

Report to Congress on Traumatic Brain Injury in the United States:

Understanding the Public Health Problem among Current and Former Military Personnel

June 2013

The Report to Congress on Traumatic Brain Injury in the United States: Understanding the Public Health Problem among Current and Former Military Personnel is a publication of the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) in collaboration with the Department of Defense (DOD) and the Department of Veterans Affairs (VA).

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Suggested Citation: The CDC, NIH, DoD, and VA Leadership Panel. Report to Congress on Traumatic Brain Injury in the United States: Understanding the Public Health Problem among Current and Former Military Personnel. Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the Department of Defense (DoD), and the Department of Veterans Affairs (VA). 2013.

Dear Colleague:

Since the mid-2000s, public health and health care-communities have become aware of the increased rates of traumatic brain injury (TBI) among active duty U.S. military personnel. In response to these public health concerns, Congress passed the *Traumatic Brain Injury Act of 2008*, which requires the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH), in consultation with the Department of Defense (DoD) and the Department of Veterans Affairs (VA), to determine how best to improve the collection and dissemination of information on the incidence and the prevalence of TBI among persons who sustained these injuries while in the military; and to make recommendations on the manner in which CDC, NIH, DoD, and VA can collaborate further on the development and improvement of TBI diagnostic tools and treatments.

This report, *Traumatic Brain Injury in the United States: Understanding the Public Health Problem among Current and Former Military Personnel*, presents the major findings and recommendations of the members of the CDC, NIH, DoD, and VA Leadership Panel. These findings and recommendations are the product of a review of relevant scientific literature and a thorough examination of current TBI-related activities and programs conducted by the four agencies/departments. The report describes the public health importance of military service-related TBI, recommends how better to measure the magnitude of its medical and socio-economic impact, and suggests ways in which the four agencies/departments can collaborate further on the development and improvement of TBI-related diagnostic tools and treatments.

Incorporating the recommendations of this report into public health policy and public health and clinical practice will help our nation to address the full impact and long-term consequences of TBI, will inform the development of more effective primary prevention strategies and policies, diagnostic tools and therapeutic interventions, and will allow for improved rehabilitation and reintegration of military and civilian TBI survivors in the United States.

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Preface

Since the beginning of Operation Enduring Freedom (OEF) (Afghanistan) and Operation Iraqi Freedom (OIF), public health and health care-communities have become aware of the increased rates of traumatic brain injury (TBI) among active duty U.S. military personnel. Epidemiologic and clinical studies suggest that many of these military service-related injuries have serious long-term health and socioeconomic consequences.

In response to these public health and medical concerns, Congress passed the Traumatic Brain Injury Act of 2008 (*TBI Act of 2008*), which requires the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH), in consultation with the Department of Defense (DoD) and Department of Veterans Affairs (VA), to determine how best to improve the collection and dissemination of information on the incidence and prevalence of TBI among persons who were formerly in the military; and to make recommendations on the manner in which CDC, NIH, DoD, and VA can collaborate further on the development and improvement of TBI diagnostic tools and treatments. To that end, the CDC, NIH, DoD, and VA formed a Leadership Panel of experts with extensive experience in epidemiologic and clinical research, and in treating and managing TBI and its consequences.

This report presents the major findings and recommendations of the Leadership Panel and a review of relevant scientific literature and a thorough examination of current TBI-related activities and programs conducted by the four agencies/departments. It describes the public health importance of military service-related TBI, recommends how to measure the magnitude of the health and socioeconomic impact of TBI and suggests ways in which the four agencies/departments can collaborate further on the development and improvement of TBI diagnostic tools and treatments.

Goals of the Report

To respond to the mandate of the *TBI Act of 2008* and to accomplish the goals of this report, CDC, NIH, DoD, and VA formed a Leadership Panel comprising representatives from each of these four agencies/departments. These persons were researchers and investigators with extensive experience in TBI-related epidemiologic and clinical research and in treating and providing rehabilitation for TBI survivors. To prepare their respective contributions to the report, members of the panel reviewed all current TBI-related activities and programs conducted by the four agencies/departments and relevant scientific literature.

This report represents the culmination of the Leadership Panel's deliberations and summarizes findings and recommendations. By sharing the results of this effort, CDC, NIH, DoD and VA aim to:

- **Raise Awareness:** Describe the public health importance of TBI among people currently or formerly in the military;
- **Improve Surveillance:** Recommend how to better measure the magnitude and impact of this condition in this population and the country; and
- **Strengthen Collaboration:** Suggest how the four agencies/departments can collaborate further on the development and improvement of TBI-related diagnostic and prognostic tools, treatment, management, and rehabilitation.

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Executive Summary

Background and Key Findings

Traumatic brain injury (TBI) is one of the highest priorities in public health and medicine because of its magnitude, cost, and consequences (e.g., death and disability), and because it is often preventable. The Centers for Disease Control and Prevention's (CDC) National Center for Injury Prevention and Control (NCIPC) estimates that each year approximately 1.7 million civilians in the United States sustain a TBI. Of these TBI injuries, which can occur alone or in combination with other injuries, about 1.36 million are treated and released from emergency departments (EDs), 275,000 are hospitalized, and 52,000 die. However, not all of these ED visits, hospitalizations and deaths are attributable to TBI, but might be due to other co-occurring injuries. These data suggest that the majority of TBIs (approximately 80%; *Coronado, Thurman, Greenspan, and Weissman, 2009*) are mild. These figures might not reflect the true incidence of TBI because they do not include people who are treated in physicians' offices or outpatient facilities or those seeking medical care in non-civilian facilities (*Faul, Xu, Wald, and Coronado, 2010*).

