The Defense Health Research Consortium

May 13, 2026

The Honorable Mitch McConnell
Chairman
Subcommittee on Defense
Senate Committee on Appropriations
Washington, DC 20510

The Honorable Christopher Coons
Vice Chair
Subcommittee on Defense
Senate Committee on Appropriations
Washington, DC 20510

Dear Chair McConnell and Vice Chair Coons:

As you begin work on the Fiscal Year (FY) 2027 Defense Appropriations Act, we thank you for your continued support of the critical and highly successful Congressionally Directed Medical Research Programs (CDMRP) at the Department of Defense (DoD). The CDMRP plays a vital role in advancing research that protects the health and readiness of our Armed Forces, military families, and veterans, while also benefiting civilian populations.

For FY 2027, we urge you to increase funding for these critical programs above FY 2024 levels by at least five percent plus inflation, to approximately $1.62 billion. This investment is essential to ensure our nation is prepared to meet current and future public health-related threats and challenges to our national security. An increase in funding is particularly vital to mitigate the impact of inflation on the purchasing power of individual CDMRP programs, as well as the 57 percent reduction in spending for these programs resulting from the enactment of the Full-Year Continuing Appropriations and Extensions Act (Public Law 119-4).

We appreciate your bipartisan efforts to fund CDMRP at $1.27 billion in FY 2026. However, this level remains well below the $1.51 billion funding level for CDMRP enacted in FY 2024. Without full restoration and growth, these programs will experience research interruptions that could have long-term implications for the health and readiness of our warfighters.

The highly innovative research portfolio supported by the CDMRP fuels scientific discovery by funding high-impact research not typically sponsored by the National Institutes of Health (NIH), the Department of Veterans Affairs (VA) or other federal agencies. Many of the programs' unique award mechanisms are specifically designed to propel the exploration of revolutionary ideas and concepts. These programs prioritize research with the potential to deliver significant impact —both within their respective scientific fields of research and the health and well-being of the men and women in the U.S. Armed Services. CDMRP grants study a range of conditions, including cancers, respiratory diseases, neurodegenerative disorders, and other toxic exposure outcomes, added as the result of the PACT Act as VA benefit presumptive service-connected health conditions. Defense health research programs are worthy of continued federal support for the following reasons:

- Directly relevant to DoD-prevalent conditions: As the enclosed white paper demonstrates, the medical research programs at DoD directly impact and are aimed at improving the health and lives of current and former members of the U.S. military, their families, and the public. Programs provide groundbreaking research on traumatic brain injury and psychological health, toxic exposures including Gulf War Illness and burn pits, respiratory health, spinal cord injury, hearing and vision loss, and newer conditions such as Long COVID. Research also focuses on existing and emerging infectious diseases that may threaten operational readiness and health security, and why diseases like ALS, multiple sclerosis and Parkinson's disease occur at greater rates in those who have served in the military. CDMRP has also funded orthopedic research that has resulted in new limb-sparing techniques to save and restore functions of injured extremities, as well as outcomes research benefiting injured warfighters in need of orthotic and prosthetic devices.

  Equally important, this disease-specific approach includes important medical research programs related to several forms of cancer (breast, pancreatic, kidney, blood, colorectal, bladder, brain tumors, lung, ovarian, prostate, stomach, liver, esophageal, melanoma, rare and childhood cancers), autoimmune diseases and other disorders (like neurofibromatosis and tuberous sclerosis complex) that have led to breakthroughs on nerve regeneration, traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD).

- Complementary – and not duplicative – of other federal research: Defense health research program grants neither duplicate nor supplant NIH or VA research efforts, but rather enhance those efforts. They fund highly innovative projects – support that is typically unavailable through other federal programs. For example, programmatically-related VA research funding is only available to VA employees (at least 0.625 full-time equivalent). CDMRP funds the best-qualified proposals from researchers and research teams at top research universities and medical centers. The NIH and DoD medical research portfolios have symbiotic relationships, allowing NIH-funded basic research to serve as a foundation for ground-breaking, disorder-targeted research at DoD. NIH and DoD program officers meet regularly to ensure collaboration and prevent duplication.

- Cutting-edge and focused on cures: While the NIH funds high-quality basic biomedical research, the defense health research programs provide essential emphasis on and support for finding innovative cures or new therapies for medical conditions. For several disorders, DoD breakthroughs have led to new clinical trials, new drug products, and novel procedures that are making a difference in the everyday lives of affected patients and families. For example, research funded by DoD led to the development of two treatments for tuberous sclerosis complex approved by Food and Drug Administration. The ALS Research Program is supporting translational research and has developed four

potential treatments for the disease, for which an effective treatment currently does not exist. The CDRMP's impact is undeniable: 61 FDA-treatments including 16 cancer drugs, a rapid blood test to detect traumatic brain injuries and more than 600 clinical trials for cutting-edge drugs and vaccines.

- Agile, adaptable, and collaborative: Each of the separate programs is guided by a specific vision and mission statement, which in addition to incorporating Congressional direction, reflects rapid change in knowledge, addresses research gaps, and prevents duplication. Annual funding prevents out-year budget commitments, which in turn further enhances programmatic flexibility. Many DoD programs identify, develop and fund collaborative and consortium-based research**,** helping to bring unique, interdisciplinary, inter-institutional, collaborative efforts to bear on complex medical research issues unlikely to be solved though the inherent limits of individual researchers.

- Competitive and unique peer review process: While Congress allocates funding through the annual Defense Appropriations Act to specific medical conditions, it does not direct the programs' dollars to specific researchers. These programs utilize an efficient multi-tiered process that includes multiple stages of peer review, including two levels of formal peer review of final proposals. Proposals are scored in a number of key areas such as scientific merit and impact for patients and the military, providing a robust comparative basis for helping accomplish the program's mission of finding and funding the best research related to these important medical conditions.

- Consumer review: All CDMRP programs incorporate the full and equal participation of consumer reviewers at every stage of the multi-tiered review process – a novel and valuable practice in medical research funding. Consumers – people actually affected by the disease or medical condition – help ensure the program's funded research will have the greatest impact on those who are affected. Consumer reviewers also help inform and educate their disease advocacy communities and others.

- Generating economic growth across the United States: Research activities promote job growth and encourage long-term economic development through innovation. It has been estimated that for every dollar awarded in biomedical research grants, more than two dollars of additional business activity is created. Defense health research grants are awarded to researchers in every state in the country.

In short, CDMRP represents a model of effective and efficient stewardship of taxpayer dollars, delivering meaningful benefits to active-duty servicemembers, veterans, the broader patient population, and the nation's economy. Perhaps most importantly, DoD's innovative approach to funding biomedical research has led to several significant breakthroughs and achievements, contributing to national security and the health and welfare of U.S. Armed Forces personnel and their families. Continued federal funding will only build on these successes.

Lastly, we encourage the timely enactment of the FY 2027 Defense Appropriations Act to ensure continuity in the defense health research programs. We recognize the continuing challenges inherent in advancing appropriations bills through the "regular order" process. However, sustained and predictable investment in this important research is critical to ensure that our nation is prepared for future public health challenges that threaten our current military populations and their families, as well as veterans and the general civilian population. The failure to enact an FY 2025 Defense Appropriations Act led to the devastating 57 percent cut to CDMRP, demonstrating the importance of Congress enacting the Defense bill with full funding for CDMRP. Some of the programs that received no funding or significantly reduced funding in FY 2025 still have not had funding restored to their FY 2024 levels.

We, the undersigned respectfully request your support for increasing the appropriation for CDMRP by at least five percent plus inflation in the FY 2027 Defense Appropriations Act.

Sincerely,

Alliance for Vision Research
ALS Arizona
ALS Association
ALS Network
ALS New Mexico
ALS Northwest
ALS of Nevada
ALS United
ALS United Connecticut
ALS United Greater New York
ALS United Illinois, Indiana, and Missouri
ALS United of Georgia
ALS United Ohio
ALS United, North Carolina
ALS United Rocky Mountain
American Academy of Allergy, Asthma & Immunology
American Academy of Ophthalmology
American Academy of Physical Medicine and Rehabilitation
American Association of Orthopaedic Surgeons
American Brain Tumor Association
American Cancer Society Cancer Action Network, Inc.
American College of Rheumatology
American Congress of Obstetricians and Gynecologists
American Epilepsy Society
American Gastroenterological Association

American Lung Association
American Parkinson Disease Association (APDA)
American Psychological Association Services
American Society for Gastrointestinal Endoscopy
American Society of Hematology
American Urological Association (AUA)
Angelman Syndrome Foundation
Aplastic Anemia & MDS International Foundation
APS Foundation of America, Inc
Arthritis Foundation
Association for Clinical Oncology (ASCO)
Association of American Cancer Institutes
Association of Schools and Colleges of Optometry
Asthma and Allergy Foundation of America
Autism Speaks
Bladder Cancer Advocacy Network (BCAN)
Blue Faery: The Adrienne Wilson Liver Cancer Association
CACNA1A Foundation
Cancer ABCs
Cancer Support Community
Case Western Reserve University School of Medicine
Celiac Disease Foundation
Children's Cardiomyopathy Foundation
Children's Hospital Association
Children's Tumor Foundation
Cholangiocarcinoma Foundation
Christopher & Dana Reeve Foundation
Coalition for National Trauma Research
Coalition to Cure CHD2
COMBINEDBrain
Connect Melanoma
Crohn's & Colitis Foundation
CURE Epilepsy
Cure HHT
Cure SMA
CureGRIN Foundation
Danny Did Epilepsy Foundation
Deadliest Cancers Coalition
Debbie's Dream Foundation: Curing Stomach Cancer (DDF)
Debra of America
Defense Health Research Consortium
Dravet Syndrome Foundation
Duke Health
Duke University
Dup15q Alliance
Epilepsies Action Network
Epilepsy Alliance America

Epilepsy Foundation Alabama
Epilepsy Foundation Alaska
Epilepsy Foundation Arizona
Epilepsy Foundation Arkansas
Epilepsy Foundation Central & South Texas
Epilepsy Foundation Florida
Epilepsy Foundation Greater Orange County
Epilepsy Foundation Indiana
Epilepsy Foundation Iowa
Epilepsy Foundation Los Angeles
Epilepsy Foundation Louisiana
Epilepsy Foundation Maryland
Epilepsy Foundation Metro D.C.
Epilepsy Foundation Mississippi
Epilepsy Foundation Montana
Epilepsy Foundation Nebraska
Epilepsy Foundation Nevada
Epilepsy Foundation New England
Epilepsy Foundation New Jersey
Epilepsy Foundation New Mexico
Epilepsy Foundation North Carolina
Epilepsy Foundation North Dakota
Epilepsy Foundation of America
Epilepsy Foundation of Colorado & Wyoming
Epilepsy Foundation of Delaware
Epilepsy Foundation of Greater Chicago
Epilepsy Foundation of Michigan
Epilepsy Foundation of Minnesota
Epilepsy Foundation of Missouri and Kansas
Epilepsy Foundation of Northeastern NewYork, Inc.
Epilepsy Foundation of Southeast Tennessee
Epilepsy Foundation of Texas
Epilepsy Foundation of Wisconsin
Epilepsy Foundation Ohio
Epilepsy Foundation Oklahoma
Epilepsy Foundation Oregon
Epilepsy Foundation South Carolina
Epilepsy Foundation South Dakota
Epilepsy Foundation Utah
Epilepsy Foundation Washington
Epilepsy Foundation West Virginia
The Epilepsy Institute dba Epilepsy Foundation of Metropolitan New York
Esophageal Cancer Action Network
FDMAS Alliance
Fight Colorectal Cancer
FORCE: Facing Our Risk of Cancer Empowered
Foundation for Angelman Syndrome Therapeutics

Foundation for Peripheral Neuropathy
Foundation to Eradicate Duchenne
Friedreich's Ataxia Research Alliance (FARA)
GBS|CIDP Foundation International
GI Cancers Alliance
GO2 for Lung Cancer
Hearing Loss Association of America
Hepatitis B Foundation
HIV Medicine Association
Hope for Stomach Cancer
Hydrocephalus Association
Infectious Diseases Society of America
International Myeloma Foundation
Interstitial Cystitis Association
Invisible Wounds Foundation
Johns Hopkins University & Medicine
Kidney Cancer Association
KidneyCAN
The LAM Foundation
Lennox-Gastaut Syndrome (LGS) Foundation
Long COVID Campaign
LUNGevity Foundation
Lupus and Allied Diseases Association, Inc.
Lupus Foundation of America
Lupus Research Alliance
Lymphoma Research Foundation
Malecare Cancer Support
Massachusetts ME/CFS & FM Association
ME/CFS San Diego
MEAction Maryland
MEAction NC
Melanoma Research Foundation
Mesothelioma Applied Research Foundation
The Miami Project to Cure Paralysis
The Michael J. Fox Foundation for Parkinson's Research
The Myalgic Encephalomyelitis Action Network (#MEAction)
National Alliance of State Prostate Cancer Coalitions
National Ataxia Foundation
National Autism Association
National Brain Tumor Society
National Fragile X Foundation
National Health Council
National Kidney Foundation
National LGBT Cancer Project
National Multiple Sclerosis Society
Neurofibromatosis (NF) Midwest
Neurofibromatosis Network

NF Northeast
North American Spinal Cord Injury Consortium
Ovarian Cancer Research Alliance
Pancreatic Cancer Action Network (PanCAN)
Parent Project Muscular Dystrophy
Patient-Led Research Collaborative
Penn State University
Phelan-McDermid Syndrome Foundation
PKD Foundation
Prevent Cancer Foundation
The Prostate Cancer Clinical Trials Consortium
Prostate Cancer Foundation
Pulmonary Fibrosis Foundation
The Quinism Foundation
Rally Foundation for Childhood Cancer Research
Rare Epilepsy NEtwork (REN)
RASopathies Network
ReNU2 United
Research!America
Ring 20 USA
The Sergeant Sullivan Circle
SHEPHERD Foundation
The Society of Thoracic Surgeons
Solve M.E.
Susan G. Komen
TB Alliance
Texas NF Foundation
Theresa's Research
TSC Alliance
Unite 2 Fight Paralysis
United Soldiers and Sailors of America-USASOA
United Spinal Association
University of Colorado Anschutz
University of Iowa
University of Pittsburgh
University of Washington
UsAgainstAlzheimer's
Vasculitis Foundation
Veterans for Common Sense
VHL Alliance
Virginia Commonwealth University
Washington State University
Weill Cornell Medicine
Wool + Wander
ZERO Prostate Cancer
cc: Members, U.S. Senate
Enclosure: "Relevance to National Security and Military Families"

Defense Health Research Programs
Relevance to National Security and Military Families
Updated May 7, 2026

- **ALS**: According to studies by the Department of Defense (DoD), Department of Veterans Affairs (VA), National Institutes of Health (NIH) and Harvard University, people who have served in the military are approximately twice as likely to develop ALS as the general population[1]. Most recently, researchers found an increased risk of ALS among those who served in Iraq and Afghanistan[2]. The VA has recognized the connection between ALS and military service by establishing a presumption of service connection for ALS[3]. The VA presumes that ALS was incurred in or aggravated by service in the military. Moreover, the presumption applies to any veteran who served, from any branch of the military, regardless of where or when a veteran served (home or abroad, during a time of peace or conflict) and regardless of when they were diagnosed with the disease following discharge (e.g., 1 year after service or 50 years). The DoD ALS Research Program is supporting translational research and has developed four potential treatments for the disease, for which there is no cure.

- **Arthritis**: According to the Centers for Disease Control and Prevention, over 1 in 3 veterans have arthritis, compared to 1 in 4 in the general population.[4] Arthritis carries with it enormous physical, financial and societal costs, but for veterans and service members, the costs are multiplied. One study found osteoarthritis (OA) rates to be 26 percent higher in service members aged 20 to 24 compared with the same age group in the general population. From the same study, individuals over age 40 were twice as likely to develop OA after returning to civilian life.[5] Data from the U.S. Army's Physical Evaluation Board reveals that among permanently disabling conditions, arthritis was the most common unfitting condition, with 94.4 percent of cases attributed to combat injury.[6] Arthritis is responsible for rising DoD and VA health care costs stemming from joint pain, loss of function, and joint replacement surgery. Research can help identify better joint injury management to reduce the effects of joint degeneration in this population, and help identify ways to prevent joint injury during military training and service.

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[1] Horner, R. D. et. al., 2003, 2008. Occurrence of amyotrophic lateral sclerosis among Gulf War veterans; Haley, R. et. al. 2003. Excess incidence of ALS in young Gulf War veterans; Weisskopf, M. G. 2005, 2009. Prospective study of military service and mortality from ALS; Institute of Medicine, 2006. Amyotrophic Lateral Sclerosis in Veterans: Review of the Scientific Literature.

