

Neurologic Health in Gulf War Veterans



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Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses

June 25, 2018 San Francisco, CA

Considerations for Designing an Epidemiologic Study for Multiple Sclerosis and Other Neurologic Disorders in Pre and Post 9/11 Gulf War Veterans

Committee on Designing an Epidemiologic Study for Multiple Sclerosis and Other
Neurologic Disorders in Veterans of the Persian Gulf and Post 9/11 Wars

Board on the Health of Select Populations

Institute of Medicine

Published December 2015

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

THE NATIONAL ACADEMIES PRESS
Washington, DC
www.nap.edu

**COMMITTEE ON DESIGNING AN EPIDEMIOLOGIC STUDY FOR MULTIPLE
SCLEROSIS AND OTHER NEUROLOGIC DISORDERS IN VETERANS OF THE
PERSIAN GULF AND POST 9/11 WARS**

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ABSTRACT Objective: To assess the feasibility of proceeding with a study as outlined in the committee's statement of task (SOT). Methods: Reviewed

Statement of Task

An ad hoc committee under the auspices of the Institute of Medicine will design and manage an epidemiologic study to determine the incidence and prevalence, as well as the risk (to the extent possible) of developing multiple sclerosis and other neurologic diseases as a result of service in the 1990-1991 Persian Gulf and post 9/11 Global Operations theaters. Other neurologic diseases to be considered include Parkinson's disease and brain cancers, as well as central nervous system abnormalities that are difficult to precisely diagnose. The committee will identify its data needs, request those data from the Department of Veterans Affairs, and will analyze the data. The resulting report will describe the study design, methods, and results on the neurologic outcomes of interest. The report will also include recommendations for legislative or administrative actions as deemed appropriate by the committee regarding data collection and/or follow-up related to the neurologic diseases under consideration.

The Department of Veterans Affairs (VA) requested that the Institute of Medicine (IOM) of the National Academies of Sciences, Engineering, and Medicine conduct a study to respond to Public Law 110-389 enacted in 2008 (see Appendix A) to determine the incidence and prevalence, as well as the risk of developing multiple sclerosis (MS) and other neurologic diseases as a result of service in the 1990-1991 Persian Gulf and post 9/11 (that is, OEF/OIF/OND)¹ Global Operations theaters. Specifically, the other neurologic diseases to be

considered are migraines, Parkinson's disease, and brain cancers, as well as central nervous system abnormalities that are difficult to precisely diagnose. The committee's statement of task

APPROACH TO THE TASK

In January 2015, the IOM convened a committee of 13 experts, in the fields of neurology, epidemiology, and statistics, to address the task and the feasibility of proceeding with the study. At its first meeting in March 2015, the committee met with VA officials to learn about the burden of illness with regard to neurologic outcomes in veterans who have been deployed to the gulf region, to gain an understanding of the available data that might be useful in addressing its task, and to learn about past and ongoing efforts that have been undertaken in this area (Bossarte, 2015; Schneiderman, 2015; Wallin, 2015). The committee members examined VA utilization reports (see Appendix B) detailing the use of VA health services by Gulf War and OEF/OIF/OND veterans. Those reports detail the number of unique veterans with primary diagnoses or diagnoses in any position by *International Classification of Diseases* (ICD) codes that are obtained from veterans' medical records; they are not based on a review of patient records or a confirmation of diagnoses. The utilization reports provided the committee with a starting point for understanding the burden of illness in the veteran populations of interest, and to compare the outcomes of interest in the deployed versus the nondeployed, when available, in those veterans using VA health care. The VA representatives also discussed previous studies that have been conducted to gather information about the incidence and risk of MS in US veterans (for example, the studies by Wallin et al., 2012, 2014). The committee members also were presented with information regarding the datasets that are available through the VA Office of Public Health's Epidemiology Program. As the legislation directed VA to contract with the IOM to conduct the study, and the contract specified using existing VA data, the committee focused its efforts on understanding VA data.

