

WRIISC *Advantage*

Spring 2022

INSIDE THIS EDITION:

Exposure Education for Providers

WRIISC Research Advances

**Research Studies for Gulf
War Veterans**

**Veterans Make
RESEARCH Possible**



This edition of WRIISC Advantage focuses on WRIISC research happenings and our continued dedication to advancing the health of Veterans through discovery...

DIRECTORS' CORNER

Research at WRIISC continues to serve the mission to inform and advance clinical care for all Veterans. Researchers at WRIISC not only generate their own original findings, but also synthesize information learned across research studies and apply it to clinical care Veterans receive. In turn, through clinical evaluations, WRIISC experts learn about the types of health concerns that Veterans have that warrant future investigation. WRIISC clinical experience and research lead to WRIISC educational programs that are transforming health care for Veterans. Read more to find out about some of our research with a focus on our work related to Gulf War Veterans. We hope you enjoy this edition!

Helena Chandler PhD
Director, NJ WRIISC

Matt Reinhard, PsyD
Director, DC WRIISC

Wes Ashford, MD, PhD
Director, CA WRIISC

Veterans Make Research Possible

Veteran volunteers are essential in order for researchers to conduct studies and obtain information needed to develop new concepts and share findings. Positive feedback from past WRIISC research participants includes:

"Loved this treatment. I hope that the results of this study will encourage other sites to offer this treatment."

"Very much enjoyed the opportunity to provide feedback on what might work best when assessing Veterans with post deployment health concerns."

"It is good to know that this research may help other service members like me."

"One of the things [the] Health Coaching [study at the DC WRIISC] helped me understand better is my role in obtaining good health."

WRIISC is especially in need of Veteran volunteers that served in Operation Desert Storm/Shield (ODS/S). Make a difference in Veterans Health by participating!

Volunteering in a research study may or may not help you personally, but your efforts will improve future health for other Veterans. A brief description of WRIISC research studies currently recruiting Gulf War Veterans (GWV) is as follows.

JOINT SITE STUDIES

Predictors of Response to Insomnia Treatments for Gulf War Veterans

POPULATION: GWV who have had difficulty sleeping or insomnia for at least three months.

PURPOSE: To compare the effectiveness of two different sleep therapies in treating insomnia in GWV. (NJ/DC/CA WRIISC)

The Gulf War Illness Clinical Trials and Interventions Consortium (GWICTIC)

POPULATION: GWV

PURPOSE: Develop better treatment interventions for Gulf War Illness (GWI). (NJ/CA WRIISC)

Investigative Deep Phenotyping of GWV Health

POPULATION: GWV with a VA primary care physician who either have records of symptom onset within 5 years of deployment or documentation of the absence of symptoms since the time of deployment

PURPOSE: Understand the biological reasons for the development of symptoms related to GWI. (DC/CA WRIISC)

NJ WRIISC

Collaborative Specialty Care for Gulf War Illness

POPULATION: GWV enrolled in the VA Health Care System

PURPOSE: To learn whether collaborative care among specialty providers who work together on a patient's case can improve the health and quality of care that GWV receive.

Examining Sources of Delayed Onset Physical Fatigue after Exercise in Gulf War Illness

POPULATION: GWV

PURPOSE: To understand the source of symptoms (especially fatigue) in different body systems that are made worse after exercise or strenuous exertion.

Health Coaching for Chronic Multi-Symptom Illness

POPULATION: Veterans with chronic multi-symptom illness (CMI), including GWI

PURPOSE: To learn if health coaching improves outcomes for Veterans with CMI.

Individualization of Exercise Training Prescription Using Autonomic Nervous System (ANS) Function Among Patients with Chronic Multi-Symptom Illness

POPULATION: Open to GWV and Veterans from all eras

PURPOSE: Explore the optimal manner to administer exercise interventions for Veterans with CMI through using objective heart rate variability (HRV) metrics of intensity.

Assessing the Impact of the War Related Illness and Injury Study Center Health Coaching Program

POPULATION: All Veterans (including GWV) over the age of 18 approved for receiving clinical care at DC and CA WRIISC

PURPOSE: Examine the impact of a clinical health coaching program aimed at promoting adherence to the clinical recommendations and increasing health behaviors in treatment-seeking Veterans receiving care at the WRIISC.

Multi-Modal Observational Study of Veterans with Traumatic Brain Injury (TBI) and Varying Symptoms

POPULATION: All Veterans (including GWV) over the age of 18 approved for receiving clinical care at DC WRIISC

PURPOSE: Remote psychophysiological evaluations of autonomic and brain monitoring wearables to evaluate patterns of neural activity and behavior that predict exposure history.