[2] Zivkovic, S. et. al., 2014. Increased Prevalence of ALS in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans.

[3] 38 CFR 3.318 – Presumptive service connection for amyotrophic lateral sclerosis.

[4] Centers for Disease Control and Prevention. Arthritis Help for Veterans. Retrieved from https://www.cdc.gov/features/arthritis-among-veterans/index.html.

[5] Cameron KL, et al. Incidence of Physician-Diagnosed Osteoarthritis Among Active-Duty United States Military Service Members. Arthritis and Rheumatology. 2011. 62(10); 2794-2982. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/21717422.

[6] Rivera, J. D., Wenke, J. C., Buckwalter, J. A., Ficke, J. R., & Johnson, A. E. (2012). Posttraumatic Osteoarthritis Caused by Battlefield Injuries: The Primary Source of Disability in Warriors. The Journal of the American Academy of Orthopaedic Surgeons, 20(0 1), S64–S69. http://doi.org/10.5435/JAAOS-20-08-S64. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3689418/.

- **<u>Asbestos Diseases</u>**: For more than a century, military service members have been exposed to asbestos. According to the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC), all types of asbestos are classified as Class I Carcinogens.[7] Asbestos exposure can cause many diseases including mesothelioma, cancers of the lung, larynx, and ovaries, and lung and pleural diseases such asbestosis.[8] Asbestos has been widely used in manufactured goods and can still be found in shipyards, existing structures such as military barracks, vehicles, airplanes, and aboard ships.[9] There is no "safe" level of asbestos exposure for any type of asbestos fiber.[10] Inhaling or ingesting asbestos can cause fatal disease. The latency from exposure to diagnosis is commonly 10 - 50 years. Among non-smokers, asbestos exposure increased the rate of lung cancer 5-fold.[11] In addition to the military, family members of service members have also been exposed when fibers are carried home on clothing into military housing which may also be constructed with asbestos-containing materials. Recent asbestos exposures have been reported in the branches of the military serving in Iraq, the Middle East, and Southeast Asia. According to the Institute for Health Metrics and Evaluation database, 40,764 American workers died from asbestos-caused diseases in 2019.[12]

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[7] American Cancer Society, *Known and Probable Human Carcinogens,* 2021. <https://www.cancer.org/cancer/cancer-causes/general-info/known-and-probable-human-carcinogens.html>

[8] Center for Disease Control, *Occupational Safety and Health Guideline for Asbestos: Potential Human Carcinogen.* 1988. <https://www.cdc.gov/niosh/docs/81-123/pdfs/0041.pdf >

[9] U.S. Department of Veteran Affairs. *Public Health: Asbestos.* December 17, 2017. <https://www.publichealth.va.gov/exposures/asbestos/index.asp>

[10] United States Department of Labor. *Asbestos.* Occupational Safety and Health Administration. 2014. <https://www.osha.gov/asbestos>

[11] Markowitz, Steven; Levin, Stephen; Miller, Albert, et. al. American Journal of Respiratory and Critical Care Medicine/AJRCCM. *Asbestos, Asbestosis, Smoking and Lung Cancer: New Findings from the North American Insulator Cohort.* March 22, 2013. <https://www.thoracic.org/newsroom/press-releases/resources/Markowitz>

[12] Asbestos Disease Awareness Organization, *The Irrefutable Fact: Over 40,000 American Workers Died from Preventable Asbestos-Caused Diseases in 2019/ February 15, 2021* https://bit.ly/2N0yANd

- **Autism**: According to the Centers for Disease Control and Prevention, 1 in 31 children have an autism spectrum disorder (ASD)[13]. For a six-year period from calendar years 2018 to 2023, there were 109,073 children, ages 1–18, with an autism diagnosis and eligible for TRICARE benefits[14]. Military families are affected substantially by the financial and emotional costs of raising a child with autism and this impact extends to the performance and readiness of service members and their units. It is well known that children with autism, if they receive prompt treatment and early intervention services, can improve their long-term functional prospects dramatically.[15] Research supported by the Autism Research Program has addressed current needs such as difficulties accessing care associated with mobile military families[16] and gastrointestinal (GI) disorders which are among the most common medical conditions associated with autism.[17] Additional research will help to improve treatment and intervention directly serving the interests of service members and DoD families impacted by autism as well as the medical, educational, healthcare and service professionals who serve the needs of the autism community within and beyond.

[13] Baio, John et. al. 2018. Prevalence of Autism Spectrum Disorder among Children Aged 8 Years – Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2014
[14] https://www.nationalacademies.org/read/29139/chapter/2#8
[15] Dawson, G. et. al. 2009. Randomized, Controlled Trial of an Intervention for Toddlers with Autism: The Early Start Denver Model: Pediatrics.
[16] Ingersoll, B. and Wainer, A. 2013. Initial efficacy of project impact: A parent-mediated social communication for young children with ASD. J Autism Dev Disord 43:2943-52.
[17] Bornstein, Joel. et. al, 2015. The Gut-Brain Interaction and Autism Spectrum Disorder.

- **Bladder Cancer:** Bladder cancer is the 6th most common cause of cancer in the United States, and the 4th most common cancer within the U.S. veteran population.[18] [19] Smoking is a leading risk factor associated with bladder cancer, but male sex, advancing age, and white race are also strong risk factors. Despite mounting evidence in the 1950s of the adverse health effects of smoking and tobacco use, the military continued to include cigarettes in rations until 1975.[20] Smoking prevalence in the veteran population is reported to be 27% compared to 21% in the non-veteran population.[21] It has also been estimated that the prevalence of smoking is 43% higher in the population treated by VA hospitals compared to age matched controls [22]From 1961 to 1971, approximately 1,000,000 gallons of Agent Blue, containing high levels of arsenic were sprayed over the southern region of Vietnam.[23] Inorganic arsenic compounds have been linked to cancer of the bladder.[24] In addition, from the 1950s through the 1980s, people serving or living at the U.S. Marine Corps Base Camp Lejeune, North Carolina, were potentially exposed to drinking water contaminated with industrial solvents, benzene, and other chemicals. This chemical exposure may have led to adverse health conditions, including bladder cancer.[25]

[18] American Cancers Society. Bladder Cancer Statistics. Retrieved from http://www.cancer.org/cancer/bladdercancer/detailedguide/bladder-cancer-key-statistics, accessed March 9, 2016.
[19] Zullig et al, 2013, Cancer Incidence among Patients of the United States Veterans Affairs (VA) Healthcare System, Mil Med. 2012 June ; 177(6): 693–701.
[20] Joseph, Anne M.; et al. (2005). "The Cigarette Manufacturers' Efforts to Promote Tobacco to the U.S. Military". Military Medicine170: 874–880.
[21] Brown, D.W., 2010 Smoking Prevalence among US Veterans, J Gen Intern Med. Feb; 25(2): 147–149.
[22] Office of Quality and Performance, Veterans Health Administration.Health behaviors of veterans in the VHA: tobacco use. 1999 Large Health Survey of Enrollees. Washington, DC, Veterans Health Administration, 2001.
[23] H.R.2519 - Victims of Agent Orange Relief Act of 2013113th Congress (2013-2014).
[24] NCI Cancer Trends Progress Report, Retrieved March 9, 2016 from https://progressreport.cancer.gov/prevention/arsenic.
[25] US Department of Veterans Affairs, July, 2015, CAMP LEJEUNE: PAST WATER CONTAMINATION, IB 10-449.

- **Bone Marrow Failure Disorder:** Myelodysplastic Syndrome (MDS) is a rare bone marrow failure disorder that increases the risk of developing Acute Myeloid Leukemia (AML), a fast growing cancer of the blood. Exposure to benzene, historically used extensively by the military, has been well established as a risk factor for myeloid malignancy, and is significantly associated with development of MDS and AML.[26][27][28] Both ground troops and onboard support personnel have been at risk for significant exposure to dioxin, benzene and Agent Orange herbicide during the Vietnam war. [29][30][31] More recently, veterans stationed at Camp Lejeune between 1953 and 1987 were found to have potential exposure to industrial solvents in well water, inclusive of benzene, as recognized by the VA. Evidence shows a link between exposure to chemicals found in the drinking water at Camp Lejeune and MCAS New River and both MDS and aplastic anemia, a bone marrow failure disorder in which the bone marrow stops producing enough blood cells.[32] The Bone Marrow Failure Research Program supports critical research into disease etiology and therapy development pathways. Continued research into bone marrow failure etiology and molecular genomics is essential to saving lives.

- **Brain Cancer and Pediatric Brain Tumors:** Today, an estimated 700,000 people in the United States are living with a primary brain tumor, and approximately 85,000 more will be diagnosed in 2021. Brain cancer is the deadliest form of childhood cancer, which is the number one disease-related killer of children under 15. Brain cancer does not discriminate, inflicting men, women, and children of all races and ethnicities, including members of the armed services. This connection was illustrated in a 2014 report by the PRCRP to Congress, linking brain cancer with exposure to ionizing radiation during military service.[33] The report also pointed to a study by Hicks et. al indicating children of men in the Air Force having higher incidence rate of pediatric brain tumors.[34] A subsequent report published by the PRCRP in 2015 highlighted environmental hazards including radiation and insolvents as increasing the risk of brain cancer development. Specifically, high risk exposure related to a brain cancer diagnosis can include but are not limited to chemical weapons, or storage, ionizing radiation, herbicides, electromagnetic fields, jet fuel, organic materials, biological agents, and ultraviolet radiation.[35]

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[26] Irons, R. D. and P. J. Kerzic (2014). "Cytogenetics in benzene-associated myelodysplastic syndromes and acute myeloid leukemia: new insights into a disease continuum." Ann N Y Acad Sci 1310: 84-88.
[27] Poynter, J. N., M. Richardson, M. Roesler, C. K. Blair, B. Hirsch, P. Nguyen, A. Cioc, J. R. Cerhan and E. Warlick (2017). "Chemical exposures and risk of acute myeloid leukemia and myelodysplastic syndromes in a population-based study." Int J Cancer 140(1): 23-33
[28] Smith, M. T., L. Zhang, C. M. McHale, C. F. Skibola and S. M. Rappaport (2011). "Benzene, the exposome and future investigations of leukemia etiology." Chem Biol Interact 192(1-2): 155-159.
[29] Armitage, J. M., M. E. Ginevan, A. Hewitt, J. H. Ross, D. K. Watkins and K. R. Solomon (2015). "Environmental fate and dietary exposures of humans to TCDD as a result of the spraying of Agent Orange in upland forests of Vietnam." Sci Total Environ 506-507: 621-630.
[30] Landgren, O., Y. K. Shim, J. Michalek, R. Costello, D. Burton, N. Ketchum, K. R. Calvo, N. Caporaso, E. Raveche, D. Middleton, G. Marti and R. F. Vogt, Jr. (2015). "Agent Orange Exposure and Monoclonal Gammopathy of Undetermined Significance: An Operation Ranch Hand Veteran Cohort Study." JAMA Oncol 1(8): 1061-1068.
[31] Ross, J. H., A. Hewitt, J. Armitage, K. Solomon, D. K. Watkins and M. E. Ginevan (2015). "Exposure to TCDD from base perimeter application of Agent Orange in Vietnam." Sci Total Environ 511: 82-90.
[32] http://www.benefits.va.gov/COMPENSATION/claims-postservice-exposures-camp-lejeune-water.asp
[33] https://cdmrp.army.mil/prcrp/reports/14prcReport.pdf
[34] Hicks N, Zack M, Caldwell GG, Fernbach DJ, and Falletta JM. 2006. Childhood cancer and occupational radiation exposure in parents. Cancer 53:1637-1643.
[35] https://cdmrp.army.mil/prcrp/reports/15prcReport.pdf (pg. 7-11)

- **Breast Cancer**: According to recent demographic reports, active duty and select reserve females and female spouses under the care of the United States military health system total approximately 1.3 million women.[36] Assuming normal risk of developing breast cancer across a woman's lifetime (1 in 8), 162,500 cases of breast cancer are expected to be diagnosed within that population. Furthermore, a 2009 study suggested that active-duty females have a higher incidence of breast cancer than the general population, which would increase the expected number of breast cancer cases.[37] Therefore, breast cancer is a significant issue for the United States military health system. Additionally, military families are affected substantially by the financial and emotional costs of breast cancer and this impact extends to the performance and readiness of service members and their units. The Breast Cancer Research Program has invested in research to better understand how and why breast cancer is initiated, factors that increase risk, and more advanced ways to detect and treat this disease including innovative treatments for breast cancer that are both more effective and less toxic (e.g. sentinel lymph node biopsy, trastuzumab and palbociclib for HER2+ breast cancer, ribociclib and abemaciclib for HR+ breast cancer, vaccines and immunotherapies for breast cancer, nanoparticle-based drug delivery systems).[38]

- **Cancer in Adolescents and Young Adults**: Approximately 70,000 adolescents and young adults between the ages of 15 and 39 are diagnosed with cancer each year in the United States. In fact, cancer is the leading cause of disease-related death for this age group. The National Cancer Institute has found that "evidence suggests that some cancers in adolescents and young adults may have unique genetic and biological features. Researchers are working to learn more about the biology of cancers in young adults so that they can identity molecularly targeted therapies that may be effective in these cancers."[39] Unfortunately this age population is not recognized as a unique oncology care group. Adolescents and young adults have no medical "home." Providers must make care and treatment decisions using research and facilities designed for pediatric or older adult patients. This has led to a lack of improvement in survival rates since the War on Cancer began more than 40 years ago.[40] Nearly 90% of servicemembers, their spouse, and children fall within the NCI definition of an adolescent or young adults impacted by cancer.[41]

[36] http://download.militaryonesource.mil/12038/MOS/Reports/2016-Demographics-Report.pdf
[37] Cancer Epidemiol Biomarkers Prev. 2009 Jun;18(6):1740-5. doi: 10.1158/1055-9965.EPI-09-0041.
[38] http://cdmrp.army.mil/bcrp/pbks/bcrppbk2018.pdf
[39] https://www.cancer.gov/types/aya
[40] https://www.ncbi.nlm.nih.gov/pubmed/25568146
[41] https://s3.amazonaws.com/rallywebcollateral/wp-content/uploads/2017/03/08143634/DODCDMRPFY17Request_whitepaper_2.pdf

- **<u>Celiac disease</u>:** Celiac disease is recognized as one of the world's most common genetic autoimmune disorders, affecting 1% of the population. Despite this recognition, most cases remain undiagnosed.[42] Prevalence has increased markedly (4-5-fold) since 1950 for reasons not understood. Incidence has also increased in the general population and in active service military personnel[43], with a peak onset in the second or third decades of life. Currently, there is no medication or cure for celiac disease. Nor is there an effective method for prevention. The only course of action is to follow a strict gluten-free diet. Studies show from 30 to 50 percent of celiac disease patients on a gluten-free diet continue to report symptoms and/or have intestinal damage. There is a wide range of both gastrointestinal and extraintestinal symptoms, and some patients are asymptomatic entirely.[44] Fatigue and chronic abdominal pain are common symptoms. Increased fracture risk, anemia, and other consequences of malabsorption can have substantial impact on patients' quality of life. Not only is living with celiac disease a daily struggle, it is a disease that dramatically increases the mortality risk for other diseases -- 6x increased risk for death from non-Hodgkin's lymphoma; 3x increased risk for death from liver disease; 2.6x increased risk for death from pneumonia[45] ; and, 4x risk for small bowel cancer.[46] Demographics support the estimate that thousands of active, Guard, and Reserve service members are currently suffering from celiac disease or are in danger of developing the disease, making them eligible for service-connected disability. Based upon TRICARE covered lives, it is estimated that an additional 77,000 retirees and family members may also suffer from celiac disease. Further research will benefit those suffering from celiac disease by generating strategies to prevent the disease and providing critical guidance on mitigation efforts effecting readiness.

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[42] Caio G, Volta U, Sapone A, Leffler DA, De Giorgio R, Catassi C, Fasano A. Celiac disease: a comprehensive current review. BMC Med. 2019 Jul 23;17(1):142. doi: 10.1186/s12916-019-1380-z. PMID: 31331324; PMCID: PMC6647104.

[43] Rubio-Tapia A, Kyle RA, Kaplan EL, Johnson DR, Page W, Erdtmann F, Brantner TL, Kim WR, Phelps TK, Lahr BD, Zinsmeister AR, Melton LJ 3rd, Murray JA. Increased prevalence and mortality in undiagnosed celiac disease. Gastroenterology. 2009 Jul;137(1):88-93. doi: 10.1053/j.gastro.2009.03.059. Epub 2009 Apr 10. PMID: 19362553; PMCID: PMC2704247.