based on available Department of Veterans Affairs (VA) data. Results: In examining the burden of illnesses, the committee found that the existing data suggest that Gulf War deployed veterans do not have a higher prevalence of the diseases of interest than the nondeployed Gulf War veterans, with the exception of headache and migraine. The burden of illness in the post-9/11 veterans cannot be compared to the nondeployed, as almost the entire cohort of those veterans has been deployed. Moreover, the VA survey data and administrative databases alone are inadequate for assessing the effects of deployment, as they are limited to users of VA health care, which comprise only 36% to 60% of the entire veteran population of interest. Conclusion: While technically feasible to conduct a study as outlined in the committee's SOT, the committee decided not to proceed with the study because it would be limited to using existing VA data (as stated in the VA contract with the Institute of Medicine of the National Academies of Sciences, Engineering, and Medicine), it would repeat the work of others, and it likely would not advance the knowledge significantly beyond what is already known. However, if additional data were made available, then a rigorous study likely could be conducted that advances knowledge on these issues.

Some Highlights from Past Work

DOI: 10.1111/anie.12010

ORIGINAL ARTICLE

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Scandinavica

The Gulf War era multiple sclerosis cohort: 3. Early clinical features

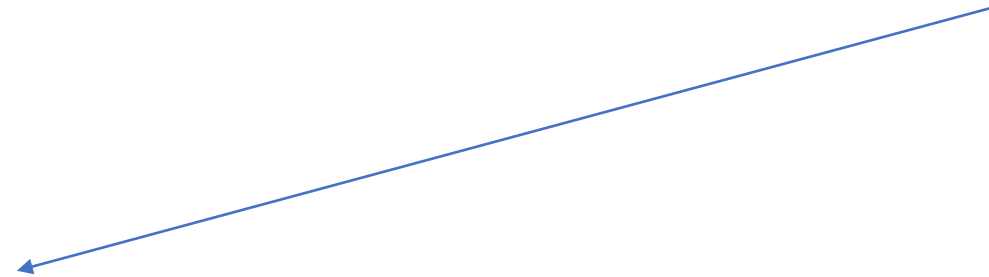
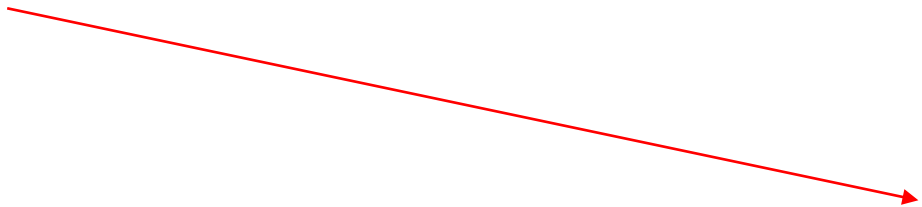
M. T. Wallin^{1,2,3}  | W. J. Culpepper^{1,3} | H. Maloni¹ | J. F. Kurtzke^{1,2,†}

Objectives: To present clinical features at diagnosis for a large nationwide incident cohort of multiple sclerosis (MS) among those serving in the US military during the Gulf War era (GWE).

Materials & Methods: Medical records and databases from the Department of Veterans Affairs (VA) for cases of MS with onset in or after 1990, active duty between 1990 and 2007 and service connection by the VA, were reviewed for diagnosis and demographic variables. Neurological involvement was summarized by the Kurtzke Disability Status Scale (DSS) and the Multiple Sclerosis Severity Score (MSSS).

Results: Among 1919 cases of clinically definite MS, 94% had a relapsing-remitting course and 6% were primary progressive at diagnosis. More males of all races and blacks of both sexes were progressive. At diagnosis, functional system involvement was pyramidal 69%, cerebellar 58%, sensory 55%, brainstem 45%, bowel/bladder 23%, cerebral 23%, visual 18%, and other 5%. Mean DSS scores were: white males, females 2.9, 2.7; black males, females 3.3, 2.8; and other-race males, females 3.2, 2.6. Mean and median MSSS were marginally greater in black males and other males compared to the other sex-race groups.

Conclusions: In this incident cohort, males and blacks had significantly higher proportions of primary progressive MS. DSS at diagnosis was significantly more severe in blacks and significantly less so in whites and in women vs men, but MSSS was only marginally greater in black males and other-race males. This morbidity assessment early in the course of MS provides population-based data for diagnosis, management, and prognosis.



