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"FOUNDATION OF CARE: EXAMINING RESEARCH AT THE DEPARTMENT OF VETERANS AFFAIRS"

NOVEMBER 1, 2023

Good afternoon, Chairman Tester, Ranking Member Moran and members of the committee. I appreciate the opportunity to discuss VA efforts to ensure our research programs improve the health and well-being of the Nation's Veterans. I am accompanied today by Dr. Patricia Hastings, Chief Consultant, Health Outcomes Military Exposures (HOME) within VHA Patient Care Services, and Dr. Sumitra Muralidhar, Director of the Million Veteran Program.

Office of Research and Development (ORD) Overview

For nearly 100 years, VA's research program has focused on enhancing the well-being of Veterans and the Nation through scientific discovery. VA research has proudly contributed to major medical advances that serve as the foundation for much of American medicine, including the first implantable pacemaker; the first liver transplant; new prosthetics; the first ever clinical trials in the United States that formed the ability to later produce evidence leading to the approval of the shingles vaccine; and findings that support the use of therapies for posttraumatic stress disorder (PTSD) within VA. More recently, via access to national electronic health record data, VA researchers have made significant contributions to the Nation's understanding of and response to COVID-19. VA has produced several key findings related to diabetes, cardiovascular health, kidney disease and in an area referred to as post-acute sequelae of COVID-19 also known as long-COVID.

Because we are embedded within the VA health care system as an intramural research program that exclusively funds eligible VA employees qualified to do research, the research we fund is firmly grounded in the experience of clinicians and researchers working directly with Veterans in VA medical centers. Most of our researchers are faculty members at academic medical centers, and we can draw upon the best and the brightest researchers across the country. In fact, the ability to conduct research is one of the features that allows VA to attract and retain talented clinicians.

VA is indeed an extraordinary system to conduct biomedical research. Chief among its features is our mission to serve Veterans. In fact, 9.2 million of these extraordinary former Service members are enrolled in VA health care. Caring for these individuals and those who preceded them has resulted in one of the richest health care datasets in the world. When paired with skilled researchers and modern scientific computing, the opportunities for discovery that benefit Veterans and the Nation are vast. The capacity for VA research to do good goes well beyond the data: we support a full range of research approaches, including basic, translational, clinical, epidemiological, health services and rehabilitation research.

The President's Fiscal Year (FY) 2024 Budget requests \$938 million in discretionary appropriations for VA's Medical and Prosthetic Research account to continue the investment in VA's capabilities as a national research enterprise, including research in support of American Pandemic Preparedness plan goals. This request builds upon the historic investment from the President's FY 2023 Budget to continue to increase funding to advance VA's research missions in areas such as military environmental exposures; traumatic brain injury; cancer and precision oncology; and mental health.

Given previous investments in VA to support broader efforts in advancing precision oncology research, VA is positioned to be an active leader and partner in the second Cancer Moonshot initiative through clinical trials and cutting-edge analyses of human tissues and tumors. This research has significantly contributed to advancements in health care for Veterans and Americans from every walk of life.

As an enterprise, VA is a tremendous source of biomedical evidence and research capability for Veterans and the Nation. We are building on that critical work to better link VA research efforts into an integrated enterprise. We intend to focus this actively coalescing enterprise on work that will fulfill our mission of improving Veterans' lives through research.

As a system, we are working on increasing all Veterans' access to high-quality clinical trials; enhancing the substantial real-world impact of VA research; putting VA data to work for Veterans; actively promoting diversity, equity and inclusion within our sphere of influence; and building community through VA research. Our research focuses on several cross-cutting clinical research priorities that reflect VA's unique opportunity and special responsibility to improve the health and quality of life of Veterans. These priorities include military environmental exposures; suicide prevention; PTSD; pain and opioid use; cancer; traumatic brain injury; and COVID-19. In addition, we are continuing important research on the prosthetic needs of women Veterans with limb loss; have made significant progress in implementing our plan to reduce, refine and replace sensitive animal species in VA research; and are advancing the use of artificial intelligence in biomedical research. VA efforts have prioritized Veterans' access to highquality clinical trials and have increased the substantial real-world impact of our research. Consequently, we have increased opportunities to engage a broader community of investigators, funders and other stakeholders with shared interests to enable more robust research on how we care for Veterans.

Setting priorities is an essential part of stewarding the research appropriations given to us. ORD follows an iterative, multi-stakeholder process, outlined in the Government Accountability Office report "Efforts to Prioritize and Translate Research into Clinical Practice," completed in January 2020. These priorities factor into funding decisions and underpin enhanced central coordination of research. In addition, ORD responds to timely priorities identified by VA, VHA, Congress, Veterans Service Organizations and other key stakeholders.

Accordingly, ORD's current priorities correlate with our overall mission of improving Veterans' health and well-being via basic, translational, clinical, health services and rehabilitation research; applying scientific knowledge to develop effective individualized care solutions for Veterans; attracting, training and retaining the highest-caliber investigators and nurturing their development as leaders in their fields; and ensuring a culture of professionalism, collaboration, accountability and the highest regard for research volunteers' safety and privacy.