[44] Leonard MM, Sapone A, Catassi C, Fasano A. Celiac Disease and Nonceliac Gluten Sensitivity A Review. JAMA. 2017;318(7):647-656. doi:10.1001/jama.2017.9730. PMID 28810029

[45] Holmes GKT, Muirhead A. Mortality in coeliac disease: a population-based cohort study from a single centre in Southern Derbyshire, UK. BMJ Open Gastroenterol. 2018 Apr 17;5(1):e000201. doi: 10.1136/bmjgast-2018-000201. PMID: 29686881; PMCID: PMC5911148.

[46] Ilus T, Kaukinen K, Virta LJ, Pukkala E, Collin P. Incidence of malignancies in diagnosed celiac patients: a population-based estimate. Am J Gastroenterol. 2014 Sep;109(9):1471-7. doi: 10.1038/ajg.2014.194. Epub 2014 Jul 22. PMID: 25047399.

- **<u>Cholangiocarcinoma</u>:** Bile duct cancer, or cholangiocarcinoma, is a rare but severe disease affecting the biliary system, which includes the bile ducts, gallbladder, and certain cells in the liver. It is the second most common form of liver cancer, and certain risk factors disproportionately affect veterans, particularly those who served in Southeast Asia.[47] Veterans who served in regions such as Vietnam, Laos, or Thailand may have unknowingly been exposed to liver flukes, tiny parasitic worms that infect the biliary system. This exposure occurs through eating raw or undercooked fish contaminated with these parasites. Over time, the scarring and inflammation caused by liver flukes increase the risk of developing bile duct cancer.[48] Additionally, other risk factors for cholangiocarcinoma include environmental toxins such as dioxin exposure.[49] The U.S. Department of Veterans Affairs states that "Veterans who served anywhere in Vietnam between January 9, 1962, and May 7, 1975 are presumed to have been exposed to herbicides, as specified in the Agent Orange Act of 1991".[50] For many veterans, these risks were tied directly to their service, making it not just a health issue but a service-related concern. Delays in recognition and diagnosis compound the health burden of bile duct cancer on veterans.[51] Symptoms such as jaundice, abdominal pain, and weight loss often manifest late, making early detection crucial. Additionally, veterans may face unique challenges navigating the VA health system to access specialized care for rare conditions like cholangiocarcinoma. Understanding and addressing the unique risks for veterans is essential to improving outcomes. Raising awareness about service-related exposures, such as liver flukes and Agent Orange exposure, can lead to earlier diagnoses and better treatment options. Furthermore, expanded research and targeted health programs can ensure veterans receive the care and support they deserve.

[47] El-Serag HB, Engels EA, Landgren O, et al. Risk of hepatobiliary and pancreatic cancers after hepatitis C virus infection: a population- based study of U.S. veterans. Hepatology. 2009;49(1):116-123.
[48] Banales JM, Cardinale V, Carpino G, et al. Expert consensus document: Cholangiocarcinoma: current knowledge and future perspectives consensus statement from the European Network for the Study of Cholangiocarcinoma (ENS-CCA). Nat Rev Gastroenterol Hepatol. 2016;13(5):261-280.
[49] Anderson, Christopher D., et al. Diagnosis and Treatment of Cholangiocarcinoma. The Oncologist. 2004; 9:43-57.
[50] U.S. Department of Veteran Affairs. (2025, April 23). Exposure to Agent Orange in Vietnam. https://www.publichealth.va.gov/exposures/agentorange/locations/vietnam.asp#:~:text=For%20the%20purposes%20of%20VA,statement%20of%20personally%20going%20ashore.)
[51] El-Serag HB, Engels EA, Landgren O, et al. Risk of hepatobiliary and pancreatic cancers after hepatitis C virus infection: a population- based study of U.S. veterans. Hepatology. 2009;49(1):116-123.

- **Colorectal Cancer:** According to a study published in the June 2009 issue of Cancer Epidemiology, Biomarkers & Prevention, researchers found that colorectal cancer was one of the most common forms of cancer among active-duty military personnel. Yet, screening rates among military personnel for colorectal cancer remain low. As published in the 2009 Humana Military's Clinical Quality Report Card, only 58 percent of those in the military were up to date with screening in 2008. The Peer Reviewed Cancer Research Program (PRCRP) has supported research into treatments for colorectal cancer, including research into treatments that would block the growth of metastatic colorectal cancer. CA093415[52], CA111002[53], CA100879[54], CA100512P1[55], CA093176[56])

- **Congenital Heart Disease**: Congenital heart disease (CHD) is the most common class of birth defects and the leading cause of birth defect-related infant mortality. Nearly 1 in 100 babies are born with a CHD and more than five percent will not live to see their first birthday.[57] [58] Even those who receive successful intervention are not cured. Children and adults born with CHD require ongoing, costly, specialized cardiac care, and face a lifelong risk of permanent disability and premature death. As a result, healthcare utilization among the CHD population is significantly higher, and health care costs are estimated to be 10 to 20 times greater for this community than the general population. There are higher rates of birth defects, including CHD, for children born in military families. Research conducted through the Department of Defense has found high altitudes play a role. There are some suggestions that the reduced oxygen at high elevations [such as in the mountains of Afghanistan] may adversely affect the pregnancy and the growth of the fetus, but there is little understanding of the effect on the developing fetus of travel to high altitudes.[59] This is especially true early in the pregnancy when the heart and other organs are just forming (8-12 weeks) and the Service member may not yet know or have not verbalized that she is pregnant. Other studies have suggested higher prevalence of CHD among infants conceived in Gulf War veteran families. Further research in these areas will benefit the children conceived of military families and will have broader implications for all American families.

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[52] Feng Z, Liu L, Zhang C, et al. 2012. Chronic restraint stress attenuates p53 function and promotes tumorigenesis. PNAS 109:7013-7018.
Hu W, Feng Z, and Levine A. 2012. The regulation of multiple p53 stress responses are mediated through MDM2. Genes Cancer 3:199-208. (PMC3494373).
Yu H, Yue X, Zhao Y, et al. 2014. LIF negatively regulates tumor suppressor p53 through Stat3/ID1/MDM2 in colorectal cancers. Nat Comm 5:5218.

[53] Lightfoot YL, and Mohamadzadeh M. 2013. Tailoring gut immune responses with lipoteichoic acid-deficient Lactobacillus acidophilus. Front Immunol 6;4:25.
Lightfoot YL, Yang T, Sahay B, et al. 2013. Targeting aberrant colon cancer-specific DNA methylation with lipoteichoic acid-deficient Lactobacillus acidophilus. Gut Microbes 4(1):84-88.
Owen JL, and Mohamadzadeh M. 2013. Macrophages and chemokines as mediators of angiogenesis. Front Physiol 5(4):159.

[54] Lu J, Ye X, Fan F, et al. 2013. Endothelial cells promote the colorectal cancer stem cell phenotype through a soluble form of Jagged-1. Cancer Cell 23(2):171-185.

[55] Pitts TM, Newton TP, Bradshaw-Pierce EL, et al. 2014. Dual pharmacological targeting of the MAP Kinase and PI3K/mTOR pathway in preclinical models of colorectal cancer. PLoS One 9(11):e113037.

[56] Song BP, Jain S, Lin SY, et al. 2012. Detection of hypermethylated vimentin in urine of patients with colorectal cancer. J Mol Diagn 14(2):112-119.

[57] Hoffman JL, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002;39(12):1890-1900.

[58] Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in Atlanta, 1998-2005. J Pediatr. 2008;153:807-13.

[59] http://www.dtic.mil/dtic/tr/fulltext/u2/1048533.pdf

- **Crohn's Disease and Ulcerative Colitis (Inflammatory Bowel Diseases)**: The prevalence of Crohn's Disease and Ulcerative Colitis (collectively known as inflammatory bowel diseases-IBD) increased by two to threefold among veterans from 1998 to 2009. Researchers found nearly 17,000 unique incident cases of Crohn's Disease and over 26,000 cases of Ulcerative Colitis within the military population during this time. Due to the population studied, 94% of the cases were in men. In 2009, the age and gender standardized prevalence rate of Crohn's Disease was 287 per 100,000 VA users and the prevalence rate for Ulcerative Colitis was 413 per 100,000 VA users.[60] Despite having a large population study, much is yet to be known about etiology or cause of these diseases, therefore continued research in this area is necessary to advance knowledge about IBD.

- **Epilepsy**: According to 2015 estimates, a staggering 3.4 million Americans report living with epilepsy.[61] Individuals who serve in the military are especially susceptible to developing a type of epilepsy called post-traumatic epilepsy (PTE), defined as a recurrent seizure disorder following traumatic brain injury (TBI). [62] TBIs can take the form of bumps, blows to the head, blasts or penetrating injuries,[63] such as those seen so often in the line of duty. In fact, over 400,000 active-duty service members were diagnosed with a TBI from 2000-2019.[64] These injuries can have a devastating impact on troops; for example, a reported 53% of a group of Vietnam veterans with penetrating brain wounds developed epilepsy, [65] and within a group of veterans of the Afghanistan and Iraq conflicts, those with TBI were almost 19x more likely to develop epilepsy than those without TBI.[66] Furthermore, people with epilepsy including that which is a result of head injury are largely prohibited from admission into the armed services according to DoD regulations, reducing the pool of eligible recruits.[67] Currently, there is no known prevention for PTE following TBI, and treatments for PTE are only partially effective and can have severe drawbacks.[68] There is also no known treatment or cure for many other types of epilepsy that afflict our troops and the general population.[69]

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[60] Hou JK, Kramer JR, Richardson P, Mei M, El-Serag HB. The Incidence and Prevalence of Inflammatory Bowel Disease Among U.S. Veterans: A National Cohort Study. Inflamm Bowel Dis. 2013 Feb 27. [Epub ahead of print] PubMed PMID: 23448789.

[61] Zack MM, Kobau R. National and state estimates of the numbers of adults and children with active epilepsy — United States, 2015. *MMWR*. 2017;66:821–825.

[62] Pitkänen A and Bolkvadze T. Head Trauma and Epilepsy. Jasper's Basic Mechanisms of the Epilepsies [Internet] 4th Edition 2012. Noebels JL, Avoli M, Rogawski MA, et al., editors.

[63] Marr A, Coronado V, editors. Central Nervous System Injury Surveillance: Annual Data Submission Standards for the Year 2002. Atlanta: U.S. Department of Health and Human Services, CDC, National Center for Injury Prevention and Control; 2004.

[64] DoD Worldwide Numbers for TBI, Defense and Veterans Brain Injury Center, 2020

[65] Salazar AM, Jabbari B, Vance SC, Grafman J, Amin D, Dillon JD. Epilepsy after penetrating head injury. I. Clinical correlates: a report of the Vietnam Head Injury Study. *Neurology* 1985; 35(10): 1406-1414.

[66] Pugh MJ, Orman JA, Jaramillo CA, Salinsky MC, Eapen BC, Towne AR, Amuan ME, Roman G, McNamee SD, Kent TA, McMillan KK, Hamid H, Grafman JH. The prevalence of epilepsy and association with traumatic brain injury in veterans of the Afghanistan and Iraq wars. *J Head Trauma* 2015; 30(1):29-37.

[67] DoD Instruction 6130.03, Volume 2, Medical standards for military service: retention. https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/613003v2p.pdf?ver=2020-09-04-120013-383

[68] Szaflarski JP, Nazzal Y, Dreer LE. Post-traumatic epilepsy: Current and emergent treatment options. Neuropsychiatr Dis Treat 2014; 10:1469-1477.

[69] Kwan P, Brodie MJ. Early identification of refractory epilepsy. *New England Journal of Medicine* 2000;342(5):314-9.

Committed to a vision of "a time when post-traumatic epilepsy can be prevented or optimally managed," the CDMRP Epilepsy Research Program (ERP) has funded epilepsy research since 2015. The ERP aims to understand the basic mechanisms by which TBI produces PTE and the extent of PTE following TBI within the military. Epidemiological work funded by the ERP has shown that post-9/11 veterans with a self-reported history of moderate/severe TBI were more likely to have epilepsy than those without TBI or those with mild TBI. This work also showed that post-9/11 veterans with TBI who developed PTE report worse quality of life than those who had TBI but no PTE.[70] Promising preclinical projects include the identification of a molecular target known as C1q that may help reduce post-TBI neuroinflammation and epileptic brain activity. In addition, the ERP has funded development of animal models including a large animal model of PTE that has already led to a better understanding of how early post-TBI dysfunctional brain activity occurs.

- **Esophageal Cancer**: Esophageal cancer is the seventh leading cause of cancer-related death among American men in both the military and the general population. In addition, four out of five patients (more than 80 percent) die within five years of receiving an esophageal cancer diagnosis. It is one of America's deadliest cancers, largely because little effective treatment, scarce early detection and no screening guidelines exist for this disease. Further, those at greatest risk for esophageal cancer are men over the age of 55 who have a history of gastro-esophageal reflux disease (GERD), tobacco and/or alcohol use, and/or obesity[71] – all risks that are higher in the country's veteran population compared to the general population.[72] Our military personnel and veterans also have additional risks. In fact, the VA has already established that there is a presumption of service connection for esophageal cancer. One reason for this step is that the radiation some veterans have been exposed to has been shown to be linked to the disease.[73] There is also a link to the contaminated drinking water at U.S. Marine Corps Base Camp Lejeune, North Carolina from the 1950s to the 1980s.[74] Veterans and their families who were stationed there were potentially exposed to drinking water contaminated with industrial solvents, benzene, and other chemicals that have been linked to esophageal cancer. Finally, some of the burden of esophageal cancer is linked to military-encouraged smoking. It is well documented that the military continued to include cigarettes in rations until 1975[75] and overall, veterans are more likely to be smokers than the general population.[76]

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[70] Pugh MJ, Kennedy E, Gugger JJ, Mayo J, Tate D, Swan A, Kean J, Altalib H, Gowda S, Towne A, Hinds S, Van Cott A, Lopez MR, Jaramillo CA, Eapen BC, McCafferty RR, Salinsky M, Cramer J, McMillan KK, Kalvesmaki A, Diaz-Arrastia R, MINUTE Study Group. The Military Injuries: Understanding post-traumatic epilepsy study: Understanding relationships among lifetime traumatic brain injury history, epilepsy, and quality of life. J Neurotrauma 2021; 38(20): 2841-2850.

[71] Cancer Facts & Figures 2021, American Cancer Society, cancer.org, 1/2021 accessed 2-18-2021.

[72] Using Health Factors Data for VA Health Services Research, Paul G. Barnett, Adam Chow and Nicole E. Flores February 2014, p. 28; VA/DoD Clinical Practice Guideline for SCREENING AND MANAGEMENT OF OVERWEIGHT AND OBESITY, Department of Veterans Affairs, Department of Defense, 2014, p. 3; Research Letter, JR Kramer, Shakhatreh , AD Naik, Z Duan, HB El-Serag, , JAMA Internal Medicine, January 2014, Use and Yield of Endoscopy in Patients With Uncomplicated Gastroesophageal Reflux Disorder, p E1.

[73] https://www.law.cornell.edu/cfr/text/38/3.309

[74] https://www.va.gov/disability/eligibility/hazardous-materials-exposure/camp-lejeune-water-contamination/

[75] Joseph, Anne M.; et al. (2005). "The Cigarette Manufacturers' Efforts to Promote Tobacco to the U.S. Military". Military Medicine170: 874–880.

[76] Brown, D.W., 2010 Smoking Prevalence among US Veterans, J Gen Intern Med. Feb; 25(2): 147–149.

