Chapter 22

DISCUSSION SUMMARY: METHODOLOGICAL CONSIDERATIONS TO DESIGN A PULMONARY CASE SERIES AND A NATIONAL, BROAD-BASED REGISTRY FOR VETERANS OF OPERATION IRAQI FREEDOM AND OPERATION ENDURING FREEDOM

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INTRODUCTION

In Iraq and Afghanistan, concentrations of air contaminants, such as combustion products and particulate matter, are frequently much higher than they are in the United States. The US Department of Defense (DoD) has evaluated air pollution at several locations in theater and performed risk assessments of the potential long-term health effects.[1,2] In 2010, the DoD published the proceedings of a symposium co-sponsored by the Armed Forces Health Surveillance Center and the Uniformed Services University of the Health Sciences titled Assessing Potentially Hazardous Environmental Exposures Among Military Populations.[3] The symposium focused on airborne hazards, including environmental monitoring and medical surveillance.[4–6] Several other recent studies have focused on air pollution in theater, including a comprehensive Institute of Medicine (IOM) study potential health effects of burn pit emissions.[1,2,7–9] The long-term health effects of air pollution in theater are uncertain; therefore, epidemiological, clinical, and laboratory research studies are underway.

Individual cases have been reported of service members and veterans who developed various pulmonary diseases after returning from deployment to Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). However, no controlled epidemiological studies have followed up these individual cases to determine if there were linkages between them, such as living at the same military base in theater or belonging to the same military unit or military occupational specialty. The rates of chronic pulmonary diseases in deployed service members have been compared with the rates in nondeployed service members in a number of controlled, population-based studies. To date, the evidence is inconclusive.[7,8,10–15] Controlled epidemiological studies of pulmonary diseases in OIF/OEF veterans and nondeployed veterans are continuing.

In response to case reports of pulmonary diseases, the Department of Veterans Affairs (VA) and the DoD have recently discussed the possible establishment of a pulmonary disease registry for veterans of OIF and OEF. During the Joint VA/DoD Airborne Hazards Symposium in August 2012, one work group discussed the scientific issues that need to be considered to develop a registry; this chapter summarizes that discussion. The purpose of this chapter is to describe issues related to development of two possible types of medical data collection: (1) a case series that is targeted to specific pulmonary diseases and (2) a national, broad-based registry related to deployment to OIF and OEF.

During the past few years, Congress introduced multiple bills that would require the VA to establish a burn pit registry. This potential requirement for a new VA registry was discussed during the August 2012 symposium. In January 2013, President Obama signed legislation that requires the VA to establish a registry. The provisions of this law are outlined in the section on National, Broad-based Registry Related to Operation Iraqi Freedom and Operation Enduring Freedom.[16]

CASE SERIES THAT ARE TARGETED TO SPECIFIC PULMONARY DISEASES

Existing Case Series of Pulmonary Diseases in Veterans of Operation Iraqi Freedom and Operation Enduring Freedom

This section reviews the small case series that has been published or presented during the August 2012 Airborne Hazards symposium, followed by a summary of the work group discussion during that symposium. This discussion focused on the general methodological issues related to the development of a pulmonary case series.

DoD and VA physicians at different locations have identified individual cases of OIF/OEF veterans who developed pulmonary diseases after returning home. During the August 2012 symposium, several physicians presented clinical case summaries of patients who had pulmonary diseases and who had served in Iraq or Afghanistan. Each of these cases demonstrated divergent pulmonary pathology. These individual cases raised more questions than they answered related to the types of environmental exposures or other risk factors that they experienced in OIF or OEF, which may or may not have contributed to the etiology of their diseases. Currently, there is no coordinated process in the DoD and the VA to collect data on these patients and to provide long-term follow-up, if warranted.

Physicians at Vanderbilt University (Nashville, TN) evaluated 80 soldiers who had deployed to Iraq or Afghanistan and who were referred for an evaluation of dyspnea on exertion.[17] Some of the soldiers reported exposure to the large fire at a sulfur mine in Iraq in 2003; however, others did not report any specific exposures.[14] These 80 soldiers received a variety of diagnoses, including asthma, bronchitis, sarcoidosis, and several other pulmonary diseases.[17] Of the 49 soldiers who underwent surgical lung biopsy, 38 were diagnosed with constrictive bronchiolitis.