Research Related to Military Environmental Exposures

A tremendous amount is yet to be learned about the impacts of military exposures on Veterans' health. VA has completed 4.3 million toxic exposure screenings, with approximately 42.5% reporting a concern of exposure. To make rapid progress requires coordination across the Federal Government. ORD is leading the interagency Toxic Exposures Research Working Group (TERWG), mandated by section 501 of the Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics Act of 2022 (the PACT Act). The TERWG includes 35 representatives from eight Federal departments and several agencies. As required by the PACT Act, the TERWG will deliver a strategic plan for coordinating efforts to deliver meaningful results to Veterans.

VA also is conducting research with an emphasis on advancing military exposure assessments and understanding effects on Veterans' health outcomes. For example, ORD recently began funding a study at the Nashville VA Medical Center on new technology for non-invasive detection of constrictive bronchiolitis (CB). This condition is a concern to Veterans and is difficult to diagnose. Non-invasive methods to diagnose and monitor Veterans with CB would dramatically improve the ability of VA to safely identify and provide care to Veterans with this condition.

Understanding the effect of military environmental exposures is a critical research focus for VA. We are committed to lead and partner in growing a high-quality evidence base and enhancing capabilities for state-of-the art research on military exposures so that VA can provide care and benefits to Veterans based on the best available evidence. Military environmental exposures can lead to short-term acute health outcomes and acute or delayed onset of diseases. We committed to urgently and proactively addressing the potential health effects of military environmental exposures of Veterans.

VA's overarching approach for addressing military environmental exposures includes the interrelated tenets of policy; research; communication, education and operations. These activities complement the research, review of presumption, education, risk, communication and clinical care already implemented through HOME; the War Related Illness and Injury Study Center (WRIISC) at three sites; the Airborne Hazards Open Burn Pit Center of Excellence; the Women's Operational Military Exposure Network to meet the unique concerns of women Veterans; the Complex Exposure Threats Center that studies and provides care for new or novel exposures such as directed energy; and the Metal Exposures Depleted Uranium Center.

Approximately 3.5 million U.S. Service members have deployed to Iraq, Afghanistan, Kuwait, Qatar, Djibouti, United Arab Emirates, Syria, Kyrgyzstan and surrounding areas since February 24, 1991. Prior cohorts of Veterans such as Vietnam and Atomic Veterans have had unique exposures depending on the circumstances of their military service. Defining health outcomes from all types of military exposures as well as emerging environmental threats is one of our top priorities.

VA uses a repeating cycle through which scientific evidence, policy and clinical programs continuously inform and improve through subsequent iterations, leading to improvements in Veterans' care. Science forms the foundation of policy decisions regarding the provision of evidence-based clinical care. In turn, the evaluation of clinical programs, trends in health care utilization and trends identified through health surveillance help identify knowledge gaps and determine priority areas for further research. To best understand and serve the needs of Veterans, VA must identify knowledge gaps and emerging threats, conduct research and use data to make evidence-based decisions about policy, care and benefits.

VA has expanded its portfolio of military environmental exposures research efforts to inform care and policy. VA is making this research investment in a complementary and parallel fashion with clinical programs and policies. This research investment is enabled through strategic planning at a national level and executed by clinician researchers, many of whom perform clinical and research duties at their local VA medical center.

One of the major challenges in the field of military environmental exposures is a lack of exposure assessment at the individual level. Improved exposure monitoring during military service may help make more precise determinations of the types and amounts of specific exposures incurred by Service members and will address a key gap in the field. Other critical areas of focus include developing clinical diagnostic tests to identify health conditions as early as possible and translating research findings into care that will make a difference in Veterans' lives.

HOME also conducts population-based epidemiological research to help answer questions about the associations of certain health outcomes and military environmental exposures. The WRIISCs and specialty centers also conduct military environmental exposures research to include clinical best practices. Education of Veterans and healthcare providers is an important part of these efforts. The Airborne Hazards and

Burn Pits Center of Excellence in New Jersey has completed the case definition for Deployment Related Respiratory Disease, which is part of a continuum of illness that may include CB. HOME works closely with the Department of Defense (DoD) on the Individual Longitudinal Exposure Record—a VA-DoD collaboration to track in-service exposures—to improve clinical care, research and Veteran disability claims processing.

Because military environmental exposure data frequently is unavailable, it can be difficult for VA to link health outcomes to a specific exposure. To address this gap in the science and data, ORD is designing new experiments to generate that data. One example of our efforts regarding environmental hazards is VA Cooperative Studies Program #595, the Service and Health Among Deployed Veterans study. We are actively enrolling over 6,000 Veterans across six VA recruitment sites to better understand the respiratory health of Southwest Asia-deployed Veterans. The study's primary objective is to assess the impact of fine particulate matter air pollution on pulmonary function. Investigators are using National Aeronautics and Space Administration (NASA) satellite data to quantify and provide an objective measure of exposure that has thus far eluded prior and current research efforts. Through a VA-led study, VA is partnering with DoD, NASA and academia to ensure its success.