- **<u>Fibrous dysplasia/McCune-Albright syndrome (FD/MAS)</u>**: The mutation that causes FD/MAS is located in a very important gene (GNAS) that is necessary for the maintenance of healthy bone. For that reason, the study of FD/MAS has a track record of yielding broad insights about bone biology, like the discovery that bone is the body's source of a key kidney-regulating hormone.[77] FD/MAS provides a unique natural experiment to study key signaling pathways that have implications for treatments of DoD-prevalent conditions, like blast-induced heterotopic ossification, chronic bone pain, skeletal fractures, osteoporosis, and osteoarthritis. Heterotopic Ossification (HO) is a condition where bone forms in soft tissue where bone does not normally exist. Studies have found that blast-induced HO affects approximately 65% of combat-wounded warriors, resulting in obstacles to mobility, use of prostheses, recovery, and returns to service.[78] HO can be caused by the inverse of the gene mutation that causes FD/MAS.[79] The study of the basic biology of FD/MAS could increase understanding of HO because FD/MAS is caused by the activating mutation of GNAS and HO can be caused by the inactivating mutation of the very same gene. Studying FD/MAS can also provide a window into the mechanisms of pain. Because people with FD/MAS transition to chronic pain in a predictable time frame, and exhibit both major forms of pain (nociceptive and neuropathic), this population a convenient sample to track the biochemical, physiological, and neurological emergence of chronic bone pain, from beginning to end.[80][81]

[77] Riminucci M, Collins MT, Fedarko NS, Cherman N, Corsi A, White KE, Waguespack S, Gupta A, Hannon T, Econs MJ, et al. FGF-23 in fibrous dysplasia of bone and its relationship to renal phosphate wasting. J Clin Invest. 2003;112(5):683-92.
[78] Alfieri KA, Forsberg JA, Potter BK. Blast injuries and heterotopic ossification. Bone Joint Res. 2012;1(8):192-7.
[79] Brewer N, Fong JT, Zhang D, Ramaswamy G, Shore EM. Gnas Inactivation Alters Subcutaneous Tissues in Progression to Heterotopic Ossification. Front Genet. 2021;12:633206.
[80] Kelly MH, Brillante B, Collins MT. Pain in fibrous dysplasia of bone: age-related changes and the anatomical distribution of skeletal lesions. Osteoporos Int. 2008;19(1):57-63.
[81] Tucker-Bartley A, Lemme J, Gomez-Morad A, Shah N, Veliu M, Birklein F, Storz C, Rutkove S, Kronn D, Boyce AM, et al. Pain Phenotypes in Rare Musculoskeletal and Neuromuscular Diseases. Neurosci Biobehav Rev. 2021;124:267-90.

- **Food Allergies**: Food allergy affects approximately 7.6 percent of children[82] and 10.8 percent[83] of adults in the United States. Active duty service members with a history of food-allergy anaphylaxis or a systemic reaction to food do not meet military accession or retention standards. In spite of this, the incidence rate of food-allergy anaphylaxis among active component service members approximates that found in the general population and appears to be increasing.[84] Inadequate knowledge or misconceptions of current military-specific standards regarding food allergy and how these apply to enlistment, induction, and retention in the US military can lead potentially to inaccurate counseling because each military service has specific regulations that affect the evaluation and decision-making process. Both civilian and military allergists play an essential role in the evaluation, counseling, and management of patients with a food allergy history. Understanding the service-specific language and regulations regarding food allergy will improve the allergist's awareness, counseling, and management of these individuals.[85] Further, in the military, an IgE-mediated food allergy can be disqualifying for entry and specific career specialties. However, given the increasing numbers of service members affected by this condition, the military may wish to consider new policies to allow applicants and members with avoidable food allergies to serve successfully. Future studies are needed to evaluate whether food allergies have any unique consequences in this population.[86]

[82] Gupta RS, Warren CM, Smith BM, et al. The Public Health Impact of Parent-Reported Childhood Food Allergies in the United States. Pediatrics. 2018:142(6):e20181235. (2019). Pediatrics March 2019, 143 (3) e20183835; DOI: https://doi.org/10.1542/peds.2018-3835.

[83] Gupta, R. S., Warren, C. M., Smith, B. M., Jiang, J., Blumenstock, J. A., Davis, M. M., … Nadeau, K. C. (2019). Prevalence and Severity of Food Allergies Among US Adults. JAMA Network Open 2019; 2(1): e185630. doi:10.1001/jamanetworkopen.2018.5630

[84] Clausen S, Stahlman S. Food-allergy anaphylaxis and epinephrine autoinjector prescription refills, active component service members, U.S. Armed Forces, 2007-2016.

[85] Food allergy guidance in the United States Military: A work group report from the American Academy of Allergy, Asthma & Immunology's Military Allergy and Immunology Assembly. J Allergy Clin Immunol 2018; 141(1):54-59

[86] Lee RU, Stahlman S. Increasing incidence and prevalence of food allergies in the US Military 2000-2017. J Allergy Clin Immunol-Practice 2020; 8(1):361-63.

- **Gulf War Illness**: According to a 2014 update report of the Congressionally-mandated Research Advisory Committee on Gulf War Veterans' Illnesses (RAC), "Scientific research [since 2008] . . . supports and further substantiates . . . that Gulf War illness is a serious physical disease, affecting at least 175,000 veterans of the 1990-1991 Gulf War, that resulted from hazardous exposures in the Gulf War theater."[87] Studies reviewed in the report found an elevated incidence of Lou Gehrig's disease (ALS)[88] among Gulf War veterans as well as significantly elevated rates of death due to brain cancer[89] among those who were most exposed to the release of nerve gas by the destruction of the Khamisiyah Iraqi arms depot. In addition to improving the health of Gulf War veterans, important discoveries made by the GWIRP will also help protect current and future American servicemembers who are at risk of similar toxic exposures.[90]

- **Hepatocellular Carcinoma**: Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, accounting for approximately 69% of liver cancers in the United States.[91] HCC typically develops in people with chronic liver disease, most commonly related to hepatitis B virus, hepatitis C virus, cirrhosis, alcohol-associated liver disease, or metabolic dysfunction-associated steatotic liver disease.[92] This is especially relevant to veterans because hepatitis C has long been an important public health issue in the veteran community, and the Veterans Health Administration has operated a national hepatitis C screening and treatment program since 1998.[93] Studies of the Veterans Health Administration population found that hepatitis C-related HCC incidence declined after the widespread use of direct-acting antiviral treatment, but non-hepatitis C-related HCC increased after 2015, underscoring the need for continued prevention, surveillance, and research.[94] The VA recommends liver cancer surveillance for eligible patients with cirrhosis because earlier detection can expand access to potentially curative or life-extending treatments.[95] Continued research into HCC prevention, early detection, and treatment would directly benefit service members, veterans, and military families affected by liver disease and liver cancer.

- **Hereditary Ataxia**: Hereditary Ataxia refers to a group of rare, neurodegenerative diseases that are genetically inherited.[96] There are over 100 known types of Hereditary Ataxia, which can present at any life stage and include symptoms such as difficulty with mobility, speech and swallowing, fine motor skills, and life shortening cardiomyopathy. Hereditary Ataxias are progressive conditions and can lead to extreme disability and premature death. It is estimated that 10 in 100,000 people have a form of Hereditary

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[87] Research Advisory Committee on Gulf War Veterans' Illnesses, Gulf War Illness and the Health of Gulf War Veterans: Research Update and Recommendations, 2009-2013, p. 1. U.S. Government Printing Office, Washington, D.C., 2014.
[88] Research Advisory Committee on Gulf War Veterans' Illnesses, pp. 23-25.
[89] Research Advisory Committee on Gulf War Veterans' Illnesses, pp. 23-26.
[90] Research Advisory Committee on Gulf War Veterans' Illnesses, pp. 1; 4; 5; 13; 78; 83. And: Institute of Medicine, N. R. C., 2010. Gulf War and Health: Volume 8 - Health Effects of Serving in the Gulf War. The National Academies Press, Washington, DC, pp. 10; 260-64.
[91] American Cancer Society, Cancer Facts & Figures 2026.
[92] National Cancer Institute, "Liver Cancer Causes, Risk Factors, and Prevention."
[93] U.S. Department of Veterans Affairs, "Screening Veterans for Hepatitis C Infection."
[94] Beste LA et al., "Hepatitis C–Related Hepatocellular Carcinoma Incidence in the Veterans Health Administration," JAMA.
[95] U.S. Department of Veterans Affairs, "Hepatocellular Carcinoma Surveillance."
[96] Perlman, S. (2023). Hereditary ataxia overview. Genereviews®[internet]. https://www.ncbi.nlm.nih.gov/books/NBK1138/

Ataxia.[97] [98] Currently, there is one FDA approved treatment to slow neurological symptoms in a single type of Hereditary Ataxia, Friedreich's Ataxia, and no treatments that address the underlying cause of any type of Hereditary Ataxia. The impact to the military is compounded by the breadth of this disease. Given its prevalence, Hereditary Ataxia is present within the military population, where its progressive nature would likely render affected service members unfit for duty over time.[99] Many types of Hereditary Ataxia present in early to mid-adulthood- the same age range as many active-duty service members.[100] Alternatively, active military who have relatives, including children, with Hereditary Ataxia may find that they are not mission ready as they must become their primary caregiver. Since this is a genetic disease, those caregivers may even find themselves caring for multiple members of their family and facing uncertainty about their own future health status. Additionally, Hereditary Ataxia requires a complex team of doctors, caregivers, and rehabilitation specialists, which would impose high costs on the VA health system.[101] Developing a deeper understanding of the underlying mechanisms that cause Hereditary Ataxia would not only lead to treatments but could shed light on other neurological conditions, including ALS, Alzheimer Disease, and Parkinson Disease, that share similar traits and are known to be common in military populations.[102] Moreover, Hereditary Ataxias provide a well-defined biological model that can clarify cerebellar injury mechanisms. Insights can guide the development of outcome measures, imaging biomarkers, and functional assessments specifically tailored to cerebellar dysfunction.[103] Cerebellar-focused clinical outcome and harmonized MRI protocols are increasingly validated in Hereditary Ataxias and are immediately translatable to blast- and TBI-related cerebellar injury for detection, monitoring, and triage.[104] [105] Such tools could strengthen return-to-duty evaluations and inform long-term care strategies for deployed personnel with blast exposure or repetitive mild TBI.

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[97] Ashizawa, T., Figueroa, K.P., Perlman, S.L. et al. Clinical characteristics of patients with spinocerebellar ataxias 1, 2, 3 and 6 in the US; a prospective observational study. Orphanet J Rare Dis 8, 177 (2013). https://doi.org/10.1186/1750-1172-8-177

[98] Hafiz, S., De Jesus, O. (2023). Ataxia. StatPearls [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK562284/

[99] Defense Health Agency. (2024, February 29). Evaluation of the TRICARE Program: Fiscal Year 2024 Report. https://www.health.mil/Reference-Center/Reports/2024/09/23/Annual-Evaluation-of-the-TRICARE-Program-FY24

[100] Epidemiology Program, Health Outcomes, Military Exposures, Office of Patient Care Services, Department of Veterans Affairs. (2021). Post Deployment Health Surveillance Tables of Prevalence and Incidence: 2010-2019. https://www.publichealth.va.gov/docs/epidemiology/PDSR_Dec_2019.pdf

[101] Stephen, C.D., Brizzi, K.T., Bouffard, M.A. et al. The Comprehensive Management of Cerebellar Ataxia in Adults. Curr Treat Options Neurol 21, 2019). https://doi.org/10.1007/s11940-019-0549-2

[102] Beard JD, Kamel F. Military service, deployments, and exposures in relation to amyotrophic lateral sclerosis etiology and survival. Epidemiol Rev. 2015;37(1):55-70. doi: 10.1093/epirev/mxu001. Epub 2014 Oct 31. PMID: 25365170; PMCID: PMC4325667. https://pmc.ncbi.nlm.nih.gov/articles/PMC4325667/

[103] Klockgether, T., Grobe-Einsler, M. & Faber, J. Biomarkers in Spinocerebellar Ataxias. Cerebellum 24, 104 (2025). https://doi.org/10.1007/s12311-025-01856-5

[104] Potashman, M., Popoff, E., Powell, L. et al. Psychometric Validation of the Modified Functional Scale for the Assessment and Rating of Ataxia (f-SARA) in Patients With Spinocerebellar Ataxia. Cerebellum 23, 2095–2108 (2024). https://doi.org/10.1007/s12311-024-01707-9

[105] Öz, G., Cocozza, S., Henry, PG. et al. MR Imaging in Ataxias: Consensus Recommendations by the Ataxia Global Initiative Working Group on MRI Biomarkers. Cerebellum 23, 931–945 (2024). https://doi.org/10.1007/s12311-023-01572-y

- **<u>Hydrocephalus</u>**: Hydrocephalus is a chronic neurological condition that affects over one million people in the US. Hydrocephalus has no cure and the only treatment option is brain surgery. Often thought of as a pediatric condition, children can be born with hydrocephalus or develop it after birth, with the premature baby population being at particular risk of post-hemorrhagic hydrocephalus as a result of a brain bleed. Hydrocephalus is the leading cause of brain surgery in children. However, anyone at any time can develop hydrocephalus as it can be caused by a traumatic brain injury, tumor, infection, or as part of the aging process for reasons which are still not understood. This makes hydrocephalus' impact and reach within our military population deep and wide. Families can be affected if their children are born with or develop the condition. Active service members and veterans who have experienced traumatic brain injury are particularly vulnerable to developing hydrocephalus. Since 2000, more than 450,000 U.S. service members have sustained a traumatic brain injury.[106] Over 60,000 are at risk of developing hydrocephalus due to the severity of the injury.[107] [108] [109] [110]The Department of Defense does not currently track the development of hydrocephalus, so, while Normal Pressure Hydrocephalus (NPH) affects elderly adults, it is not known if previous injury, even mild injury, increases the risk of NPH. It is estimated that NPH affects over 800,000 seniors in the United States, including over 180,000 veterans. [111] [112]

[106] Evaluation of the DoD's Management of Traumatic Brain Injury. Department of Defense Office of Inspector. 2023 https://www.dodig.mil/reports.html/article/3346218/evaluation-of-the-dods-management-of-traumatic-brain-injury-dodig-2023-059/#:~:text=As%20highlighted%20in%20the%20DoD,exposure%20during%20combat%20and%20training

[107] Groswasser, Z., Cohen, M., Reider-Groswasser, I., & Stern, M.J. (1988). Incidence, CT findings and rehabilitation outcome of patients with communicative hydrocephalus following severe head injury. Brain Inj, 2, 267-272.

[108] Licata, C., Cristofori, L., Gambin, R., Vivenza, C., & Turazzi, S. (2001). Post-traumatic hydrocephalus. J.Neurosurg. Sci, 45, 141- 149.

[109] Marmarou, A., Foda, M.A., Bandoh, K., Yoshihara, M., Yamamoto, T., & Tsuji, O. et al. (1996). Posttraumatic ventriculomegaly: Hydrocephalus or atrophy? A new approach for diagnosis using CSF dynamics. J.Neurosurg, 85, 1026-1035.

[110] Mazzini, L., Campini, R., Angelino, E., Rognone, F., Pastore, I., & Oliveri, G. (2003). Posttraumatic hydrocephalus: A clinical, neuroradiologic, and neuropsychologic assessment of long-term outcome. Arch. Phys. Med. Rehabil, 84, 1637-1641.

[111] Jaraj D, Rabiei K, Marlow T, Jensen C, Skoog I, Wikkelsø C. Prevalence of idiopathic normal-pressure hydrocephalus. Neurology.2014;82:1449–1454. doi: 10.1212/WNL.0000000000000342.

[112] The Veteran Population Projection Model 2014. U.S. Department of Veterans Affairs. http://www.va.gov/vetdata/Veteran_Population.asp.

