerships with nations that have a shared stake in the security and prosperity of each region and facilitate broader DOW and U.S. Government collaborations or host nation surveillance. Routine public health surveillance is critical for preparedness against emerging influenza viruses.

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