Every Veteran's story matters, and that is why we are so focused on research and connecting it to health outcomes. "Put VA data to work for Veterans" is VA's broad strategic research priority. Our integrated health system means we are leveraging rich health datasets to accelerate discoveries and drive better outcomes. VA publishes its findings in peer-reviewed journals, which informs not only VA but also the Nation to improve many areas of care for Americans and indeed has global impacts.

VA research is very focused on Veteran health and needs, and it is core to VA's mission. Through research on military environmental exposures and in many other areas of importance to Veterans' health, VA will continue to provide and lead the way to serve the Nation's Veterans.

Million Veteran Program (MVP)

The signature example of our partnership with Veterans and the associated data assets held by VHA is the Million Veteran Program (MVP). MVP is a national, voluntary research program to study how genes affect health. MVP partners with Veterans who primarily receive their care in the VA health care system. Each Veteran agrees to contribute their blood samples and health information. Over 985,000 Veterans have enrolled so far with hopes to reach the million enrollee milestone by Veterans Day 2023.

Protecting the privacy and confidentiality of MVP participant data is the program's highest priority. Data from MVP participants is protected throughout the life cycle from the point of collection through data use. Tubes used for collecting blood samples as well as survey data and data from the electronic health record are marked with a code and do not contain personally identifiable information such as name, social security number or date of birth. Only a few authorized MVP staff have access to the participant's identity and can link the various data to an individual Veteran. Data is stored on secure servers

within the VA firewall, and the servers are in a secure, isolated architecture from the VA network so that any perturbations to the network do not affect MVP data.

Furthermore, before providing data access to researchers, a new code is assigned to the dataset. Approved researchers access data in this secure server architecture and conduct their analysis. Only summary results of the analyses can be downloaded from the servers. No individual-level data leave the servers. With the goal of making MVP data accessible to the broader research community outside VA in the future, data storage and access currently are being beta-tested by a small group of VA researchers in the VA Data Commons at the University of Chicago. Here, MVP data are completely deidentified and researchers do not access the data directly. Instead, they select the cases and controls needed for their analysis, and the analysis is completed by an automated tool with results returned to the researchers. Researchers use MVP data to study diseases such as diabetes, cancer and other service-related conditions. The amount and types of data generated by MVP and curated for researchers are expanding and will in the future include whole genome sequence data, methylation, metabolomes and proteomes.

MVP is the largest database of genetic information on African Americans in the world with over 170,000 participants enrolled thus far. In the cohort overall, 25% of enrollees are from minority racial and ethnic backgrounds. The program has completed the largest genome-phenome analysis (large scale analysis of the association between genetic variations and health conditions) in history by partnering with the Department of Energy on their supercomputer, SUMMIT, and provisioned summary results to all VA researchers. A manuscript describing this analysis is currently under a revise-and-resubmit request by the journal *Science*. Once published, the summary results also will be made available to the broader research community through the National Institutes of Health's portal, *Database of Genotypes and Phenotypes*.

By providing genotype data to MVP researchers, over 350 peer-reviewed papers in high-impact journals have been published since 2018, with over 50 papers published in 2023 alone. Because so many Veterans have volunteered to participate, MVP is able to shed unprecedented light on conditions that affect Veterans from all backgrounds. For example, the *American Journal of Psychiatry* recently published a study that identified 12 DNA variants associated with risk of suicide and highlights the genetic link between suicide and factors such as impulsivity, chronic pain, attention deficit hyperactivity disorder and heart disease. The findings suggest that suicide risk shares some genetic similarities for risk for these conditions and could help identify new prevention and treatment strategies. MVP contributed the largest dataset from Veterans for this study, with 14,089 cases and 395,064 controls. The study included data from 22 cohorts for 43,871 included cases and 915,025 matched controls.

Researchers are using MVP data to learn about the genes that may affect whether combat Veterans develop PTSD. The team hopes to gain new insight into the effects of PTSD on the brain so that new and improved treatments can be explored. This genomic research project on PTSD is one of the largest ever done.

MVP researchers also are examining how differences in a person's genes affect gene expression or how the information in DNA is translated into actual physiological changes within the body. Studying changes in gene expression will help researchers understand the genetic risk factors of different diseases. Researchers are looking at numerous health conditions such as PTSD, depression, diabetes and heart disease. Researchers will use the results to improve treatments and develop precision medicine, which is treatment customized to individual patients.

Conclusion

VA research is very focused on Veteran health and needs, and it is core to VA's mission. Through research on military environmental exposures and in many other areas of importance to Veterans' health, VA will continue to provide and lead the way to serve the Nation's Veterans. VA consistently has produced scientific findings across a range of diseases and conditions that enable VA to make real differences in the lives of Veterans and all Americans. This public benefit is due to the dedicated efforts of countless VA scientists and research staff over a long history and to those Veterans who selflessly served their Nation in the Armed Forces and continue their service through participation in research.

Mr. Chairman, this concludes my testimony. Thank you for the opportunity to testify today and for your continued support of our mission. I am happy to respond to any questions you or the Committee may have.