The Role of the Brain Stem in Gulf War Illness Pathology

POPULATION: GWV with GWI

PURPOSE: Determine relationships between brain stem circuits, pain and sleep in GWI.

Non-Pharmacological Treatments for Insomnia in Chronic Traumatic Brain Injury

POPULATION: Veterans with mild TBI and current insomnia

PURPOSE: To assess the relative efficacy of two non-pharmacological interventions for insomnia in Veterans suffering from chronic TBI.

If you would like to obtain more specific information about any of these research findings, contact the associated WRIISC site. Stay tuned as WRIISC researchers embark on new journeys to study Veterans' health constantly and new research findings will continuously emerge.

Exposure Education for Providers- You spoke we listened

Veterans have raised concerns that many providers within and outside the VA are not always aware of the exposures they may have experienced during deployment and their concerns about health. To address this concern, WRIISC education products are being actively promoted to increase awareness and recognition.

Environmental exposure clinicians have long understood that core competency on military environmental exposure concerns is of increasing importance for providers who serve Veterans. In recognition of this, the VA's Secretary recently directed that all Veterans Benefits Administration (VBA) and Veterans Health Administration (VHA) compensation and pension providers and VHA clinicians must complete WRIISC's E-Learning Module 1 – Assessing Deployment Related Environmental Exposures. This training was also made available on the Center for Disease Control and Prevention (CDC) education and training website.



To further strengthen provider skills in Military Environmental Exposures, this past September WRIISC and Health Outcomes Military Exposures (HOME) partnered with the American College of Preventive Medicine (ACPM) to offer a certification program with ACPM. WRIISC's five E-learning modules serve as the core clinical education for VA and non-VA providers to develop a Level 1 certification program in Military Environmental Exposures. Providers can earn this certification in addition to receiving continuing medical education credits upon successful completion of the five modules by passing the comprehensive exam. An advanced level certification is also being developed which will consist of a series of case studies and clinical exposure scenarios. Certification will be earned upon successful completion of a comprehensive exam. We have engaged military exposure subject matter experts from across VA to help build this important training!

More information on these exciting certifications at:

<https://www.acpm.org/education-events/military-environmental-exposures-certification/>

WRIISC Research REVELATIONS

Here are just some recent key findings WRIISC researchers have made for Gulf War Veterans through their critical work. Many of these findings will lead to the development of better treatments for the conditions or symptoms studied.

NJ WRIISC

- Not all Gulf War Veterans (GWV) with Gulf War illness (GWI) experience post-exertional malaise (PEM) (or the worsening of symptoms following even minor physical or mental exertion) 24 hours after exercise, and more research is needed to determine the extent that exercise worsens symptoms in GWI.
- PEM responses in GWV with GWI were not related to select cardiorespiratory measures (oxygen, carbon dioxide, ventilation, heart rate, work rate, and leg muscle pain) and perceptual responses to exercise.
- An inability to modulate brain activation as task demands change from easier to more difficult may underlie fatigue in GWI.
- Brain responses to nonpainful changes in skin temperature (thermal stimuli) in GWV with chronic medically unexplained pain are sensitive to pain anticipation. Accounting for the influence of pain anticipation in future investigations of central nervous system dysfunction in Veterans with chronic unexplained pain is important.
- Results of a study on cardiopulmonary exercise testing for GWV provided a future framework for evaluating 2-day cardiopulmonary exercise testing reliability for GWV, and reinforced the importance of carefully considering measurement error when interpreting findings of testing.
- GWV with GWI adopt a unique exercise ventilatory (air in and out of the lungs) pattern characterized by reduced respiratory frequency, despite similar ventilation relative to controls. Although the reason for this pattern remains unresolved, findings suggest that the components of ventilation should be considered when evaluating clinical conditions with unexplained exertional symptoms.
- Patients with GWI use a variety of self-management strategies, many of which are consistent with clinical practice guidelines for treating GWI, including lifestyle

changes and non-pharmacological strategies. Providers should encourage effective self-management approaches for patients, especially those that patients want to use.

- Providers may need education and training to facilitate diagnosis of and service-connection for medically unexplained symptom (MUS) conditions. Greater acknowledgment and validation of MUS conditions would increase patient engagement with healthcare as well as provider and patient satisfaction with care.
- Factors related to institutional betrayal (situations in which the institutions people depend upon for safety and well-being cause them harm) have a profound impact on perceptions of care and the patient-provider relationship for Veterans living with GWI. Future research and policy aimed at improving healthcare for people living with MUS should consider the concept of institutional betrayal.