- **<u>Kidney Cancer</u>**: Kidney cancer affects military personnel, their dependents and veterans at a much higher rate than the general US population. Military Health System states between 2010-2019 49,472 active service members and other Department of Defense beneficiaries were diagnosed with kidney cancer.[113] Kidney cancer is the fourth leading cancer in incidence among patients of the United States Veterans Affairs Healthcare System.[114] Congress passed the PACT Act in 2022. This Act expanded benefits to active service members and veterans exposed to toxins and specifically designated kidney cancer as a presumptive condition for disability benefits.[115] Under the Act, the VA expanded its Airborne Hazards and Open Burns Bits Registry (AHOBPR) and Toxic Exposure Screenings. More than 4 million screenings have occurred through August 2023.[116] Researchers, including experts at VA, are actively studying airborne hazards like burn pits and other military environmental exposures.[117] The EPA, under the Safe Drinking Water Act, has finalized their rule on PFAS in drinking water. A large study shows that participants with high concentrations of PFAS are more than twice as likely to develop kidney cancer.[118] The Department of Defense has identified 687 installations with known or suspected release of PFAS (Per- and Polyfluorinated Substances).[119] According to the Centers for Disease Control and Prevention, US Marines and their families stationed at Camp Lejeune have a 35% higher risk of contracting kidney cancer than their US counterparts due to contaminated drinking water.[120] With incidences of smoking more prevalent among service members and veterans than in civilian populations, and a higher chance of exposure to chlorinated solvents, petrochemicals, and heavy metals associated with increased risk of renal cell carcinoma, kidney cancer is especially relevant to the military.[121]

[113] https://cdmrp.health.mil/pubs/annreports/2021annrep/2021annreport.pdf
[114] https://pubmed.ncbi.nlm.nih.gov/28810986/
[115] https://www.va.gov/resources/the-pact-act-and-your-va-benefits
[116] https://www.publichealth.va.gov/exposures/burnpits/participants.asp
[117] https://www.publichealth.va.gov/exposures/burnpits/index.asp
[118] Shearer J, et al. Serum concentrations of per- and polyfluoroalkyl substances and risk of renal cell carcinoma. J Natl Cancer Inst,September 18, 2020. DOI: 10.1093/jnci/djaa143.
[119] Firefighting Foam Chemicals: DOD Is Investigating PFAS and Responding to Contamination, but Should Report More Cost Information (GAO-21-421: June 2021), United States Government Accountability Office, Report to Congressional Committees
[120] Bove, F.J., Ruckart, P.Z., Maslia, M. et al. Evaluation of mortality among marines and navy personnel exposed to contaminated drinking water at USMC base Camp Lejeune: a retrospective cohort study.Environ Health 13, 10 (2014). https://doi.org/10.1186/1476-069X-13-10
[121] Congressionally Directed Medical Research Programs: 2021 Annual Report (September 30, 2021), Department of Defense, US Army Medical Research and Development Command, page 36. https://cdmrp.health.mil/pubs/annreports/2021annrep/2021annreport.pdf

- **Leukemia/Lymphoma/Multiple Myeloma**: Many of the blood cancers are linked to chemical and radiologic exposure during deployment. Leukemia, non-Hodgkin Lymphoma (NHL), Hodgkin Lymphoma (HL), and multiple myeloma have all been connected to chemical weapons, or storage, ionizing radiation, herbicides, electromagnetic fields, jet fuel, organic materials, etc. The Selected Cancers Cooperative Study Group showed that veterans of the Vietnam War had a 50% increase of risk of HL as compared to subjects who had not served in Vietnam. Evidence associates an increased risk for NHL, HL, and chronic lymphocytic leukemia to Vietnam War service and exposure to herbicides such as Agent Orange.[122]

- **Lung Cancer**: Lung cancer is by far the leading cause of cancer death in the US, accounting for about 1 in 5 of all cancer deaths.[123] Numerous studies over the years published by the Institute of Medicine, Cancer, Military Medicine, Chest and others have shown that lung cancer incidence and mortality rates, due to much higher smoking rates and exposures to known carcinogens during active duty, are an estimated 25% – 30% higher in the military than in civilian populations.[124] [125] [126] [127]Of growing concern is the lung cancer risk among ground troops deployed during the Gulf Wars whose exposures included asbestos, chromium, diesel exhaust, radon, crystalline silica, pesticides, pollutants and particulate matter from burn pits, oil well fires and the destruction of chemical weapons including sarin gas. Research focused on these veterans is urgently needed. Given lung cancer's long latency period, and the fact that the average age of Gulf War veterans is now in the mid-fifties, research projects and clinical practice should incorporate CT screening as a platform. Lung cancer is the second most common cancer diagnosed in Veterans and only 21% of lung cancers are caught at stage I.[128] Survival for screen-detected lung cancer especially when the lung cancer is in its earliest stages is much higher than metastatic lung cancer.[129] While surgery with curative intent can be offered to patients with early-stage lung cancer, the addition of new neoadjuvant (immunotherapies) or adjuvant (immunotherapies or targeted therapies) can further increase cures rates in early-stage disease.[130] [131]

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[122] Frumkin H. Agent Orange and cancer: an overview for clinicians. CA Cancer J Clin. 2003;53:245–55.
[123] Key Statistics for Lung Cancer. American Cancer Society. Accessed February 13, 2023. https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html.
[124] Stuart Bondurant and Roberta Wedge. Combating Tobacco Use in Military and Veteran Populations, , Editors; Committee on Smoking Cessation in Military and Veteran Populations; Institute of Medicine 2009. http://www.nap.edu/catalog.php?record_id=12632
[125] Harris RE, Hebert JR, Wynder EL. Cancer risk in male veterans utilizing the Veterans Administration medical system. Cancer 1989;64:1160-8.
[126] A Study of Cancer in the Military Beneficiary Population, Guarantor: Raymond Shelton Crawford III, MD MBA, Contributors: Raymond Shelton Crawford III, MD MBA; Julian Wu, MD MPH; Dae Park, MD; Galen Lane Barbour, MD; Military Medicine, Vol. 172, October 2007.
[127] Wilson, M.. Prevalence of tobacco abuse in a United States Marine Corp Infantry Battalion Forward Deployed in the Haditha Triad Area of Operations, Al Anbar, Iraq. CHEST. 2008;134: s53001
[128] Leah Zullig; Mil Med. 2017 Jul;182(7):e1883-e1891. doi: 10.7205/MILMED-D-16-00371.
[129] International Early Lung Cancer Action Program Investigators; Claudia I Henschke,et al; N Engl J Med. 2006 Oct 26;355(17):1763-71. doi: 10.1056/NEJMoa060476.
[130] Mariano Provencio et al; Am Soc Clin Oncol Educ Book. 2022 Apr;42:1-18. doi: 10.1200/EDBK_358995.
[131] Yi-Long Wu et al; N Engl J Med. 2020 Oct 29;383(18):1711-1723. doi: 10.1056/NEJMoa2027071. Epub 2020 Sep 19.

- **Lupus**: Lupus is a debilitating autoimmune disease that causes the immune system to erroneously attack health, living tissue. It is up to three times more common among African Americans, Hispanics and Native Americans.[132] Lupus affects over one-and-a-half million persons in the U.S. --90 percent of whom are women. Defense Department data show that women now make up a much greater share of our armed forces than they have at any time in U.S. history. Women account for 16 percent of active duty Service Members, 19 percent of the Air Force, 18 percent of the Navy, 14 percent of the Army, and 8 percent of the Marines.[133] A 2018 Council of Foreign Relations report found that the active-duty female force is racially diverse—56 percent of female recruits are Hispanic and there are nearly as many black women as white women in the Army.[134] Lupus often strikes young women of childbearing age who experience symptoms such as intense fatigue and exhaustion, joint pains, cognitive and memory problems, and skin rashes. It can also manifest in kidney problems, premature heart disease, strokes, or lung inflammation. Research shows that Lupus is becoming more prevalent among women in the military.[135] In 2009, as many as 20,000 active duty soldiers and veterans were receiving care for lupus through TRICARE or the Veteran's Administration healthcare system.[136] There are a number of possible reasons that could help to explain the growing rates of Lupus including post-traumatic stress disorder, chemicals and toxins, as well as certain drugs and infectious agents.[137] Research projects are studying these triggers to determine what effect they have on the immune system.

[132] Wallace, D.J., and Hahn, B.H. Dubois' Lupus Erythematosus and Related Syndromes. (8th ed.) Philadelphia, PA: Elsevier Saunders. 2013.
[133] 2015 Demographics: Profile of the Military Community. Department of Defense. Accessed January 21, 2020.
[134] Demographics of the U.S. Military. Council on Foreign Relations. Accessed January 21, 2020.
[135] O'Donovan, et al. Elevated Risk for Autoimmune Disorders in Iraq and Afghanistan Veterans with Posttraumatic Stress Disorder. Biological Psychiatry. 2015. Accessed January 21, 2020.
[136] Lupus, the Prototypical Autoimmune Disease, and the Military. Lupus Foundation of America, Inc. 2009. Accessed January 21, 2020.
[137] Department of Defense: Lupus Research Program. Accessed January 21, 2020.

- **<u>Malaria</u>:** While malaria has been eliminated from the United States since 1951, it has been and remains a direct threat to members of the United States military serving overseas.[138] During World War II, General Douglas MacArthur was quoted as saying, "This will be a long war if for every division I have facing the enemy, I must count on a second division in hospital with malaria and a third division convalescing from this debilitating disease!"[139] Nearly eighty years later, malaria remains the number one infectious disease threat to U.S. military forces deployed worldwide.[140] In 2003, 80 out of 220 or 36% of Marines deployed to Liberia contracted Plasmodium falciparum malaria due to low prophylaxis adherence, 46 of which required medical evacuation. Given the threat malaria poses to service members, the Department of Defense, through the Walter Reed Army Institute of Research (WRAIR) and the Naval Medical Research Center (NMRC) conducts malaria-related research and development efforts for drugs, diagnostics and vaccines, helping to establish and enhance partnerships around the world and achieve FDA-approval of new tools in the fight against malaria. WRAIR's role within the DOD is critical, as they are the only institution in the world focused on developing the treatments to prevent malaria in healthy adults.[141] Among its recent successes, the scientists at WRAIR made significant contributions to the development of the RTS,S malaria vaccine which is currently being piloted in Kenya, Malawi, and Ghana, as well as the development of tafenoquine, a single dose cure for Plasmodium vivax malaria which was approved by the FDA in July 2018.[142]

- **<u>Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS):</u>** Studies in Military Behavioral Health Journal and elsewhere estimate that one in six veterans have chronic fatigue syndrome[143] [144]. A study of 2,000 Gulf War veterans found that the odds of developing chronic fatigue syndrome for deployed veterans were 40 times as much as those for undeployed veterans [145]. Active-duty personnel who develop ME/CFS may become incapacitated and ineligible for deployment or even routine duties. ME/CFS is a serious and often debilitating disease characterized by severe fatigue, cognitive impairment, and post-exertional malaise (profound exhaustion following physical or mental effort that would not typically affect healthy people). The disease burden of ME/CFS (years lived with disability/100,000 adults) exceeds that of stroke and is comparable to that of anxiety disorders and migraine [146]. Before the COVID-19

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[138] Pages, F., Faulde, M., Orlandi-Pradines, E., & Parola, P. (2010). The past and present threat of vector-borne diseases in deployed troops. Clinical Microbiology and Infection, 16(3), 209-224.
[139] Paul F Russell, 'Introduction', in Preventive medicine in World War II, op. cit., note 1 above, p. 2.
[140] Moss, Kellie and Josh Michaud. 2013. The U.S. Department of Defense and Global Health: Infectious Disease Efforts. Kaiser Family Foundation pg. 17
[141] Lezaun, J. (2018). The deferred promise of radical cure: pharmaceutical conjugations of malaria in the global health era. Economy and Society, 1-25.
[142] Hounkpatin, A. B., Kreidenweiss, A., & Held, J. (2019). Clinical utility of tafenoquine in the prevention of relapse of Plasmodium vivax malaria: a review on the mode of action and emerging trial data. Infection and drug resistance, 12, 553.
[143] Kipen HM, Hallman W, Kang H, Fiedler N, Natelson BH. Prevalence of chronic fatigue and chemical sensitivities in Gulf Registry Veterans. Arch Environ Health. 1999;54(5):313-318.
[144] McAndrew LM, Chandler HK, Serrador JM, Quigley KS, Natelson BH, Lange G. Comparison of the functional health limitations of Iraq or Afghanistan Veterans to Desert Shield/Storm Veterans with chronic fatigue syndrome. Mil Behav Health. 2016;4(3):299-306.
[145] Eisen SA, Kang HK, Murphy FM, et al. Gulf War veterans' health: medical evaluation of a U.S. cohort. Ann Intern Med. 2005;142(11):881-890
[146] Bonuck K, Gao Q, Congdon S, Kim RS. Long COVID disability burden in US adults. Commun Med (Lond). 2026;6(1):177.

pandemic, about three million adults in the US were affected by ME/CFS; but because many people with Long Covid subsequently develop ME/CFS, the current prevalence is likely much higher, with estimates of over 71.2 million afflicted worldwide[147] [148]. Despite its high disability burden, ME/CFS remains severely underfunded, receiving less than 1% of the NIH funding warranted by its burden (one study lists it as the most underfunded disease) [149]. Thus, support from other funding agencies, like the Congressionally Directed Medical Research Programs (CDMRP), is critical for helping people with ME/CFS. In particular, there is an urgent need to find reliable biomarkers for diagnosis and to develop effective treatments, as there are currently no FDA approved biomarkers or therapies for people with ME/CFS. Research on ME/CFS is also valuable for understanding other CDMRP-prioritized "low-energy" conditions, like Long COVID, lupus, multiple sclerosis, psychological health disorders, and Gulf War illness[150] , since ME/CFS symptoms and pathological mechanisms substantially overlap with these other diseases, as discussed in Military Medicine and elsewhere[151] . In some cases, individuals with these similar disorders are at significantly increased risk of later developing ME/CFS. For example, both ME/CFS and Gulf War illness are associated with initial infections or environmental stressors and their symptom profiles substantially overlap [152] [153] [154]. These shared features suggest that advances in diagnostic tools and therapeutic strategies for ME/CFS will have broader clinical relevance to the overall "low-energy" conditions community.

[147] Eckey M, Li P, Morrison B, Bergquist J, Davis RW, Xiao W. Patient-reported treatment outcomes in ME/CFS and long COVID. Proc Natl Acad Sci U S A. 2025;122(28):e2426874122.
[148] Vardaman M, Gilmour S. Letter: Time to correct the record on the global burden of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). J Transl Med. 2025;23(1):331. Published 2025 Mar 14.
[149] Bonuck K, Gao Q, Congdon S, Kim RS. Long COVID disability burden in US adults. Commun Med (Lond). 2026;6(1):177.
[150] Mantle D, Domingo JC, Golomb BA, Castro-Marrero J. Gulf War Illness, Fibromyalgia, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Long COVID Overlap in Common Symptoms and Underlying Biological Mechanisms: Implications for Future Therapeutic Strategies. Int J Mol Sci. 2025;26(18):9044.
[151] Bast E, Jester DJ, Palacio A, Krengel M, Reinhard M, Ashford JW. Gulf War Illness: A Historical Review and Considerations of a Post-Viral Syndrome. Mil Med. 2026;191(1-2):e7-e11.
[152] Kipen HM, Hallman W, Kang H, Fiedler N, Natelson BH. Prevalence of chronic fatigue and chemical sensitivities in Gulf Registry Veterans. Arch Environ Health. 1999;54(5):313-318.
[153] Mantle D, Domingo JC, Golomb BA, Castro-Marrero J. Gulf War Illness, Fibromyalgia, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Long COVID Overlap in Common Symptoms and Underlying Biological Mechanisms: Implications for Future Therapeutic Strategies. Int J Mol Sci. 2025;26(18):9044.
[154] Bast E, Jester DJ, Palacio A, Krengel M, Reinhard M, Ashford JW. Gulf War Illness: A Historical Review and Considerations of a Post-Viral Syndrome. Mil Med. 2026;191(1-2):e7-e11.

- **<u>Mefloquine neurotoxicity/chronic quinoline encephalopathy</u>**: Mefloquine is an antimalarial quinoline drug developed by the U.S. military that had been widely employed until 2013, when the DoD declared it an antimalarial drug of last resort, after research at the Walter Reed Army Institute of Research (WRAIR) identified it as neurotoxic, and the U.S. Food and Drug Administration (FDA) warned that mefloquine may cause long-lasting and even permanent adverse neuropsychiatric effects. The U.S. Department of Veterans Affairs (VA) has recently awarded several disability claims to veterans for permanent neuropsychiatric conditions, including anxiety and insomnia, that the VA has concluded were due to exposure to mefloquine while serving in the military.[155] "Neurotoxicity of mefloquine" was first included as a PRMRP topic area fifteen years ago for one year (FY 2006).[156] DoD has provided other limited funding for toxicity-relevant research, including funding by the Military Infectious Disease Research Program (MIDRP) for a project entitled, Evaluation of Multiple Potential Pharmacogenomic Risk Factors for Chronic Mefloquine Neurotoxicity [i.e. chronic quinoline encephalopathy] Through the Establishment of a Drug Safety Registry.[157] A National Academies of Sciences, Engineering, and Medicine (NASEM) committee, charged "*to assess the long-term health effects that might result from the use of antimalarial drugs by adults, in particular mefloquine, for the prophylaxis of malaria,*"[158] concluded "there is a very limited body of research that directly addresses the pathways by which these drugs might result in persistent changes that produce adverse events that may or may not be reversible." Consistent with prior PRMP funding and the recommendations of the NASEM committee for further research, support is needed to define persistent and latent central nervous system effects of antimalarial quinoline neurotoxicity, to define the adverse neurophysiological effects of antimalarial quinolines, to disentangle comorbid neuropsychiatric diagnoses confounded by antimalarial quinoline toxicity, and to develop effective treatments.

[155] Nevin RL, Ritchie EC. FDA Black Box, VA Red Ink? A Successful Service-Connected Disability Claim for Chronic Neuropsychiatric Adverse Effects From Mefloquine. Federal Practitioner. 2016;33(10):20–24.
[156] Peer Reviewed Medical, FY06 Topic Areas: https://cdmrp.army.mil/prmrp/topicareas/topicareas06.
[157] U.S. Army Medical Research and Materiel Command. Congressionally Directed Medical Research Programs. 2017 Annual Report. https://cdmrp.army.mil/pubs/annreports/2017annrep/2017annreport.pdf
[158] National Academies of Sciences, Engineering, and Medicine 2020. Assessment of Long-Term Health Effects of Antimalarial Drugs When Used for Prophylaxis. Washington, DC: The National Academies Press. https://doi.org/10.17226/25688.