Methodological concerns have been raised about this case series.[7,18] Questions have been raised whether the diagnoses of constrictive bronchiolitis were actually correct, because the majority of cases lacked evidence of airway obstruction

on pulmonary function tests, which has traditionally been a diagnostic feature of this disease. In addition, the majority of these cases (75%) did not demonstrate findings of mosaic air trapping or centrilobular nodularity on high-resolution chest computed tomography, both of which are features that are seen in constrictive bronchiolitis. Concerns have also been raised about the lack of blinding of the pathologists in this study, which could have led to bias. Results of this case series cannot be used to draw conclusions on the etiology (causes) of the individual cases. To address the methodological concerns, the DoD recently funded scientists at National Jewish Health (Denver, CO) to provide an independent pathological review of the Vanderbilt cases.[9] This pathological review will be blinded; it will include the development of a morphometric diagnostic tool for small airways diseases, such as constrictive bronchiolitis, and it will include characterization of particles associated with the lesions.

Physicians at Brooke Army Medical Center (BAMC) in San Antonio, TX, are conducting a series of studies that are systematic clinical evaluations of active duty soldiers with pulmonary symptoms.[7,9] To date, this group has evaluated approximately 100 soldiers. The first study—titled Study of Active-Duty Military for Pulmonary Disease Related to Environmental Dust Exposure (STAMPEDE)—was presented during the August 2012 symposium.[19] The purpose of the study was to evaluate 50 active duty soldiers for evidence of lung disease. These soldiers had returned from OIF/OEF in the past 6 months and had developed new-onset pulmonary symptoms. Of the 50 cases, 12 received a diagnosis of asthma and 7 received other diagnoses. There was no evidence of constrictive bronchiolitis or interstitial lung disease in any of the 50 cases. No pulmonary diagnosis was made in 31 of the cases after a comprehensive workup. No surgical lung biopsies were required as part of STAMPEDE. Patients did undergo transbronchial lung biopsies through bronchoscopy if interstitial changes were seen on chest computed tomography. The overall conclusion was that most cases had a normal evaluation. This series of studies of systematic clinical evaluations of active duty soldiers is continuing at BAMC.[7,9]

The three VA War-Related Illness and Injury Study Centers (WRIISCs)—located in East Orange, NJ, Palo Alto, CA, and Washington, DC—evaluate veterans who have pulmonary symptoms.[8] For example, the East Orange Veterans Affairs Medical Center (VAMC) evaluated 35 veterans during 2012. These evaluations included cardiopulmonary exercise testing. The Baltimore VAMC has similarly performed thorough evaluations of OIF/OEF veterans who have had pulmonary symptoms since January 2012.

In general, medical evaluation methods used in these small case series have been too disparate to permit combined analyses from different sites. The DoD and VA could build on the foundation of separate case series to establish a shared, systematically collected case series of OIF/OEF veterans who have developed pulmonary diseases. The DoD and VA could develop this as a consortium for sharing information on pulmonary cases among military treatment facilities (MTFs) and VAMCs. The consortium could consist of a network of DoD and VA sites that would report to a central coordinating site.

During the August 2012 symposium, the work group discussed the potential utility of a coordinated, shared case series. The purpose of the case series would have to be carefully defined during its development to align expectations with the purpose. If a mechanism to pool similar cases from MTFs and VAMCs nationally could be established, this mechanism could yield a larger collection of cases and more useful data that could be used to identify commonalities among the cases. This could help generate hypotheses related to possible risk factors for the development of pulmonary diseases, which are related to military service or not. The case data would be used optimally as part of a case-control study. The remainder of this section describes the general methodological considerations needed to design a pulmonary case series, and it also summarizes the work group's discussion during the 2012 symposium.