DC WRIISC

- Dispositional mindfulness (DM) (the trait of awareness and attention to one's thoughts and feelings in the present moment) has beneficial effects for GWV with GWI on multiple self-reported health measures, cognitive performance, and electrical activity of the brain. DM also moderated the effect of deployment related stress on post-traumatic stress disorder (PTSD) symptoms of GWV with GWI.
- A randomized clinical trial assessed the potential benefits of combining mindfulness meditation and auricular acupuncture for GWV with GWI and observed significant reductions in fatigue and pain interference at post-treatment.
- Autonomic activity modulated self-reported GWI symptom severity for GWV. This could inform targets for treatment and recovery.
- Military service members and Veterans with TBI had poorer sleep quality compared to civilians, possibly reflecting unique stressors associated with prior military experiences and other physical and/or psychological traumas that combine to heightened vulnerability. *
- Veterans with a history of blast exposures had high post-concussive symptoms and posttraumatic stress levels. *
- Veterans that have been exposed to traumatic brain injuries and

blasts with greater post-concussive symptoms experience worse sleep. *

- A clinical trial of a remote meditation and aerobic exercise program paired with health coaching improved depression, sleep quality, and mental health-related quality of life among Veterans with CMI. *
- A comprehensive exposure assessment tool revealed exposure duration and frequency were associated with self-report behavioral health measures, cognitive performance and actigraphy based sleep metrics. *
- Military/Veterans have poorer sleep quality compared to civilians even in the absence of TBI, reflecting unique stressors associated with prior military experiences. The findings from the meta-analysis suggests that military service members and Veterans with TBI are particularly at a higher risk of poor sleep and its associated adverse health outcomes. *

CA WRIISC

- Completed the first randomized controlled trial (one group participated in yoga but the other did not) to demonstrate that yoga is effective for treating symptoms of GWI, especially pain and fatigue. Results support further evaluation of yoga for treating Veterans with GWI.
- First study in Veterans to show that yoga delivered via telehealth had similar benefits to in-person yoga. This complements prior evidence for the efficacy of yoga and supports the use of yoga in healthcare settings. *
- Brainstem volume may be selectively affected by GWI, and that the resulting progressive shrinkage of the brainstem could in turn mediate or moderate GWI-related symptoms such as fatigue and depression. The brainstem should be carefully considered in future research focusing on the cause of GWI.
- A special type of radiological scan (Diffusion tensor tractography or DTI) is an effective and efficient way to explore Veterans' brain circuits, in this case connections involved in pain processing. *
- First study to demonstrate that white matter abnormalities are found in brains of Veterans with depression even in the presence of co-occurring PTSD and TBI. *

**Study includes non-Gulf War Veterans*

RESEARCH MATTERS

WRIISC continues to conduct research that relates to Veterans' health. Below is a study published by the DC WRIISC research team.

PUBLICATION TITLE: Emotion dysregulation and heart rate variability improve in US Veterans undergoing treatment for posttraumatic stress disorder: Secondary exploratory analyses from a randomized controlled trial

QUESTION: How do PTSD treatment of standard therapy (cognitive processing therapy), or a breathing based meditation therapy (Sudarshan kriya yoga; SKY) impact emotional regulation?

FINDINGS: Questionnaire responses indicated that both types of treatment had a beneficial effect on emotional regulation. However, only SKY treatment moved heart rate variability (HRV) towards a healthier profile (i.e., higher beat-to-beat variability in heart rate).



MEANING: This study adds to a growing body of literature suggesting breathing based meditation can improve autonomic regulation (certain body processes, such as blood pressure and the rate of breathing) and balance. Findings are also consistent with literature that demonstrates slow, deep, relaxed, diaphragmatic breathing increases HRV, improves emotion regulation, and reduces clinical symptoms of PTSD.

ADDITIONAL INFORMATION: This research is in press in the journal BMC Psychiatry. Contributors from CA WRIISC: Danielle C. Mathersul, Kamini Dixit, Jay Schulz-Heik, Timothy J. Avery & Peter J. Bayley

HIGHLIGHTING WRIISC'S COLLABORATING PARTNERS

Partnering with individuals and teams across VA, Department of Defense (DoD) and other federal agencies, as well as universities and research foundations continues to be critical to advancement in the field of Veterans health.

Cardiovascular physiologist Loren E. Wold, PhD, FAHA, FAPS, is a distinguished researcher and professor in the Department of Physiology and Cell Biology at the Ohio State University. He is also Associate Dean for Research Operations and Compliance in the College of Medicine and the Editor-in-Chief of the Elsevier journal Life Sciences. Throughout Dr. Wold's impressive career, he's impacted the world of science through his work and influenced generations of students and researchers.