- **Melanoma**: A 2000 "Annals of Epidemiology" study comparing mortality among WWII veterans of the Pacific and European Theaters found that Pacific Theater Prisoner of War veterans had an estimated 3-fold higher risk of dying from melanoma than veterans of the European Theater, concluding that exposure to high levels of solar radiation in young adulthood is associated with a higher risk of melanoma mortality.[159] Given this information, U.S. military personnel currently stationed in Iraq and Afghanistan, where the intensity of sun exposure is similar to that of the Pacific, have the potential for a long-term risk of melanoma. According to the American Cancer Society, the American Academy of Dermatology and the Melanoma Research Foundation, skin cancer is the most commonly diagnosed cancer in the United States. Melanoma, the deadliest type of skin cancer, kills an estimated 10,000 Americans each year. Furthermore, people of all ages, races and genders are at risk. Melanoma is the most common form of cancer for young adults 25-29, the second most common form of cancer for young people 15-29 and SEER data suggests that the majority of people diagnosed with melanoma are white men over the age of 50.[160] [161] [162]

- **Mesothelioma**: There is a long history of asbestos exposure in military service, and a significant elevated risk of mesothelioma in the military population.[163] A study of occupational exposures and subsequent mesothelioma diagnoses found that one third of mesothelioma cases involved Navy and shipyard exposures.[164] Due to disease development latency (i.e., disease of today is caused by exposure from 25-50 years ago) and asbestos' continued presence on US Navy ships (Comptroller General of the United States, 1979), the expectation is that mesothelioma development among service members will not stop. Among other branches of military, recent exposures have been reported among service members engaged across a variety of military interests abroad, particularly in Iraq and Afghanistan. In addition, smoking has been shown to negatively affect survival in mesothelioma patients.[165] The prevalence of tobacco use among military personnel, and specifically smoking, is reported to be significantly higher than that of the general population.[166]

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[159] Annals of Epidemiology, Vol. 10, Issue 3, April 2000, pages 192-195.
[160] Bleyer A, O'Leary M, Barr R, Ries LAG (eds): Cancer epidemiology in older adolescents and young adults 15 to 29 years of age, including SEER incidence and survival: 1975-2000. Bethesda, MD: National Cancer Institute; 2006
[161] Melanoma of the Skin, Cancer Fact Sheets, National Cancer Institute, SEER database, 2007. http://seer.cancer.gov
[162] Howlader N, Noone AM, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations). Bethesa, MD: National Cancer Institute; http://seer.cancer.gov/csr/1975_2009_pops09/; Accessed August 22, 2012.
[163] Comptroller General of the United States. (1979). Navy's Efforts to Protect Workers From Asbestos Exposure.Comptroller General of the United States.
[164] K. J. BUTNOR, A. S. (2002). Malignant Mesothelioma and Occupational Exposure. The Annals of Occupational Hygiene, 150–153.
[165] Flores, R. M., Zakowski, M., Krug, L., Rosenzweig, K., & Rusch, V. (2007). Prognostic Factors in the Treatment of Malignant Pleural Mesothelioma at a Large Tertiary Referral Center. Journal of Thoracic Oncology, 957-965.
[166] Wilson, M. A. (2008). PREVALENCE OF TOBACCO ABUSE IN A UNITED STATES MARINE CORP INFANTRY BATTALION FORWARD DEPLOYED IN THE HADITHA TRIAD AREA OF OPERATIONS, AL ANBAR, IRAQ.Chest Journal.

- **Multiple Sclerosis**: There are currently over 70,000 veterans with diagnosed multiple sclerosis (MS), and over 15,000 of those veterans have a service-connected disability for MS.[167] MS is an inflammatory and degenerative disease of the central nervous system that typically starts with relapses and transitions to a progressive phenotype. MS is the most frequent progressive neurological disease of young adults with a mean age of diagnosis of 30 years.[140] Common symptoms include ataxia, numbness and tingling, blindness, pain, paralysis, bladder dysfunction, and fatigue. The progression, severity and specific symptoms of MS in any one person cannot yet be accurately predicted. The incidence of MS in military Veterans is among the highest in North America with Blacks having the highest rates followed by Whites, Hispanics, Asians and Native Americans.[141] MS is a common reason for military disability retirement and there is a presumptive period for a service connected benefit for MS. Individuals who have their initial symptoms of MS while they are in active duty military or within seven years of their honorable discharge are eligible for a service-connected disability. In 2003, the VHA funded the MS Center of Excellence to coordinate interdisciplinary clinical care, education and research for Veterans with MS. Each year, the Veterans Health Administration provides care to more than 30,000 veterans with MS.[140] The MSCoE ensures cost-effective access to FDA-approved MS disease modifying medications at the earliest time point and utilizes telemedicine platforms to reach Veterans with MS separated from specialty care by distance and disability.[140, 142] A recent publication highlighted a novel proteomic signature in the serum of Veterans with MS through the use of a military MS cohort with samples from the Department of Defense Serum Repository.[143] This proteomic signature is a starting point for further immunological characterization of this MS case subset and may be clinically useful as an antigen-specific biomarker for high-risk patients with clinically or radiologically isolated neuroinflammatory syndromes. By studying the military MS population, scientists might be able to understand the cause and triggers of MS and develop more effective treatments and preventive measures.

[167]Veterans Health Administration, VA Multiple Sclerosis Center of Excellence Database. FY 1998-FY2024.

- **Neurofibromatosis (NF)**: NF research critically addresses areas of great clinical need directly affecting the health of our soldiers. The genetic information learned from NF research holds the key to understanding a number of health issues that affect the war fighter, as well as the general population, including cancer, bone fracture and repair, vascular disease, wound healing and nerve regeneration, deafness, behavioral and psychosocial issues, learning disabilities, muscle weakness, and pain. For example, NF often requires surgical removal of nerve tumors, which can lead to nerve paralysis and loss of function, similar to nerve damage sustained by the war fighter after injury. Understanding how nerves and skin might be regenerated and functionally restored will have significant quality of life value for affected individuals. Current NF research aims to develop a rapid approach for taking a person's skin stem cells and differentiating them into cell types that need replacing after injury. This work will advance skin regeneration research and elucidate the potential of skin derived stem cells to make other cell types such as nerve cells, to restore function after injury. In another example, orthopedists, NF-ologists and tissue engineers are collaborating to investigate innovative technologies that will improve the healing of challenging and recurring bone breaks in NF patients, research that directly benefits war fighters with major bone breakages. Therefore, due to the nature of the wounds and recovery that soldiers are enduring, NF research is of particular benefit to the military mission. Proposals include: NF080017[168], NF120087[169], NF110052[170] and NF110052[171]

- **Osteoarthritis (OA)**: Current research suggests that stresses placed on joints during military training activities, increased rates of injury, and increased weight of military packs have led active duty soldiers and veterans to have twice the rate of Osteoarthritis (OA) when compared to non-military populations. In fact, OA is the leading cause of disability and medical discharge in active service members under the age of 40. Rheumatoid arthritis (RA) strikes at the peak one's career (mid-late thirties/forties) and often leads to early retirement and disability. CDMRP research funding for OA and RA could help identify arthritis prior to the onset of symptoms. This research could help identify medical and physical interventions to prevent or minimize joint damage and slow or stop the arthritis disease process before joints are permanently damaged. Targeted research efforts would focus on examining genetic factors, ways to improve diagnosis, screening, and treatment options. (Proposals: 101035[172], 120839[173], 130776[174])

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[168] Elefteriou, Florent. Neurofibromin Function in Chondrocytes.
[169] Kim, Aerang. Phase I/II Trial of an Hsp90 Inhibitor in Combination with an mTOR Inhibitor for Patients with Refractory Malignant Peripheral Nerve Sheath Tumors.
[170] Plotkin, Scott. Phase 2 Study of Bevacizumab in Children and Young Adults With NF 2 and Progressive Vestibular Schwannomas.
[171] North, Kathryn. A Randomized Placebo-Controlled Study of Lovastatin in Children with Neurofibromatosis Type 1 (STARS)
[172] McKinley, Todd O. Mitochondrial Based-Treatments that Prevent Post-Traumatic Osteoarthritis in a Translational Large Animal Intraarticular Fracture Survival Model.
[173] Deane, Kevin D. Pathogenesis and Prediction of FutureRheumatoid Arthritis
[174] Hammond, Paula T. Cartilage-Penetrating Chondrogenic Nanoparticles for Early Posttraumatic Osteoarthritis Therapy.

- **Ovarian Cancer:** In the 45 years since the War on Cancer was declared, ovarian cancer mortality rates have not significantly improved. According to the American Cancer Society, it is estimated that in 2017, more than 22,400 American women will be diagnosed with ovarian cancer, and approximately 14,080 will lose their lives to this terrible disease. Ovarian cancer is the fifth leading cause of cancer death in women. Currently, more than half of the women diagnosed with ovarian cancer will die within five years. Of the 850,000 female service members, wives of active duty military and adult daughters of active duty military[175], approximately 11,800 will be diagnosed with ovarian cancer over the course of their lifetimes. [176] Over a five-year period, nearly 2,600 members of our military or their families may be hospitalized for ovarian cancer or suspected ovarian cancer. The cost of ovarian cancer to our military is great, not only in terms of troop readiness, but also in terms of cancer care costs: treating these cases of ovarian cancer over these patients' lifetimes could cost TRICARE an estimated $971.2 million. [177] TRICARE's potential costs to care for women with ovarian cancer could fund the Ovarian Cancer Research Program at the Department of Defense for nearly 50 years at its current funding level.

[175] Military Demographics for 2012. Available here: http://www.militaryonesource.mil/12038/MOS/Reports/2012_Demographics_Report.pdf

[176] The lifetime risk of a women developing ovarian cancer is 1.4% according to the SEER Fact Sheet available here: http://seer.cancer.gov/statfacts/html/ovary.html

[177] The average cost of frontline ovarian cancer therapy is $82,000, per the National Institutes of Health. http://costprojections.cancer.gov/annual.costs.html

- **Pancreatic Cancer**: Research has shown that there is direct evidence for increased risk of death from pancreatic cancer in some US veterans. Specifically, nurses serving in Vietnam had a 2- to 5-fold higher risk of pancreatic cancer death compared with non-deployed US military women[178] [179], and deaths of Australian Vietnam veterans from pancreatic cancer was 3-fold greater than non-veterans[180]. The reasons for this increase may be related to environmental exposures to chemical agents used in the field or in medical facilities, and the PACT Act[181] includes pancreatic cancer as a presumptive disease related to burn pit and other toxic exposures. Lifestyle propensities such as smoking, a known risk factor for pancreatic cancer, may also contribute to the increase in pancreatic cancer in US veterans[182] [183] [184]. Further, the link between type 2 diabetes and pancreatic cancer is well established[185]. Type 2 diabetes is an Agent Orange-associated presumptive disease[186], and veterans that suffer from post-traumatic stress disorder are at a greater risk of developing diabetes[187]. The Pancreatic Cancer Research Program has funded a variety of critical research areas to better detect and treat pancreatic cancer, including investigations into biomarkers to detect pancreatic cancer early or follow response to therapy, targeting the oncogene KRAS, activating the immune system, taking advantage of metabolic differences between normal and malignant pancreas cells, and a variety of highly novel therapeutic approaches. Continued support for this research is critical not only for the potential risks for developing pancreatic cancer associated with military service, but also because pancreatic cancer is currently the nation's third leading cause of cancer-related death and is predicted to surpass colorectal cancer to become second only to lung cancer by 2030.[188]

[178] Dalager, NA et al, Cancer Mortality Patterns among Women Who Served in the Military: The Vietnam Experience, J Occup & Environ Medicine 37: 298-305, 1995
[179] Kang, HK et al, HealthVIEWS: Mortality Study of Female US Vietnam Era Veterans, 1965-2010, Am J. Epidemiol 179: 721-30, 2014
[180] Wilson EJ, Horsley KW, van der Hoek R. Australian National Service Vietnam Veterans Mortality and Cancer Incidence Study 2005. Canberra: Department of Veterans' Affairs, 2005.
[181] https://www.publichealth.va.gov/exposures/benefits/PACT_Act.asp, accessed June 2024
[182] Barone E et al, Environmental risk factors for pancreatic cancer: an update. Arch Toxicol 90: 2617-2642, 2016.
[183] Odani S et al. Tobacco Product Use Among Military Veterans – United States, 2010–2015. MMWR Morb Mortal Wkly Rep 67: 7-12, 2018.
[184] Kolonel LN et al, Health-related Characteristics and Dietary Intakes of Male Veterans and Non-veterans in the Multiethnic Cohort Study (United States). J Mil Veterans Health 19: 4-9. 2011.
[185] Li D, et al. Diabetes and risk of pancreatic cancer: a pooled analysis of three large case–control studies. Cancer Causes Control 22:189–197, 2011
[186] http://www.publichealth.va.gov/exposures/agentorange/conditions/index.asp, accessed June 2024
[187] Boyko EJ, et al. Risk of Diabetes in U.S. Military Service Members in Relation to Combat Deployment and Mental Health. Diabetes Care 33:1771–1777, 2010
[188] Rahib L, et al. Estimated Projection of US Cancer Incidence and Death to 2040. JAMA Netw Open. 4(4):e214708, 2021.

- **Parkinson's research program**: Parkinson's Disease (PD) environmental risk factors overlap common soldier occupational exposures such as traumatic brain injury and neurotoxic chemical exposures. The combination of brain injury and chemical exposure triple Parkinson's risk.[189] In 2012, the Department of Veterans' Affairs (VA) made PD presumptive for TBI-connected with military service[190] and secondary service connection for diagnosable illnesses associated with traumatic brain injury.[191] In 2010, the VA made PD presumptive for exposure to Agent Orange.[192] In 2021, the VA expanded this and made Parkinsonisms (includes PD and atypical parkinsonisms) presumptive for exposure to Agent Orange.[193] In 2023, a study demonstrated a 70% higher risk of Parkinson's among Camp Lejeune veterans who were exposed to water contaminated with the chemical TCE in the 1970s and 1980s compared with veterans stationed at a Marine Corps base where water was not contaminated.[194] Concerns about burn pit exposures and PD continue. Currently funded research through the VA's Airborne Hazards and Burn Pits Center of Excellence is in progress.[195] The Parkinson's Research Program (PRP), previously titled the Neurotoxin Exposure Treatment (Parkinson's) Research Program (NETPR), is funding studies in biomarkers of TBI and PD. Environmental and occupational chemical exposures, notably pesticides, increase the risk of PD in service members and has also been a focus of the program, identifying organochlorine compounds previously used in agriculture, environmental PCBs, and permethrin used in Army uniforms as risk factors for PD.[196] Parkinson's Disease Research, Education, and Clinical Centers (PADRECCs) were established within six leading VA centers to provide treatment to veterans with PD; research in these centers has benefited from NETPR and now PRP grants and provides transition between active duty members diagnosed with PD and their state-of-the-art continuity of care for PD in the VA. PD also shares neurological effects of concerns to soldiers such as disrupted sleep, depression, and cognitive impairment. All of these "dual use" aspects that are relevant to soldiers and to the PD community and have been a focus of PRP.

[189] Ritz et al., Neurology 2012;79:2061-6.
[190] 38 CFR Part 3 Department of Veterans Affairs.
[191] *Federal Register* 2013;78:76196–209.
[192] https://www.federalregister.gov/documents/2010/08/31/2010-21556/diseases-associated-with-exposure-to-certain-herbicide-agents-hairy-cell-leukemia-and-other-chronic
[193] https://www.va.gov/opa/pressrel/pressrelease.cfm?id=5675
[194] Goldman SM, Weaver FM, Stroupe KT, et al. Risk of Parkinson Disease Among Service Members at Marine Corps Base Camp Lejeune. JAMA Neurol. 2023;80(7):673–681. doi:10.1001/jamaneurol.2023.1168
[195] https://www.ideastream.org/news/ohio-state-va-study-explores-long-term-health-effects-of-exposure-to-burn-pits
[196] Tanner et al., Alz Dementia 2014;10:213-225.