Identification of Pulmonary Cases for a Shared Case Series

Eligibility criteria for the pulmonary case series could be defined by the new onset of a specific disease after returning from deployment (eg, constrictive bronchiolitis or interstitial lung disease) or by the new onset of symptoms (eg, dyspnea on exertion). A case series based on medically validated diseases would be much more specific; therefore, it would have greater scientific utility. Patients who have been described to date were diagnosed with a wide variety of diseases. Thus, it is premature to limit the shared case series to a single diagnosis (eg, constrictive bronchiolitis). The eligibility criteria could also include a threshold level of disability. Disability would be defined on the basis of pulmonary functional abnormalities or pathological diagnoses and not on receiving compensation benefits. These criteria would exclude a veteran who has mild symptoms that do not cause abnormalities in objective tests. Progression of the disease severity over time should also be considered.

Surgical lung biopsies would not be required to include patients in this case series. Many pulmonary diagnoses can be made with confidence without biopsy, particularly when the risk of undergoing an invasive procedure outweighs the benefits gained by a pathological diagnosis. However, biopsy is the gold standard for certain nonneoplastic lung diseases, and neoplastic diagnoses require pathology specimens. If biopsy results were available for some cases, pathological results would be useful to include in a case series because they provide the most accurate data. Lung biopsy specimens can be preserved, reviewed, and used in future research.

The DoD and VA maintain electronic databases that include medical records of millions of service members and veterans. These databases could be mined to identify OIF/OEF veterans who have pulmonary diseases. A targeted approach could focus on the electronic medical records of the MTF and VAMC that evaluate a large number of pulmonary patients. These hospitals evaluate the highest proportion of patients who are difficult to diagnose, regardless of severity of disease. These hospitals also treat the most severe cases.

Coordination of a Pulmonary Disease Consortium, Including Standardized Data Collection

The DoD and VA could develop one or two central coordinating centers to collect data from the MTF and VAMC that participate in the consortium. The coordinating centers would collect periodic reports from these sites and analyze the data for patterns and trends. The coordinating centers would provide feedback on these periodic analyses to the participating sites. The three military services have pulmonary consultants who could serve as consortium coordinators for their services. The VA has a national Director of Pulmonary Medicine who could coordinate consortium activities for the VA.

To develop a shared case series, the DoD and VA would need to develop and adopt a standardized medical evaluation that would be consistently recorded to ensure comparability of results between sites. Standardized evaluations would include a thorough diagnostic algorithm. Evaluations would also require the development of standardized forms for the data entry of medical history, occupational and military histories, physical examination, and a minimal set of diagnostic tests. The minimal set of diagnostic tests could include chest X-ray films and pulmonary function tests that could be performed at all of the participating sites. At a minimum, the pulmonary function tests should include pre- and post-bronchodilator spirometry to identify mild airflow obstruction.[20–24] Medical evaluations and data reporting would need to be standardized across the participating sites. Even minor differences could prevent easy integration of the data from different sites that would lead to substantial challenges in data analysis. Central coordinating centers would collect, maintain, and analyze the results of patient evaluations.

A standardized set of questions would be needed for the occupational and military histories to combine computerized data from many patients. These questions could address common airborne hazards in theater (eg, exposure to burn pits), high concentrations of particulate matter due to sand storms, and other exposures (eg, the large sulfur fire in Iraq in 2003).[14] Questions could also address the frequency, duration, and intensity of these exposures. The DoD has collected environmental samples from many locations in theater, and data are archived at the US Army Public Health Command at Aberdeen Proving Ground, MD. DoD environmental monitoring data could be requested for specific locations in theater to compare with the occupational histories of specific patients. In a small case series, environmental monitoring data could be retrieved and used to validate self-reported exposures on the questionnaires.

Environmental monitoring data would likely be available for only a small minority of cases. In most cases, only the self-reported exposure history will be available. A more scientific exposure assessment of past exposures would not be necessary to diagnose most pulmonary diseases or to provide treatment and follow-up care. Usually, clinical care does not depend on whether the causative factor was past exposure to burn pit smoke, sandstorms, or cigarette smoking. If the exposure is continuing, identification of the environmental factors contributing to a disease is necessary as part of management and treatment, because the ongoing exposure could lead to prolongation or exacerbation of the disease.