Dr. Wold's research interests lie in studying the role of the environment on the development of cardiac disease, particularly related to air pollution and electronic cigarette exposure. His lab is currently funded by multiple NIH, VA, CDC and AHA grants/contracts as well as private foundations. In the past years, Dr. Wold has worked with WRIISC research staff on several publications, including airborne hazard exposure-related cardiac and pulmonary diseases.

Experts at VA's Airborne Hazards and Burn Pit Center of Excellence (AHBPCE), located at the NJ WRIISC, are set to work with Dr. Wold and his team of researchers on a newly funded study that will

examine the effects of airborne hazards (particulate matter < 2.5µm in diameter) on cardiopulmonary health. This project will use a mouse model that replicates airborne hazard exposures that deployed Gulf War Veterans experienced.



Pictured above is the exposure system that will be used in this study.

Information learned during this study will increase our understanding regarding airborne hazard exposures and treatments and utilize the findings to benefit Veterans' health outcomes.

We thank you, Dr. Wold, for the incredible opportunity to join forces with you to improve cardiopulmonary health in Gulf War Veterans.



Cardiovascular Physiologist
Dr. Loren E. Wold,
PhD, FAHA, FAPS

First Annual Airborne Hazards and Burn Pits Center of Excellence (AHBPCE) Research Day

The Airborne Hazards and Burn Pits Center of Excellence (AHBPCE) very successfully hosted its first virtual Research Day in February 2022! The event was a way to reach researchers and others with the exciting research currently being completed at the Center and at several partnering institutions. Investigators who are collaborating with the Center on Airborne Hazards research were invited to present their updates in the Pecha Kucha format, a unique way of "story telling" which focuses on imagery rather than text. This innovative presentation style allowed presenters to concisely

translate their research findings and condensed material to 6-7 minutes per presentation. Ms. Sharon Einbinder, Marine Corps Chief Warrant Officer 2, started the event by graciously sharing her deployment and post-deployment experiences and concerns regarding airborne hazards and burn pits. Presentation topics included Pathophysiology, Novel Technologies and Cohorts of Interest, with 10 presentations in total and great discussion during Q&A sessions. Presentations were given by researchers at the Center, our Ann Arbor, San Francisco, and Eastern Colorado Post Deployment Cardiopulmonary Evaluation Network (PDCEN) sites, Rutgers University, the Ohio State University, the University of Texas Arlington, the University of Tennessee Health Science Center and the VA Center for Innovations in Quality, Effectiveness and Safety. With researchers' approval, nine presentations were recorded to be placed on our WRIISC website and soon our facility Facebook page.

Around the WRIISC News

DC WRIISC

Dr. Michelle Costanzo

Dr. Michelle Costanzo joined the WRIISC in 2016 as a neuroscientist from the Uniformed Services University (USU) where she maintains an appointment as a Research Assistant Professor of Medicine. Dr. Costanzo now serves as the Research Director and Research Fellowship Director where she and the research team have taken innovative solutions to Veteran health concerns through telehealth, neuroimaging, computational modeling, behavioral health interventions (e.g. health coaching, exercise



NJ WRIISC

Dr. Lisa McAndrew

Dr. Lisa McAndrew's journey at the NJ WRIISC began with a post-doctoral fellowship in clinical psychology between 2008-2010 and from that point forward, she has played several important roles in the Center's growth. Currently she is the Director of Research and Fellowship Director and Acting Director of Education and Risk Communication. Throughout her years at the WRIISC her contributions as a research scientist



"I'm most proud of the projects that have transformed from a meeting idea into something that is operational and ready for Veterans. I really enjoy the Research, Clinical and Education missions of WRIISC, which are so closely integrated here in Washington DC. As a researcher, it is rare to be able to consult colleagues on the clinical implications of study design and at the same time consider the impact of findings extending beyond scholarly journals through provider webinars."

and mindfulness) and retrospective analysis from large clinical data sources (e.g. VA Corporate Data Warehouse).

Recently, Dr. Costanzo has been part of the leadership group for the VA-NIH Investigative Deep Phenotyping of Gulf War Veteran Health project that has the potential to transform knowledge of why these Veterans have been sick for decades and what can be done to help them. In another high impact project, Dr. Costanzo manages the development of a VA-DoD collaboration to assess the occupational

impact on health for the Explosive Ordnance Disposal community.