Multiple Sclerosis in Gulf War Era Veterans. 2. Military Deployment and Risk of Multiple Sclerosis in the First Gulf War

Mitchell T. Wallin^{a,c} John F. Kurtzke^{a,c} William J. Culpepper^{c,h} Parisa Coffman^a
Heidi Maloni^{a,c} Jodie K. Haselkorn^{c,e-g} Clare M. Mahan^d for the
Veterans Affairs Multiple Sclerosis Centers of Excellence Epidemiology Group

0.43–0.74). **Conclusion:** Military deployment to GW1 was not a risk factor for developing MS.

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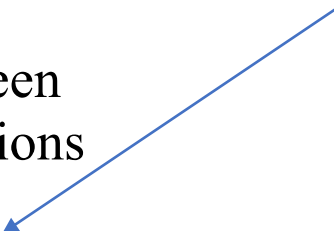
Limitations Described by the Committe

LIMITATIONS OF USING VA DATA SOURCES

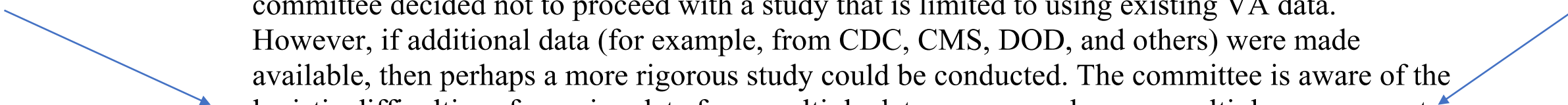
The committee limited its evaluation to existing VA data sources because these would be the only data sources available to the committee. The VA maintains hundreds of databases that collect and store information related to health and other services for veterans. Those databases include, for example, information on inpatient and outpatient procedures, diagnoses, pharmacy data, and service-connected benefits. The VA also conducts surveys of its veterans, for example, the NHS and the National Health Study for a New Generation of US Veterans (NewGen). The committee examined the potential data that could be gleaned from those databases and surveys to determine if they might be useful in designing a study as outlined in the legislation. The committee also reviewed published papers that highlighted the challenges of using those data to determine prevalence, incidence, and risk factors (as required by the legislation). The committee identified three major limitations: (1) constructing a suitable comparison group, (2) using electronic clinical data, and (3) using VA survey data.

Comparison Group-Almost all are Deployed In Combat Theaters of Operation

However, it is not easy to select a comparison group for OEF/OIF/OND active-duty service members because as of December 2011, almost all members in each service branch deployed at least once to Iraq or Afghanistan (RAND, 2013). Moreover, in contrast to the Gulf War operations, which lasted under 1 year and most service members had a single deployment, as of 2010, 47% of all OEF/OIF/OND active-duty service members, 35% of reservists, and 35% of National Guardsmen deployed more than once and their cumulative lengths of deployment averaged between 15.2 and 17.6 months depending on branch of service and component (IOM, 2013). Those who have not deployed likely differ from the deployed in important characteristics, some of which might be related to the health outcomes of interest. Many of those service members who had not deployed to Iraq or Afghanistan were new recruits in training, had been stationed elsewhere (such as Europe, Japan, or South Korea), or were supporting the operations from posts in the United States. A more representative comparison group might consist of service members who are eligible to deploy but did not. However, only 4% (20,000) of active-duty soldiers met this requirement as of December 2011 (RAND, 2013), and therefore, the statistical power for making comparisons using that group would be limited.



Conclusions



The committee examined possible data sources and data elements that would be needed (in each case, limited to VA data), considered possible study designs and appropriate algorithms to use for case ascertainment, and discussed the challenges of conducting such a study. Ultimately, the committee decided not to proceed with a study that is limited to using existing VA data. However, if additional data (for example, from CDC, CMS, DOD, and others) were made available, then perhaps a more rigorous study could be conducted. The committee is aware of the logistic difficulties of merging data from multiple data sources and across multiple government agencies, the difficulties that persist with regard to access to datasets with identifiable information, and the time and expense that would be required to complete the necessary data use agreements, data linkages, and analyses.

Given all the considerations noted, the committee did, however, consider alternative study designs for each of the neurologic outcomes and considered them separately, because each of them present different study design challenges. Identifying true cases of MS, migraines, Parkinson's disease, or brain cancer with a high degree of precision requires different approaches due to inherent differences in the nature and frequency of those illnesses. In addition, methods that accurately identify true cases suitable for estimating prevalence may not be adequate for identifying disease onset required to define incident cases, with the exception of malignant brain cancer.

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