Current capability and funding for ongoing data management must be considered before deciding on the location of the central data repositories. The coordinating centers must have an ongoing public health mission that includes information systems specialists, biostatisticians, and epidemiologists who work on health databases. The US Army Public Health Command would be a logical location for the DoD coordinating center. This Command collects data on an ongoing basis to maintain several large databases that include information from all three services. The Armed Forces Health Surveillance Center in Silver Spring, MD, would be an alternate location for the DoD coordinating center. This center has access to the great majority of health databases in the DoD, and it performs ongoing health surveillance studies.

The VA coordinating center could be located at the VA Office of Public Health in Washington, DC. This office performs environmental epidemiology studies and currently coordinates the Agent Orange and Gulf War registries. Alternatively, one of the three WRIISCs could serve as the VA coordinating center, depending on the funding mechanism that would establish the consortium. One of these centers could have an advantage, because it receives funding to perform clinical care and research. The database manager for this program could be located adjacent to clinicians, which would facilitate ongoing communications.

Longitudinal Follow-up of a Pulmonary Case Series

Patients who have advanced or diagnostically perplexing pulmonary diseases should be referred to a pulmonary specialist at the local MTF or VAMC. The pulmonary specialist would be responsible for identifying potential patients to

be included in the shared case series and would be the local point of contact for the consortium. If the patient's illness is still too difficult to diagnose, or is not responding to conventional treatment, the patient could be referred to a higher level DoD or VA referral center for further evaluation, such as the BAMC or one of the WRIISCs.

Patients who have pulmonary diseases should be followed over time and reevaluated, including after the transition of care from the DoD to VA due to separation from the military. Providers at the MTF and VAMC should plan the clinical hand-off of individual patients to ensure continuity of care and to prevent loss to follow-up, similar to the hand-off for OIF/OEF veterans who have traumatic brain injuries. Planning for a shared case series should incorporate the need for seamless transition of individual patients between DoD and VA care.

Long-term follow-up would ensure the continuity of care of individual patients, as well as illuminate the natural history of the diseases. A case series could provide useful longitudinal information, if it was designed to capture clinical follow-up data. To date, physicians who assessed the small case series have evaluated their cases at only one point in time; they have not followed the cases over time to describe the longitudinal course of the diseases. This means that DoD and VA clinicians who care for these patients have no information on the prognosis of the diseases, or if there are exposure-related conditions that could lead to unique patterns of disease progression.

By periodically evaluating trends in the case series population, investigators could elucidate the natural progression of deployment-related diseases. For example, longitudinal data analysis could address questions on the stability or progression of pulmonary function, chest imaging, or severity of disability. Some of these conditions may be rare and without widely accepted standards regarding appropriate treatment (eg, constrictive bronchiolitis). Therefore, comparisons between varying medical therapies in similar patients could foster understanding of the prognosis and the appropriate medical treatments for deployment-related diseases. The consortium could provide feedback to the participating sites on these issues of progression of the diseases and responses to treatments that could lead to improvements in clinical care.

Utility of a Shared Pulmonary Case Series

Longitudinal follow-up of pulmonary cases would enable the development of a systematic, thorough description of the cases, and it would define the natural history of the diseases. The results of a shared case series could have clinical utility to inform VA and DoD physicians who care for OIF/OEF veterans. For example, the results could be used to develop guidelines for the use of specific diagnostic tests or specific treatments for veterans who have particular respiratory diseases. Results could be published as an internal DoD or VA report and in the open medical literature.

Results of the medical evaluations could be compiled to generate hypotheses, based on patterns of disease or patterns of exposure. If patterns could be detected, improvements in treatment or prevention could possibly be developed.[24] It should be emphasized that a pulmonary case series would have multiple limitations regarding causality or association. Results could not be used to determine the etiology or pathophysiology of the diseases in individual cases. In addition, diseases that are diagnosed in individual cases could not be generalized to the entire deployed population, and no estimate of the rates of diseases could be determined.[25] However, if the cases were used as the basis of a case-control study, the association of potential risk factors with disease outcomes could be ascertained.