Dr. Costanzo's background is in cognitive neuroscience, where she has published on topics related to post-deployment health, stress and brain function and combat-related virtual reality including being awarded the 2017 Military Medicine Article of the Year. In addition to her scientific training, she has expertise in regulatory compliance and program management, ranging from her work at the National Science Foundation and the White House Office of Science and Technology Policy to her responsibilities as an investigator for NIH, USU, Walter Reed Military Medical Center and WRIISC clinical studies. In the future she intends to expand the research program to establish metrics of evidence-based knowledge for Veterans with novel exposure concerns and continue to improve recovery options for those with complex injuries.

"Both overseeing training for future generations of experts and sharing all of my research findings dedicated to advancing Veterans' health have been extremely rewarding and two of the greatest accomplishments I've made in the field to date. I am proud to be part of WRIISC Leadership team and direct my daily efforts to bettering health for Veterans".

directed towards improving the functioning of Veterans with complex post-deployment health concerns, particularly medically unexplained symptoms (e.g., GWI, chronic pain), are immense.

Specifically, Dr. McAndrew's research focuses on: (1) understanding the impact of deployment on GWI and related conditions, (2)

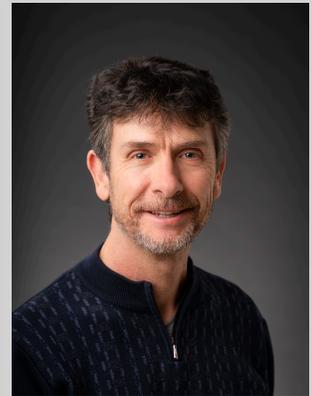
determining Veterans' experiences with GWI and related conditions (3) using Veterans' understanding to develop behavioral interventions they want to receive (4) discovering how to implement these interventions in the VA healthcare system.

We thank the WRIISC Research Directors, Drs. Costanzo, McAndrew & Bayley for their hard work and passion to help Veterans!

CA WRIISC

Dr. Peter Bayley

Dr. Peter Bayley has been a Director of Research at the CA WRIISC since 2019, and also Associate Professor (affiliated) in the Department of Psychiatry and Behavioral Sciences at Stanford University. Previous to joining the WRIISC, Dr. Bayley, neuroscientist, performed graduate and postdoctoral research at the University of California San Diego where he studied memory disorders in patients with various forms of dementia and brain damage. Dr. Bayley and his team have been leaders in research related to the use of integrative approaches, including yoga and meditation, to improve the health status of those living with chronic symptoms, including those that are medically unexplained, often seen in Veterans evaluated at the WRIISC.



"My recent clinical trials with Yoga showed that it may be an effective treatment for core Gulf War illness (GWI) symptoms of pain and fatigue. Many Veterans we evaluate at the WRIISC experience these symptoms and look to our team for treatment advice and ways which they can best manage symptoms. Yoga is one of few successful treatments for GWI that we can confidently recommend to these Veterans as we encourage them to take control of their symptoms and live better."

Dr. Bayley has been awarded over \$4 million from VA, the National Institutes of Health, and the Department of Defense to conduct his research. He has published more than 50 peer reviewed articles on a broad range of topics including memory, Alzheimer's disease, pharmacology, and PTSD. He has published many studies of yoga, including the first evaluation of telehealth yoga in Veterans. His future plans include starting a new clinical trial to evaluate transcendental meditation as a treatment for posttraumatic stress disorder in Veterans.

This national study will include the CA WRIISC as a site and will be the largest of its kind ever undertaken. He has also recently found promising results from a small-scale clinical trial investigating how to treat chronic pain in Veterans using online yoga. He plans to scale up this research to complete a larger more definitive trial looking at online yoga therapy for treating Veterans with chronic pain.



WRIISC Advantage

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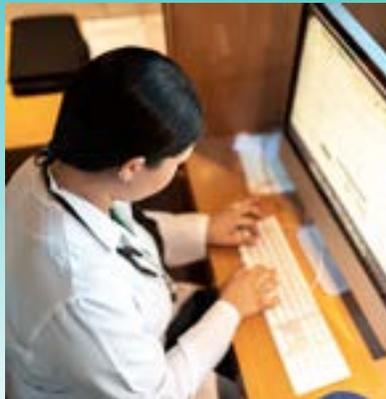
This newsletter contains a minimum of 30% post-consumer waste.

WRIISC partnered with the American College of Preventative Medicine (ACPM) to develop a certification program!

Attention Providers:

Interested in learning about Veteran military exposure concerns?

Obtain a Level 1 certification and continuing medical education credits upon successful completion of WRIISC's 5 E-learning modules comprehensive exam.



AMA certification program:

[Military Environmental Exposures Certification | ACPM](#)