- **<u>Post-Acute Sequela of COVID-19 (PASC aka "Long COVID")</u>:** The World Health Organization (WHO) recently published a definition of Long Covid[197], calling attention to one of the most concerning, yet under-recognized aspects of the COVID-19 pandemic. The most frequent prolonged symptoms are persistent fatigue, cognitive dysfunction ("brain fog") and depleted energy after even a minimal effort; having a profound impact on everyday functioning, affecting a quarter of all COVID-19 patients worldwide, with as many as 10% having long term symptoms that last for longer than 3 months.[198] While the severity of these symptoms varies among people and can fluctuate even for the same person, they can be completely disabling. This condition does not have simple diagnostics or treatments, and therefore has a clear and immediate impact on military readiness and performance. The severity of debilitating Long Covid symptoms is not correlated to the severity of the acute disease and is often affecting younger and healthy people who had a mild/moderate COVID-19 infection. Given the large numbers of people who were infected with COVID-19, the implications to the armed forces could be profound- particularly in specific units that had a higher rate of infection due to the challenges of their service environment. As a reference, it is currently estimated that Long COVID accounts for up to 15% of labor shortage and unfilled jobs in the United States.[199] While some people may recover over time, it is estimated that nearly half of Long Covid Cases meet the diagnostic criteria for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). ME/CFS, a condition associated with viral infections and previously associated with SARS-CoV-1[200], is the only COVID-triggered chronic illness currently included as a FY 21 Topic Area. As recent research is linking COVID-19 and ME/CFS[201], we strongly encourage the committee to sustain and increase investment in this area of research in order to mitigate the impact of this devastating post-viral illness on military service members and their families.

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[197] 2021. *A Clinical case definition of post COVID-19 condition by a Delphi consensus*. [ebook] World Health Organization. Available at: <https://apps.who.int/iris/bitstream/handle/10665/345824/WHO-2019-nCoV-Post-COVID-19-condition-Clinical-case-definition-2021.1-eng.pdf> [Accessed 22 February 2022].

[198] Euro.who.int. 2022. *In the wake of the pandemic: preparing for Long COVID (2021)*. [online] Available at: <https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/publications-and-technical-guidance/2021/in-the-wake-of-the-pandemic-preparing-for-long-covid-2021> [Accessed 22 February 2022].

[199] Bach, K., 2022. *Is 'long Covid' worsening the labor shortage?*. [online] Brookings. Available at: <https://www.brookings.edu/research/is-long-covid-worsening-the-labor-shortage/> [Accessed 22 February 2022].

[200] Moldofsky, H. and Patcai, J., 2011. Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. *BMC Neurology*, [online] 11(1). Available at: <https://pubmed.ncbi.nlm.nih.gov/21435231/ [Accessed 22 February 2022].

[201] Paul, B., Lemle, M., Komaroff, A. and Snyder, S., 2021. Redox imbalance links COVID-19 and myalgic encephalomyelitis/chronic fatigue syndrome. *Proceedings of the National Academy of Sciences*, [online] 118(34), p.e2024358118. Available at: <https://www.pnas.org/content/118/34/e2024358118>.

- **<u>Posttraumatic Stress Disorder and Psychological Health</u>**:
  Posttraumatic Stress Disorder: Posttraumatic stress disorder (PTSD) is the psychological health condition most commonly associated with military combat deployments.[202] [203] PTSD has been referred to as a "signature wounds of war". [204] [205] PTSD in combat veterans has been estimated to be about 14%, which equates to over 400,000 service members and veterans who have deployed to Iraq, Afghanistan, and surrounding locations.[206] Over the past decade, DoD-funded PTSD research has contributed to major advancements in the understanding, assessment, diagnosis, treatment, and prevention of PTSD in active duty military personnel. Many of these advancements are the result of leveraging the synergistic power of team science [207] that has occurred through the federal funding of two PTSD research consortia.[208] Although the DoD has continued to fund research consortia for TBI, suicide, and substance used disorders, the funding for a PTSD research consortium ended in 2020. With PTSD recovery rates in active duty military personnel limited to slightly more than 50% of those treated with current evidence-based interventions, and as the incidence of PTSD continues to persist in military populations, there is a critical need for continued funding of DoD PTSD research including support for a PTSD research consortium.

  Psychological Health: In addition to PTSD, servicemembers and veterans experience high rates of other mental health conditions, including substance use issues and depression. Servicemembers and veterans face unique stressors compared to the civilian population, through direct combat, mortuary services, moral injury, drone operation, and other defense-specific missions.[209] Many servicemembers are less likely to seek treatment for a mental health condition due to the stigma associated with receiving care in the military community as well as concerns about promotions or security clearance,

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[202] Institute of Medicine. (2014). Treatment of posttraumatic stress disorder in military and veteran populations: Final assessment. Washington, DC: The National Academies Press. https://doi.org/10.17226/18724

[203] Armed Forces Health Surveillance Center. (2011). Associations between repeated deployments to OEF/OIF/OND, October 2001-December 2010, and post-deployment illnesses and injuries, active component, U.S. Armed Forces. Medical Surveillance Monthly Report (MSMR), 18(9), 2-11. https://health.mil/Reference-Center/Reports/2011/01/01/Medical-Surveillance-Monthly-Report-Volume-18-Number-9

[204] Tanielian, T., & Jaycox, L. H. (Eds.). (2008). Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery. Santa Monica, CA: RAND Corporation. https://doi.org/10.7249/mg720

[205] Brundage JF, Taubman SB, Hunt DJ, Clark LL. Whither the "signature wounds of the war" after the war: estimates of incidence rates and proportions of TBI and PTSD diagnoses attributable to background risk, enhanced ascertainment, and active war zone service, active component, U.S. Armed Forces, 2003-2014. MSMR. 2015 Feb;22(2):2-11. PMID: 25734618.

[206] Judkins, J. L., Moore, B. A., Collette, T. L., Hale, W. J., Peterson, A. L., & Morissette, S. B. (2020). The incidence rates of posttraumatic stress disorder over a 17-year period in active duty military service members. Journal of Traumatic Stress. Advance online publication. https://doi:10.1002/jts.22558

[207] Peterson, A. L., Cifu, D. X., Joiner, T. J., Williams, R. L., Keane, T. M., Hinds, S. R., II, Gutierrez, P. M., & Kosten, T. R. (2018, August). Leveraging the synergistic power of team science: Lessons learned from DoD-funded research consortia. Poster presented at the Military Health System Research Symposium, Kissimmee, FL.

[208] Peterson, A. L., Niles, B. L., Young-McCaughan, S., & Keane, T. M. (2021). Assessment and treatment of combat-related posttraumatic stress disorder: Results from STRONG STAR and the Consortium to Alleviate PTSD. In N. Gorbunov (Ed.), Military Medicine. InTech Open.

[209] National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Care Services; Committee to Evaluate the Department of Veterans Affairs Mental Health Services. Evaluation of the Department of Veterans Affairs Mental Health Services. Washington (DC): National Academies Press (US); 2018 Jan 31. 6, Department of Veterans Affairs Mental Health Services: Need, Usage, and Access and Barriers to Care. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499497/

requiring additional research on how to best reach out to servicemembers experiencing mental health issues. [210]

- **Prostate Cancer**: Prostate cancer is the second deadliest cancer among American men, killing more than 35,000 men annually,[211] and there are more than 3.3 million prostate cancer patients in the U.S. that depend on breakthroughs in research to continue their fight. Rates of prostate cancer have been increasing in recent years, especially the incidence rate of advanced disease.[212] Prostate cancer significantly impacts both active duty servicemen, veterans, and their families; in fact, active duty males are twice as likely to be diagnosed with prostate cancer as their civilian counterparts,[213] with negative effects on their ability to serve. In addition, soldiers exposed to chemical agents such as Agent Orange in Vietnam are considered to be at increased risk of death from prostate cancer due to its association with high-grade disease in a population-based study of US Veterans[214] and prostate cancer is now considered a presumptive service-connected disability since passage of the PACT Act.[215] Prostate cancer is the most commonly diagnosed cancer in the U.S. Department of Veterans Affairs.[216] Research funded by the Prostate Cancer Research Program (PCRP) advances treatments; PCRP funding was responsible for accelerating the development of the five new treatments for advanced disease in the last ten years,[217] [218] [219] [220] bringing them to patients faster than typical development of new drugs. Moreover, the program focuses on not only developing more effective therapeutics, but has also led to the development of a new diagnostic tool.[221] By improving diagnosis to reduce over treatment and accurately distinguish life-threatening disease from indolent tumors,[222] the PCRP may have its greatest impact on active duty servicemen who can be confidently monitored through active surveillance,[223] rather than compromising their service to undergo treatment.

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[210] Acosta, Joie D., Amariah Becker, Jennifer L. Cerully, Michael P. Fisher, Laurie T. Martin, Raffaele Vardavas, Mary Ellen Slaughter, and Terry L. Schell, Mental Health Stigma in the Military, Santa Monica, Calif.: RAND Corporation, RR-426-OSD, 2014. As of May 12, 2021: https://www.rand.org/pubs/research_reports/RR426.html

[211] American Cancer Society. Cancer Facts & Figures 2024. Atlanta: American Cancer Society; 2024.

[212] American Cancer Society. Cancer Facts & Figures 2024. Atlanta: American Cancer Society; 2024.

[213] Zhu K, Devesa SS, Wu H, et al. 2009. Cancer incidence in the U.S. military population: Comparison with rates from the SEER program. Cancer Epidemiol Biomarkers Prev 18:1740-45.

[214] Chamie K1, DeVere White RW, Lee D et al. 2008. Agent Orange exposure, Vietnam War veterans, and the risk of prostate cancer. Cancer. Nov 1;113(9):2464-70. doi: 10.1002/cncr.23695.

[215] US Department of Veterans Affairs. The PACT Act and your VA benefits. 2022. Accessed at https://www.va.gov/resources/the-pact-act-and-your-va-benefits/ on August 25, 2022.

[216] Levine RD, Ekanayake RN, Martin AC, et al. Prostate Cancer Foundation-Department of Veterans Affairs Partnership: A Model of Public-Private Collaboration to Advance Treatment and Care of Invasive Cancers. Fed Pract. 2020;37(Suppl 4):S32-S37. doi:10.12788/fp.0035

[217] Ryan CJ, Smith MR, de Bono JS et al. 2013. Abiraterone in metastatic prostate cancer without previous chemotherapy. N Engl J Med. 2013 Jan 10;368(2):138-48. Erratum in: N Engl J Med. 2013 Feb 7;368(6):584.

[218] Scher HI, Beer TM, Higano CS et al. 2010. Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1-2 study. Lancet. 2010 Apr 24;375(9724):1437-46.

[219] 2018 Prostate Cancer Research Program Book. https://cdmrp.army.mil/pcrp/pbks/pcrppbk2018.pdf

[220] Abida W, Patnaik A, Campbell D, et al. Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a BRCA1 or BRCA2 Gene Alteration. J Clin Oncol. 2020;38(32):3763-3772. doi:10.1200/JCO.20.01035

[221] 2018 Prostate Cancer Research Program Book. https://cdmrp.army.mil/pcrp/pbks/pcrppbk2018.pdf

[222] http://comptroller.defense.gov/Portals/45/Documents/defbudget/fy2015/budget_justification/pdfs/09_Defense_Health_Program/DHP_PB15_Vol_I-II.pdf

[223] Tosoian JJ, Carter HB, Lepor A et al. 2016. Active surveillance for prostate cancer: current evidence and contemporary state of practice. Nat Rev Urol. 2016 Mar 8. doi: 10.1038/nrurol.2016.45. [Epub ahead of print].

- **Rare Cancers**: Out of 400 total cancers, 380 are rare cancers with a disproportionate impact on those who serve our country.[224,225] Military service members experience cancer at higher rates than civilians.[226] At least 64 forms of cancer that disproportionately affect service members are correlated with service-related exposures and almost 70 percent are rare and very few have any targeted treatment options.[227] As of April 2019, only 26 of those rare cancers have "next generation" targeted therapeutics approved by the FDA.[228] The remainder are typically treated by surgery, radiation, and chemotherapy but often chemotherapy is ineffective for rare cancers, so for many patients, there are no treatment options available.[229] With service members uniquely exposed to carcinogens, including asbestos, industrial solvents, nuclear radiation, depleted uranium, lead, fuels, PCBs, and components of Chemical Agent Resistance Coating as well as being located in Asian Pacific regions where exposures to natural organisms such as fluke worm often lead to rare cancers, military service members need access to effective treatment options regardless of cancer subtype.[2,230,231,232,233] Therefore, research into rare cancer treatments is vital to increasing survivability rates among service members.

- **Reconstructive Transplant Research**: Sustained federal funding since FY 2014 has been critical to support translational research and clinical advancements in reconstructive transplantation that yield life-changing results for wounded warriors in upper extremity, face, and urogenital transplants. Hand transplant recipients regain function, sensation and independence[234]; face transplant recipients regain the ability to speak, smell, swallow, and smile; urogenital transplant recipients feel whole again.[235] Reconstructive transplantation provides a viable solution for thousands of veterans with devastating injuries not amenable to conventional reconstruction to regain some of what was lost. This research resulted in breakthroughs in immunosuppression regimens and immunomonitoring strategies and is exploring novel strategies for organ preservation to allow for longevity, better organ matching, and broader organ exchange with ultimately improved outcomes for transplant recipients.

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[224] Rare Cancer's 'Valley of Death', American Association of Cancer Researchers, Abstract 2505, Atlanta, 2019
[225] https://cdmrp.army.mil/prcrp/reports/18prcReport.pdf
[226] Zhu K, et al. *Cancer Epidemiol Biomarkers Prev*. 2009 Jun;18(6):1740-5.
[227] Rare Isn't Rare, American Association of Cancer Researchers, Abstract 7739, Chicago, 2018
[228] https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet
[229] https://www.sofpromed.com/about-rare-cancers-and-clinical-trials
[230] https://www.asbestos.com/veterans/va-claims/
[231] https://www.cancer.net/blog/2014-11/veterans-radiation-and-cancer-risk
[232] https://www.cdc.gov/niosh/ocas/pdfs/misc/varadfs.pdf
[233] https://www.chicagotribune.com/nation-world/ct-veterans-day-vietnam-vets-rare-cancer-20161111-story.html
[234] Ruane, Michael E. "Johns Hopkins Hospital performs double arm transplant on Army soldier." *Washington Post*, 28 Jan 2013. https://www.washingtonpost.com/local/johns-hopkins-hospital-performs-double-arm-transplant-on-army-soldier/2013/01/28/d4b8e082-673c-11e2-93e1-475791032daf_story.html. Accessed 23 May 2022.
[235] Grady, Denise. "'Whole Again': A Vet Maimed by an I.E.D. Receives a Transplanted Penis." *New York Times*, 24 Apr 2018, p. D1.

- **Sleep**: Insufficient sleep and sleep disorders affect the health of an estimated 70 million Americans across all demographic groups, including military personnel. Sleep disruption, especially insomnia, is a contributing risk factor to the onset and severity of major mental health problems such as depression, bipolar disorder, substance abuse, posttraumatic stress disorder, traumatic brain injury, and suicide. [236] [237] [238] [239] [240] An increasingly detrimental condition affecting military troops is sleep-disordered breathing, including obstructive sleep apnea which results in excessive daytime somnolence, poor performance, increased frequency of road traffic accidents, and arterial hypertension.[241] Studies show that 85% of 725 troops returning home from Afghanistan and Iraq had a sleep disorder and the most common was obstructive sleep apnea (51%).If left untreated, obstructive sleep apnea has significant negative impacts on health, including early mortality. By using continuous positive airway pressure (CPAP), a treatment used to combat sleep apnea, military personnel report reductions in pain and fatigue, and improvements in cognitive function. [242] The high prevalence of sleep and circadian disturbances indicates an opportunity for research advances and informed public policy to reduce disease risk across a lifespan and improve the health of our active troops. It is important to accelerate scientific discovery of the relationship between mental health, overall health and sleep and circadian disorders, and strengthen cognitive function and military readiness through the improvement of sleep quality.

[236] Ford ES, Li C, Wheaton AG, Chapman DP, Perry GS, Croft JB. Sleep duration and body mass index and waist circumference among US adults. Obesity2014;22:598-607.
[237] Ford ES, Wheaton AG, Chapman DP, Li C, Perry GS, Croft JB. Associations between self-reported sleep duration and sleeping disorder with concentrations of fasting and 2-hour glucose, insulin, and glycosylated hemoglobin among adults without diagnosed diabetes. J Diabetes 2014;6:338-350.
[238] Ford ES, Wheaton AG, Cunningham TJ, Giles WH, Chapman DP, Croft JB. Trends in outpatient visits for insomnia, sleep apnea, and prescriptions for sleep medications among US adults: findings from the National Ambulatory Medical Care Survey, 1999-2010. Sleep 2014;37:1283-1293.
[239] Wheaton AG, Shults RA, Chapman DP, Ford ES, Croft JB. Drowsy driving and risk behaviors--10 states and Puerto Rico, 2011-2012. MMWR 2014;63(26):557-562.
[240] Fang J, Wheaton AG, Ayala C. Sleep duration and history of stroke among US adults. J Sleep Research 2014;23(5):531-537.
[241] Liu Y, Wheaton AG, Chapman DP, Cunningham TJ, Lu H, Croft JB. Prevalence of Healthy Sleep Duration among Adults – United States, 2014. MMWR Morb Mortal Wkly Rep 2016:65:137-141. DOI: http://dx.doi.org/10.15585/mmwr.mm6506al
[242] Mysliwiec, Vincent et al. "Sleep Disorders in US Military Personnel: A High Rate of Comorbid Insomnia and Obstructive Sleep Apnea." Chest 144.2 (2013): 549–557. PMC. Web. 26 Feb. 2016.