NATIONAL, BROAD-BASED REGISTRY RELATED TO OPERATION IRAQI FREEDOM AND OPERATION ENDURING FREEDOM

Existing Department of Veterans Affairs Registries Related to Deployments and the Congressional Requirement for a New Veterans Affairs Burn Pit Registry

This section describes the existing VA registries, followed by a summary of the work group discussion during the August 2012 symposium. This discussion focuses on the general methodological issues related to the development of a broad-based VA registry.

The VA has multiple registries related to specific deployments and environmental exposures, including Agent Orange, Gulf War, depleted uranium, and ionizing radiation. The VA has maintained an Agent Orange Registry for Vietnam veterans since 1978.[26] As of mid-2012, more than 561,000 veterans had received an Agent Orange examination. Approximately 4,000 veterans per month were enrolling in the Agent Orange registry as of 2012.[26] The VA has maintained a Gulf War Registry since 1992.[26] Veterans of the 1990–1991 Gulf War and OIF are eligible to enroll in the Gulf War Registry. As of mid-2012, more than 126,000 veterans had received a Gulf War examination. From 1994 to 2002, the DoD had a similar registry for active duty service members who had deployed to the 1990–1991 Gulf War.[25]

The VA's Agent Orange and Gulf War registries are voluntary (ie, any veteran who deployed can enroll). Veterans can enroll for a medical evaluation for any type of disease, even if they are asymptomatic. Approximately 10% of the

veterans who enrolled in the DoD Gulf War Registry were asymptomatic.[25] The VA Agent Orange and Gulf War registries include similar elements:

- an exposure history,
- a medical history,
- a physical examination, and
- laboratory tests, if indicated.

The exposure history relies solely on the veteran's recall and is not verified with military records. In fact, some veterans in the Agent Orange Registry were never in Vietnam.[26] These registry examinations do not provide a substitute for a VA Compensation and Pension Examination; that is, these examinations are not the first step in an application for VA disability compensation. This is confusing to some veterans.

Results of these examinations are entered into specific Agent Orange and Gulf War databases, respectively. The registry forms are paper-based, and they require data entry of multiple pages that is burdensome for the clinical staff. Registry data are not integrated with the general VA outpatient database. Data quality and usability of the databases are limited. For multiple reasons, there has been very little analysis of the data in the Agent Orange Registry, despite data collection since 1978.[26]

DoD and VA scientists performed an exhaustive analysis of the data in the DoD and VA Gulf War registries in 2002.[25] They combined the DoD and VA data on more than 100,000 patients and published a comprehensive surveillance report. This included approximately 14% of the total population of 697,000 Gulf War veterans. They concluded there was substantial clinical information in the registries that was useful to DoD and VA physicians who cared for Gulf War veterans. However, extrapolations could not be made from the registry data to the health status of the entire population of Gulf War veterans because of the substantial selection bias. Multiple research studies have demonstrated that Gulf War veterans who enrolled in the registries were sicker than Gulf War veterans who did not enroll.[25] In general, the registry data could not be used for epidemiological research.

The Disabled American Veterans (DAV), a veterans service organization, developed a burn pits registry for veterans to enroll in if they have health concerns that they believe are related to burn pit exposure. The DAV speaker at the August 2012 symposium said that 591 veterans had registered on the DAV website. They reported diseases in many organ systems, including 80 veterans who reported that they developed cancer within a few years of exposure to burn pits in theater.

During the past few years, Congress introduced multiple bills that would require the VA to establish a burn pit registry. In January 2013, President Obama signed legislation that requires the VA to establish a registry.[16] Public Law 112-260, Section 201, requires the VA to establish an "open burn pit registry for eligible individuals who may have been exposed to toxic airborne chemicals and fumes caused by open burn pits."[16(p6)] The law defines eligibility as having deployed in support of a contingency operation while serving in the military, on or after September 2001, and being based at a location where an open burn pit was used. The law does not require verification of an individual's location with military records or substantiation of exposure to burn pits. Burn pits were used at most bases in Iraq and Afghanistan; therefore, most deployed service members were located at bases with burn pits. VA implementation of the law is likely to translate into enrollment of any veteran who was deployed to OIF or OEF and who wants to volunteer for the registry.

