

DEPARTMENT OF VETERANS AFFAIRS (VA)

Research Advisory Committee on Gulf War Veterans' Illnesses (RACGWVI) Responses to Recommendations

Recommendation 1: Fund research into key focus areas, examples below, to support the diagnosis and treatment of Gulf War Illness (GWI).

- Basic and clinical studies on the role of the microbiome in the etiology and maintenance of GWI.
- Basic and clinical studies to determine the effects of dietary manipulations on the quality of life for GWVs with GWI.
- Basic and clinical studies to further evaluate the status and/or influence of mitochondrial function in GWVs, with and without, GWI.
- Determine the utility of the Department of Defense Serum Repository as a resource for Gulf War (GW)-funded investigators. Among other utilities, the repository's samples may be useful in confirming a correlation between butyrylcholinesterase inhibition (itself and as a biomarker of acetylcholinesterase) and pyridostigmine bromide exposures as potential sources which cause GWI.
- Conduct a prospective, double-blind randomized clinical trial to determine the effects of antioxidants, ubiquinol vs ubiquinone, on the quality of life for GWV with GWI.

VA Response: Concur.

VA concurs that focused diagnostic- and treatment-based research is needed to improve quality of life for Gulf War Veterans with Gulf War illnesses. The RACGWVI Committee has highlighted examples of existing promising research topics that can be followed up with attentive design and rigorous research methodology needed for subsequent evidence-based translation and implementation. VA additionally concurs that the DOD serum repository may be an underutilized resource in diagnostic and validation research. The viability and feasibility of these recommendations can be pursued through requests for application and expert scientific review.

Recommendation 2: Establish one or more Gulf War-Military Exposure Research Innovation Center(s) (GW-MERIC). The RACGWVI recommends that VA Office of Research and Development (ORD) establish one or more GW-MERIC(s) with a two-part mission: 1) To expedite and implement evidence-based clinical treatment and diagnostic research for GWV with GWI, and 2) Build upon existing collaborations and establish new VA and non-VA partnerships to leverage and expand subject matter expertise, data and specimen resources, and technology.

GW-MERIC projects should include diverse team-based approaches through supporting multi-investigator, multi-institution partnerships and recruiting new and junior investigators into the field to advance translation of research. The GW-MERIC(s) would coordinate a strategic approach supporting GWI-focused, program-directed projects and a learning healthcare system model to integrate research into clinical care.

VA Response: Concur.

- 1) Gulf War Veterans with Gulf War illnesses need accessible interventions that improve their quality of life. Operational partnerships within VA are required to effectively accomplish this recommendation. A pipeline to implement War Related Illness and Injury Study Centers validated, evidence-based research treatments and/or diagnostics could be developed and piloted through collaboration between the Office of Research and Development and clinical programs such as those managed by VA Health Outcomes Military Exposure's (HOME; 12POP5) to ensure successful clinical integration.
- 2) Developing novel and innovative approaches for treatment and diagnostics for GWI requires collaboration with other Federal agencies and academic institutions to leverage expertise, tools, and resources such as subject matter expertise, appropriate state-of-the-science technologies, and data- and biospecimen resources.

Recommendation 3: Initiate research on the relationship between COVID-19, long-haul COVID-19, and their impact on GWI. The long-term effects of COVID-19 on the health and quality of life for GWV already suffering from GWI are of critical interest and warrant further study. The RACGWVI recommends initiating studies on COVID-19 and persistent symptoms of long-haul COVID-19 including examining the similarities and differences between GWI and long-haul COVID-19 symptomology.

This research could utilize existing cohorts of GWV such as the Million Veteran Program (MVP) and data resources such as the COVID-19 supplemental survey or the VA Informatics and Computing Infrastructure (VINCI). The studies could yield insights into the characterization and management of both GWI and COVID-19.

VA Response: Concur.

This recommendation emphasizes timely and integrated support to evaluate similarities and differences of health outcomes and risk factors between GWI and COVID-19 acute and long-haul disease. In addition, the opportunity exists to compare health outcomes in GWV with and without GWI who have been exposed to SARS-CoV-2 with subsequent symptomatic COVID-19 disease. The MVP sub-study, CSP 2006 includes 1990-91 GWV who have been comprehensively characterized for those with or without GWI. This is the only large cohort (~50k) available to easily evaluate preliminary outcomes as described by the RACGWVI. Prospective studies utilizing other GWV cohorts for validation and hypothesis generating research could be adapted moving forward through release of requests for applications. Additional resources include the MVP COVID-19 supplemental survey, and the VINCI COVID Shared Data Resource.

Recommendation 4: Continue the RACGWVI subcommittee, Veteran Engagement Sessions (VES). A RACGWVI subcommittee, called VES, was established in January 2019 to support the Committee's mission to provide research education to GWV, to better understand the Veteran's experience of living with GWI and to build trust with the GWV community. Members of the subcommittee include the RACGWVI Chair, Designated Federal Officer, VA clinician and non-clinician researchers with expertise on

chronic multi-symptom illness, GWV and other VA and non-VA subject matter experts with community leadership backgrounds. The outcomes of the VES have been highly successful. Feedback from these interactions have directly led to newly funded research projects in areas not previously examined. Additionally, participation by GWV in the VES and parent RACGWVI committee meetings have increased fivefold.

The RACGWVI recommends:

- RACGWVI staff continue to work with VA and non-VA partners to facilitate maximum outreach to the 1990-91 GWV community. These communication partnerships include, but are not limited to, VA Public Affairs, VA Communications, Employee Education System (EES), War Related Illness and Injury Study Centers (WRIISC), Health Outcomes Military Exposures (HOME, formerly Post Deployment Health), Post-Deployment Integrated Care Initiative (PDICI), GWV Facebook and other Veteran social media groups.
- The RACGWVI VES subcommittee resumes in person meetings twice per year as COVID-19 travel restrictions are lifted.
- The RACGWVI VES subcommittee continue to maintain a virtual meeting platform simultaneously with in-person meetings to allow nationwide attendance to continue.
- The RACGWVI VES subcommittee pinpoint rural areas as well as areas with a high population of 1990-91 GWV.
- The RACGWVI VES subcommittee support Diversity, Equity, and Inclusion (DEI) to the VES team.

VA Response: Concur.

The VA values the voices and feedback from GWVs. This recommendation embodies *The VA Way*: ICARE and WE CARE values and the Own-the-Moment focus on the human connection and aligns with the Office of Research & Development's Enterprise priorities. The VA concurs with ongoing VES outreach for education and research direction. The marketing resources have been applied by the RACGWVI administration staff and will continue to ensure the highest potential in reaching GWVs. Diversity and inclusion to the RACGWVI subcommittee is critical for all Veteran outreaches.