- **Spinal Cord Injury:** Spinal cord injury impacts U.S. Service members, Veterans, and the American public: Between 2000 to 2009 there were 5,928 new spinal cord injuries reported in the military, and the rate of injury was nearly eight times that of the U.S. general population.[243] Currently, the U.S. Department of Veteran Affairs reports over 42,000 Veterans with a spinal cord injury (SCI).[244] SCI is a devastating condition and SCI in the military is more likely to occur in younger individuals (19 to 30) who may experience higher energy injuries.[245] In addition, SCI in the deployed military is increasingly likely to occur in areas where immediate access to neurosurgical and trauma care may be delayed due to the current organization of trauma care within the Military Healthcare System. In the U.S. population, according to the National Spinal Cord Injury Statistics Center, an estimated 17,900 new cases of SCI occur each year, and approximately 296,000 persons are living with an SCI.[246] Costs for care during the first year of the injury can be between $360,000 to $1.2 million and subsequent annual costs range from around $46,000 to over $1,000,000 per year, depending on the severity of injury and time since injury.[247]

[243] Schoenfeld et al., Nature Spinal Cord, *Spinal cord injury within the United States military* (Mar. 8, 2011); 49: 874, 876-77 https://www.nature.com/articles/sc201118.pdf.
[244] U.S. Dept. of Veterans Affairs, *VA Research on Spinal Cord Injury* (June 10, 2021); https://www.research.va.gov/topics/sci.cfm.
[245] *Id.*; Schoenfeld at 876.
[246] National Spinal Cord Injury Statistical Center, University of Alabama at Birmingham, *Facts and Figures at a Glance* (2021); https://www.nscisc.uab.edu/Public/Facts%20and%20Figures%20-%202021.pdf.
[247] *Id.*

- **Stomach Cancer**: In 2026, it is estimated that roughly 31,510 Americans will be diagnosed with stomach cancer, and approximately 10,740 will die from the disease [248]. Stomach cancer is a recalcitrant cancer, with an overall 5-year survival rate of 38 percent. The Department of Veterans Affairs considers stomach cancer to be a service connected malignancy for service members who experienced hazardous exposure to ionizing radiation [249] [250], and burn pits [251]. Further, U.S. military personnel who serve overseas have a higher encounter rate with the bacterium Helicobacter pylori (H. pylori)—a human carcinogen— which is a primary identified cause of stomach cancer [252]. Based on a recently published study [253], one-fourth of the U.S. veteran population is at risk for benign and malignant consequences of chronic H. pylori infection. The PRCRP is funding stomach cancer research with the potential to revolutionize treatment and prevention measures as well as advance our understanding of the risk factors that contribute to disease incidence. For example, the PRCRP has invested in the investigation of innovative approaches that identify pre-cancerous cells and reverse the course of pre-cancerous lesions before they evolve into malignant tumors and is also addressing important treatment gaps, such as unraveling the mechanisms driving immunosuppression to leverage the body's immune system and improve immunotherapies. The PRCRP investment in risk factor research includes investigations into genetic, environmental and infectious disease risk factors, including the increased exposure to external risk factors encountered by active-duty military personnel. They are also funding research that seeks to understand why some veterans infected with H. pylori go on to develop precancerous stomach damage and stomach cancer while others do not. All of this research benefits our veterans, military servicemembers, their families and the American public.

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[248] American Cancer Society. Cancer Facts & Figures 2026. Atlanta: American Cancer Society; 2026. www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2026/2026-cancer-facts-and-figures.pdf

[249] National Cancer Strategy, Department of Veterans Affairs, Veterans Health Administration, VHA Directive 2003-34. June 20, 2003.

[250] https://www.law.cornell.edu/cfr/text/38/3.309 – accessed February 6, 2025.

[251] www.va.gov/resources/presumptive-cancers-related-to-burn-pit-exposure/#gastrointestinal-cancers – accessed February 6, 2025.

[252] Centers for Disease Control and Prevention. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/helicobacterpylori#:~:text=pylori

[253] Shah SC, Halvorson AE, Lee D, Bustamante R, McBay B, et al. Helicobacter pylori Burden in the United States According to Individual Demographics and Geography: A Nationwide Analysis of the Veterans Healthcare System. Clin Gastroenterol Hepatol. 2024 Jan;22(1):42-50.e26. doi: 10.1016/j.cgh.2023.05.016. Epub 2023 May 26. PMID: 37245717.

- **Traumatic Brain Injury (TBI)**: Since 2000, more than 500,000 service members were diagnosed with a traumatic brain injury, which does not account for misdiagnosis or unreported incidents, with approximately 67 percent of veterans having experienced at least one TBI during their military careers.[254] [255]TBI is considered the signature injury of modern warfare in post 9-11 service members.[256] [257]Disturbingly, service members who have incurred a TBI are twice as likely to commit suicide than those who haven't.[258] Despite this fact, there is currently no imaging machine or MRI that can detect a TBI at the microscopic level, hence there is no official precision diagnostic for TBI.[259] [260]There are also no FDA-approved treatments for the injury. The Department of Defense considers protecting, treating, and optimizing brain health a top priority, and acknowledges that there are still gaps in knowledge and materiel capabilities that further research needs to close.[261] [262]

[254] https://www.health.mil/Military-Health-Topics/Centers-of-Excellence/Traumatic-Brain-Injury-Center-of-Excellence/DOD-TBI-Worldwide-Numbers
[255] https://pmc.ncbi.nlm.nih.gov/articles/PMC3997066/
[256] https://www.va.gov/budget/docs/summary/fy2024-va-budget-in-brief.pdf
[257] https://abcnews.com/Politics/traumatic-brain-injury-emerging-signature-injury-iran-war/story?id=131187835
[258] https://www.mentalhealth.va.gov/docs/data-sheets/2025/2025_Annual_Report_Part_2_508.pdf
[259] https://www.rand.org/pubs/research_reports/RRA4199-1.html
[260] https://www.fda.gov/consumers/consumer-updates/traumatic-brain-injury-what-know-about-symptoms-diagnosis-and-treatment
[261] https://health.mil/News/In-the-Spotlight/Be-a-Brain-Warrior
[262] https://www.health.mil/Reference-Center/Publications/2024/01/01/DOD-Warfighter-Brain-Health-Research-Strategy

- **Tuberculosis (TB)**: TB is the largest infectious disease killer globally, killing over 1 million people each year, and represents 30 percent of deaths from antimicrobial resistant bacteria. TB (and growing drug resistance) presents a serious concern for the US military. Thirty countries are currently classified as having a high TB burden based on the number of incident cases of TB and the severity of the disease (incident per capita).[263] Additionally, Ukraine is on the list of high burden countries for multidrug-resistant (MDR-TB), and NATO allies like Poland and Germany are currently taking in Ukrainian refugees; Germany alone has reportedly taken in over 1.2 million.[264] Overall, in Europe, where around 84,000 U.S. troops and dependents are stationed, there were nearly 162,000 cases of TB and 32,000 cases of MDR-TB. In the Western Pacific region, nearly 82,000 troops live amidst over 1.8 million cases of TB and 74,000 cases of MDR-TB according to the most recent estimates. Additionally, through the programs like the Pacific Pathways, thousands of US military members rotate through countries around the Pacific Rim like the Philippines and Thailand to strengthen alliances, where a combined 626,000 cases of TB occurred in 2024, including thousands of cases of MDR-TB.[265] [266] During deployment, the warfighter could be exposed to TB and could develop either latent or active TB in either drug sensitive (DS) or, much more ominously, drug resistant (DR) forms. An estimated 2.3 billion individuals worldwide were thought to be carriers of latent TB bacteria. Over a lifetime, around 5-15 percent of LTBI cases will progress to infectious TB. [267] LTBI's pervasiveness in the global population should be a primary concern for TB diagnoses in the U.S. military. For instance, between 2008 and 2012, most active TB cases (57.9 percent) diagnosed in the US military were associated with an existing LTBI.[268] While the healthy warfighter may not activate a latent TB infection immediately, risk increases for people under significant stress and for immunocompromised individuals.[269] Further, veterans will be at increased risk of activating a latent TB infection as they age and develop co-morbid health conditions—creating a public health risk in the U.S. Perhaps the most serious TB concern facing the U.S. military—and the broader global population—is the increase in drug resistant TB. While there are serious shortcomings in available treatment options for all forms of TB, for DR-TB it is especially problematic and worrisome. Even an MDR-TB outbreak in the U.S. could have serious consequences given the costs associated with treatment. The cost to treat and care for a patient with TB in the U.S. averages $67,000 for drug-susceptible TB, $420,000 for MDR-TB, and $801,000 for XDR-TB.[270]

[263] High Burden Countries for Tuberculosis
[264] Ukrainian refugees in Germany, four years on
[265] Pacific Pathways 2.0 to bolster presence in the theater.
[266] Global Tuberculosis Report 2025
[267] Initiation and completion of treatment for latent tuberculosis infection in migrants globally: a systematic review and meta-analysis.
[268] Tuberculosis Trends in the U.S. Armed Forces, Active Component, 1998-2012.
[269] Updates on the risk factors for latent tuberculosis reactivation and their managements
[270] CDC. "The Costly Burden of Drug-Resistant TB in the U.S." September 2022

- **<u>Tuberous Sclerosis Complex (TSCRP)</u>**: Research supported by the TSCRP is paving the way to finding cures and treatments for individuals with TSC as well as those with other neurological disorders like epilepsy and autism spectrum disorder (ASD). Research through TSCRP award W81XWH-12-1-0190[271] developed a mouse model for TSC, which in addition to its use for studying epilepsy and autism, is helping understand the consequences and potential treatment for post-traumatic brain injury (TBI) – a disorder of grave concern to the U.S. Armed Services. In 2024, the last year for which complete data are available, there were 21,397 documented traumatic brain injuries in the U.S. military. [272] A more recent award, W81XWH-14-1-0061, is testing existing FDA-approved drugs for their ability to treat or prevent epilepsy by regulating the biochemical pathway shared between TSC and TBI. Many other TSCRP awards enabled these key studies by generating the knowledge about this shared biochemical pathway. Some of the awards that built this foundation of knowledge include DAMD17-03-1-0073[273], W81XWH-04-1-0309[274], W81XWH-06-1-015[275], W81XWH-09-1-0088[276], W81XWH-10-1-0861[277], W81XWH-13-1-0040[278], W81XWH-21-1-0286[279], W81XWH-21-1-0366[280].

[271] Wong, Michael. *The Role of Brain Inflammation in Epileptogenesis in TSC*
[272] DoD Worldwide Numbers for TBI, Defense and Veterans Brain Injury Center, https://www.health.mil/Military-Health-Topics/Centers-of-Excellence/Traumatic-Brain-Injury-Center-of-Excellence/DOD-TBI-Worldwide-Numbers
[273] Gutmann, David. *Mouse Models of TSC-Related Epilepsy*
[274] Bernardo, Sabatini. *The Role of TSC1 in the Formation and Maintenance of Excitatory Synapses*
[275] McNeill, Helen. *Genetic and Molecular Analysis of the Mechanisms by which TSC Regulates Neuronal Differentiation*
[276] Yoshii, Akira. *Studying Protein Synthesis-Dependent Synaptic Changes in Tuberous Sclerosis*
[277] Manning, Brendan. *Defining the Therapeutic Implications of the Integrative Stress Response in TSC*
[278] Sahin, Mustafa. *Role of CTGF in White Matter Development in Tuberous Sclerosis*
[279] Wong, Michael. *The Role of Blood-Brain Barrier Dysfunction in Epilepsy in TSC*
[280] Anderson, Anne. *Mechanisms of Epileptogenesis and Circuit Dysfunction in a Mouse Model of TSC*

- **VHL**: Von Hippel-Lindau disease (VHL) is a genetic disease caused by a mutation in the *VHL* gene, which normally functions as a tumor suppressor[281]. It affects approximately 1 in 36,000 people, from all nationalities, ethnicities and races.[282] About 80% of people with VHL inherited it from a parent, while the other 20% of people have it as the result of a random genetic mutation. VHL is a chronic disease with no cure and no treatment, other than a lifetime of surveillance and traumatic and expensive surgeries. The manifestations of VHL include the development of tumors throughout a patient's life in up to ten different organs, including the brain, eyes, pancreas, spine and kidneys.[283] These tumors can be benign or malignant. Research into VHL will have a significant impact not just on affected service members and DoD families, but on the broader military community, because the VHL pathway is directly tied to more commonly occurring types of cancer. This could lead to the development of improved diagnostics and treatments, as well as cures, for diseases like kidney cancer and pancreatic cancer[284], both of which have a higher prevalence in US military and veterans' populations.[285] Several VHL researchers have received CDMRP grants, and VHL research has led to the discovery of at least 8 drugs currently used to treat cancer. Dr. William Kaelin, a VHL researcher, and Dr. Gregg Semenza were CDMRP grant recipients for research projects that contributed toward their 2019 Nobel Prize in Medicine.[286] Dr. Kaelin and another CDMRP grant recipient, Dr. Eric Jonasch, have been directly involved in development of a drug that recently received FDA breakthrough and orphan drug designation and will, hopefully, be used to treat both VHL and kidney cancer.[287]

[281] Maher ER, et al., von Hippel-Lindau disease: a clinical and scientific review. Eur J Hum Genet. 2011 Jun;19(6):617-23. Epub 2011 Mar 9. PMID: 21386872
[282] Varshney, Neha, et al., A Review of Von Hippel-Lindau Syndrome. J Kidney Cancer VHL. 2017; 4(3): 20–29. Epub 2017 Aug 2. PMID: 28785532
[283] Chittiboina, Prashant, et al., Von Hippel–Lindau disease. Handb Clin Neurol. 2015; 132: 139–156. Epub 2016 Nov 24. PMID: 26564077
[284] Glasker, Sven, et al., Von Hippel-Lindau Disease: Current Challenges and Future Prospects. Onco Targets Ther. 2020; 13: 5669–5690. Epub 2020 Jun 16. PMID: 32606780
[285] Zullig, Leah, et al., Cancer Incidence among Patients of the United States Veterans Affairs (VA) Healthcare System, Mil Med. 2012 June; 177 (6): 693-701
[286] https://cdmrp.army.mil/pubs/press/2019/CDMRP_Funding_Recipients_Are_Nobel_Prize_Winners
[287] https://www.eurekalert.org/pub_releases/2020-05/uotm-ntd052820.php

- **Vision**: Vision, the sense most critical for optimal military performance in battlefield and support positions, is vulnerable to acute and chronic injury. Research to effectively treat vision trauma and TBI-related visual disorders can have long-term implications for an individual's vision health, productivity, and quality of life for the remainder of military service and into civilian life. Traumatic eye injury from penetrating wounds and TBI-related visual disorders ranks second only to hearing loss as the most common injury among "active" military, accounting for upwards of 16 percent of all injuries in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF).[288] The VHA reports 202,000 OEF/OIF veterans with eye injuries since 2000 [289], as well as that upwards of 75 percent of all TBI patients experience short- or long-term visual disorders (double vision, light sensitivity, inability to read print, and other cognitive impairments). A January 2019 *Military Medicine* journal article based on a 2018 study by the Alliance for Eye and Vision Research that used prior published data from 2000-2017 has estimated that deployment-related eye injuries and blindness have cost the U.S. $41.5 billion in that timeframe, with $40.2 billion of that cost reflecting present value of a lifetime of long-term benefits, lost wages, and family care.[290]

[288] VA Office of Public Health and Environmental Hazards, 2010, "Analysis of VA Health Care Utilization among Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) Veterans"
151 Office of Public Health Epidemiologic Report, *Cumulative Frequencies of the Eye and Adnexa Enrollment OIF/OEF/OND* (FY October 2002 to second quarter, FY 2015)
[290] Kevin D. Frick and Eric L. Singman, "*Cost of Military Eye Injury and Vision Impairment Related to Traumatic Brain Injury: 2001–2017*" Military Medicine, January 2019