The VA must establish this registry within 1 year of enactment of the law. The VA is also required to include information in the registry that would enable the VA to "ascertain and monitor the health effects of the exposure" in veterans that were "caused by open burn pits."[16(p6)] This would likely require periodic analyses of data on medical diagnoses of veterans enrolled in the registry.

In January 2013, the VA started planning for this mandated burn pits registry for OIF/OEF veterans. This chapter summarizes the work group discussion during the August 2012 symposium, which focused on the methods used to develop registries in general. This chapter does not address the VA's plans for the Congressionally mandated registry, which were just beginning to be formulated.

Enrollment Criteria for a National, Broad-based Registry Related to Operation Iraqi Freedom and Operation Enduring Freedom

During the August 2012 symposium, one work group discussed issues related to developing a national registry for OIF/OEF veterans. The work group recommended that veterans could enroll in this type of broad-based national registry, regardless of their disease status. The only requirement for enrollment would be verification that the veteran was deployed. The VA already has access to the military personnel database of veterans who were deployed to OIF and OEF. The VA uses this type of open enrollment in its Agent Orange and Gulf War registries.

A broad-based registry would not be limited to individuals who have pulmonary diseases. Many veterans, who have other types of diseases, believe their health problems are from exposure to burn pits. The registry would also include asymptomatic veterans who are concerned about their exposures. Burn pits were used in most large bases in theater; therefore, the great majority of veterans perceive they were exposed to burn pit emissions.[8] Many veterans are concerned about the long-term health effects of these exposures, even if an environmental scientist objectively evaluated the air concentrations at specific locations and developed a risk assessment that concluded levels that were not hazardous.[1]

Enrollment in the registry could provide improved access to the VA medical care system. The VA currently provides free medical care to OIF/OEF veterans for 5 years after they separate from the military. Enrollment in the registry would be useful to provide access to veterans who are separated from the military more than 5 years. Veterans would not need service connection for a disability to enroll in the registry.

Coordination of a Broad-based Registry, Including Standardized Data Collection

Centralized data collection would be necessary for a broad-based national VA registry for OIF/OEF veterans. Data from the patients' medical evaluations, as documented in electronic medical records, would need to be collected and archived centrally. This centralized coordination center could also perform periodic analyses of the aggregated data to detect patterns of veterans' concerns and medical diagnoses. The most likely location for this coordination center would be the VA Office of Public Health in Washington, DC.

To develop a national, broad-based registry, the VA would need to develop and adopt a standardized medical evaluation that could be consistently recorded to ensure comparability of results among the VAMCs nationwide. This would include the development of standardized forms for the data entry of medical history, occupational and military histories, physical examination, and a minimal set of diagnostic tests. If the registry was limited to lung diseases, the medical history could be focused and the minimal set of laboratory tests could include chest X-ray films and pulmonary function tests. If the registry included patients who had diseases in any organ system, a much broader medical history and a larger number of diagnostic tests would be needed.

A standardized set of questions would be needed for the occupational and military histories to combine computerized data from many patients. This could include questions on common airborne hazards in theater, such as exposure to burn pits, high concentrations of particulate matter due to sand storms, and other exposures. The occupational and military histories would reflect the patients' perceptions of their environmental exposures. Therefore, the utility of these histories would be limited, and they could not be used to determine the etiology of disease.

In 2011, the IOM published a comprehensive review of the potential health effects of exposure to burn pits in theater.[1] The IOM concluded that there was limited or suggestive evidence of an association between exposure to combustion products and decreases in pulmonary function tests. This conclusion was based on studies of industrial workers and not on military populations exposed to burn pits. The IOM concluded that there was inadequate evidence to determine if there was an association between exposure to combustion products and several other diseases. Based on IOM conclusions, pulmonary function testing would be the only scientifically justified laboratory test to include in a standardized medical evaluation.

Instead of developing a tailored medical evaluation for registry participants, the VA might choose to use the standard electronic medical records for outpatient clinic visits and hospitalizations. The names, demographics, and exposure histories of veterans who enrolled in the registry could be matched with the VA outpatient and inpatient databases. This would pull in the results of medical evaluations that were performed during routine clinical care. This approach would provide the advantage of integrating the registry data with the VA's electronic medical record systems. It would reduce the need for data entry of paper forms. It would also improve the incorporation of registry procedures into the normal clinical work flow compared with a separate standalone system for registry examinations.[26] However, this approach would lead to more incomplete or missing diagnostic data and less consistency in the methods of medical evaluations. This would lead to substantial challenges if analyses of aggregated diagnostic data were conducted.

Initial Small-Scale Initiative to Prepare for the Development of a National Registry

A small-scale pilot project at a few VAMCs would be very useful before the VA launches a national registry for OIF/OEF veterans. This initiative could gauge the possible interest of veterans who wanted to enroll in a registry. It could also estimate the number of veterans who would enroll and assess the types of questions, symptoms, and diseases they would have. In 2013, the VA considered use of a pilot project to refine the website and processes for its Congressionally mandated burn pits registry.

A small-scale pilot project would be useful to refine the standardized medical evaluation based on the types of diseases seen. It would also be useful to refine the information technology systems needed for the electronic reporting of medical evaluations and centralized data collection. The pilot project results would also be useful to design training for clinicians who care for OIF/OEF veterans. The VA has training programs for healthcare providers. A program outlining the purpose and methods of the registry could be developed prior to the national launch.

A pilot project would also provide useful information on the types of outreach and communications the VA should perform when it launches a national registry. The VA should include information on its website describing the purpose of the registry and how to register. Younger veterans have an affinity for social media; therefore, the VA should consider using social media to publicize the registry. Veterans service organizations should be involved in planning the outreach efforts for the launch of the national registry.

Utility of a National, Broad-based Registry for Veterans of Operation Iraqi Freedom and Operation Enduring Freedom

A registry could provide value to OIF/OEF veterans; however, the registry would have limited value for scientific analyses. Results of a voluntary registry for OIF/OEF veterans would not be useful for epidemiological research to determine the strength of association or causality. Veterans who would enroll in a registry would likely represent the most severe end of the disease spectrum. Therefore, considerable selection bias would be likely in the group of veterans who enroll. The VA has performed population-based studies that demonstrated that veterans who seek VA medical care have higher rates and severity of disease, higher rates of disability, higher rates of unemployment, and lower incomes, compared with veterans who do not seek VA care.[6] Healthy OIF/OEF veterans who are not concerned about their exposures would be much less likely to enroll in the registry. This selection bias was demonstrated in analyses of veterans who enrolled in the Gulf War Registry.[25] This means the types of diseases that are diagnosed in veterans enrolled in the registry could not be generalized to the entire population of 2.6 million veterans who have deployed to OIF and OEF. In addition, no estimate of the rates of diseases could be determined.

The registry results could not be used to determine the etiology of diseases. The registry would contain self-reported exposure data from a self-selected group of veterans that would lead to recall bias and selection bias. A registry would have some utility in hypothesis generation for design of future controlled studies. A population-based epidemiological study would be required to determine if there was a relationship between exposure to burn pits and the subsequent development of pulmonary diseases or other diseases. Appropriate population-based studies that address this issue are ongoing, including the Millennium Cohort Study and other longitudinal studies. These research studies use environmental data to classify individuals into more accurate exposure categories, and they use valid medical diagnoses and smoking histories to control for confounding factors.[9–13]

Although a voluntary registry for OIF/OEF veterans would have substantial scientific limitations, it could fulfill other needs. Veterans have benefited from previous VA registries in multiple ways.[25,26] A registry evaluation could provide OIF/OEF veterans with an opportunity to receive a high-quality medical evaluation and to address their health concerns. Informed healthcare providers could provide veterans with answers to their questions about long-term health effects related to deployments. Enrolling in such a registry would provide OIF/OEF veterans with a variety of benefits, including the following:

- Information about VA medical care and benefits for which they are eligible.
- Improved access to VA medical care without the need to establish a service connection for a disability. The VA would need to make it clear that a registry evaluation would not be a substitute for a Compensation and Pension Examination (ie, enrolling in the registry would not be the first step in applying for disability compensation).
- Recognition and validation from the VA that it takes veterans health conditions and exposure concerns seriously.
- The opportunity to provide feedback to the VA during their evaluations. In turn, the VA would gain insight on the veterans' perceptions and concerns. This would enable the VA to target its health education messages, which would be the highest priority to veterans in future VA communication efforts.
- Placement on an automatic mailing list. Veterans who enroll in the Agent Orange and Gulf War registries are placed on a mailing list and automatically receive periodic newsletters tailored to their concerns.[26] The VA could improve its communication with OIF/OEF veterans by establishing a similar mailing list and sending newsletters (via mail or email) highlighting issues of particular concern to OIF/OEF veterans.

The health surveillance data derived from the registry for OIF/OEF veterans should be shared with physicians and other healthcare providers on a periodic basis. These could be VA, DoD, and private healthcare providers. Results should be published as an internal report for VA clinicians and in the open medical literature. A summary of the results should be written in plain English and published on a VA website to communicate with veterans, active duty service members, family members, and Congress.

SUMMARY

This chapter described methodological issues related to development of two possible types of medical data collection: (1) a case series that is targeted to specific pulmonary diseases; and (2) a national, broad-based registry related to OIF and OEF deployment.

Individual cases of service members and veterans who developed various pulmonary diseases after returning from deployment to OIF and OEF have been reported. DoD and VA scientists have already developed multiple, small case series at different locations. The DoD and VA could build

on this small case series foundation to establish a shared, systematically collected case series of OIF/OEF veterans. This would require collaboration to develop a standardized medical evaluation of OIF/OEF veterans that would provide data that are comparable and could be combined. The DoD and VA could develop this as a consortium for sharing information on pulmonary cases among multiple medical centers. Patients who have pulmonary diseases should be followed over time and reevaluated, including after the transition of care from the DoD to the VA after military separation. The DoD and the VA could establish one or two coordinating centers that would collect, archive, and analyze the data. Combining data from multiple sites could yield adequate numbers of cases to analyze for patterns of pathology, disease progression, and possible risk factors during military service.

The VA maintains multiple, national registries related to specific deployments, including the Agent Orange and Gulf War registries. In January 2013, Congress mandated that the VA establish a registry for OIF/OEF veterans related to burn pit exposure. This chapter described general methodological issues related to the development of a broad-based registry, focusing on the discussion during the August 2012 symposium. The work group recommended that veterans could enroll in this type of broad-based registry regardless of their disease status. The only requirement for enrollment would be verification that the veteran was deployed. The registry would not be limited to individuals who have pulmonary diseases, because many veterans who have other types of diseases believe their health problems are from burn pit exposure. The VA would need to develop and adopt a standardized medical evaluation that would be recorded consistently to ensure comparability of results among the VAMCs nationally. Instead of developing a tailored medical evaluation for the registry, the VA might choose to use the standard electronic medical records for outpatient clinic visits and hospitalizations. The names of veterans who enrolled in the registry could be matched with the VA outpatient and inpatient databases to pull in the results of medical examinations from routine clinical care. A voluntary registry could provide value to OIF/OEF veterans; however, it would have substantial scientific limitations. It would not be useful for epidemiological research to determine the strength of association or causality. In contrast, a registry could fulfill the multiple needs of veterans. Participating in the registry could provide OIF/OEF veterans with an opportunity to receive a high-quality medical evaluation and address their health concerns. In addition, the registry could inform veterans about VA medical care and benefits for which they are eligible and be used to develop an OIF/OEF veterans' mailing list for future VA communications.

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