TBI among U.S. military personnel is a critically important health concern for veterans of the current Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF); these operations comprise several subordinate operations in Afghanistan, Horn of Africa, Trans Sahara, Philippines, Kyrgyzstan, as well as earlier theaters of military operations. According to a Defense and Veterans Brain Injury Center (DVBIC) analysis of surveillance data released by the Department of Defense (DoD), 33,149 U.S. military personnel were diagnosed with a TBI in 2011 alone. This number includes service members (SMs) from the Army, Navy, Marine Corps, Air Force, and from the active duty and reserve components of the National Guard. (*U.S. Dept. of Defense: http://www.health.mil/Research/TBI_Numbers.aspx*). The U.S. Department of Veterans Affairs (VA) estimates that of the 771,874 veterans who sought care from a VA Medical Center from the start of OEF in October 1, 2001 to December 31, 2011, a total of 59,218 unique OEF and OIF veterans were evaluated or treated for a condition possibly related to a TBI (*U.S. Dept. of Veterans Affairs, 2012: <http://www.publichealth.va.gov/docs/epidemiology/healthcare-utilization-report-fy2012-qtr1.pdf>*).

In response to these public health and medical concerns, Congress reauthorized the Traumatic Brain Injury (TBI) Act of 1996 with the passage of the Traumatic Brain Injury (TBI) Act of 2008 (P.L. 110-206; U.S. GPO 2008), which requires CDC and the National Institutes of Health (NIH), in consultation with the Department of Defense and the Veteran's Administration, to

- Determine how best to improve the collection and dissemination of information on the incidence (rate at which new cases of a condition occur in the population) and the prevalence (proportion of a population at any given time that is experiencing the effects of a condition) of TBI among persons who were formerly in the military; and
- Make recommendations on the manner in which CDC, NIH, DoD, and VA can collaborate further on the development and improvement of TBI diagnostic tools and treatments.

This report responds to these mandates. It was developed through a collaborative effort of a Leadership Panel made up of representatives from the four participating agencies/departments and was reviewed, cleared, and approved by the participating agencies/departments. Members of this Leadership Panel were clinicians, researchers, investigators, and science administrators with extensive experience in epidemiologic and clinical research and in treating and managing persons with TBI.

Advances in TBI research in the past 30 years have created new opportunities for improved surveillance and for effective, acute and long-term medical care and rehabilitation; however, as detailed in this report, many important data and knowledge gaps persist. Several critical concerns and challenges related to the population of U.S. SMs who have sustained a TBI while in military service drive the recommendations included in this report. Although DoD and VA have made substantial progress in helping military personnel who have sustained a TBI, critical gaps remain in surveillance, epidemiology, clinical diagnosis, management, and rehabilitation, including a need to continue developing standard surveillance definitions, clinical definitions, and data collection methods as new knowledge and technology emerge. Some recent and current challenges include the following:

- The annual rate of TBI among active duty personnel increased substantially from 2000 to 2011. A majority of the increases occurred from 2006 through 2008 (*U.S. Department of Defense, unpublished data*).
- As is experienced in the general population, the actual rate of TBI among military personnel is potentially underestimated by existing TBI surveillance efforts. This is especially true for identification of personnel who have sustained a mild TBI.
- The total burden of TBI among current and former military personnel, including medical costs, rehabilitation costs and lost productivity/income, is difficult to determine from existing data sources.

- Evidence on the effectiveness of acute and post-acute treatment is limited. Although some guidelines and recommendations exist for the acute and post-acute treatment and rehabilitation of persons sustaining a TBI, they are generally derived from expert consensus or case series studies, as evidence-based scientific knowledge is sparse or is less than optimal to justify the strongest clinical recommendations.
- The influence of blast exposure on the risk for later developing neurodegenerative disorders is unknown.

Recommendations

The following general recommendations were developed in response to these concerns and to the questions posed in the *TBI Act of 2008*:

- **IMPROVE IDENTIFICATION:** Strengthen the identification of military service-related TBI among current military SMs and veterans, including those who do not seek care from the military or VA health-care systems. Emphasis will be given to improving data-collection initiatives and data sources to obtain a more comprehensive picture of the problem and impacts of TBI in this population. All four participating agencies should continue to foster and strengthen collaboration to this aim.
- **STANDARDIZE DEFINITIONS:** Use standard clinical and surveillance definitions and severity classification of TBI among U.S. military and civilian health-care providers and researchers to improve reporting. Update these definitions periodically as more precise, sensitive, and valid terms and definitions are available.
- **STANDARDIZE CLASSIFICATION:** Improve the coding and classification of TBI by working across agencies. All four participating agencies should continue to meet with professional, academic, health care, and coding organizations to discuss improvements in ICD-10-CM and TBI severity measures that can allow comparison of cases and outcomes.
- **ENHANCE DISSEMINATION:** Promote dissemination of information to non-VA facilities regarding TBI services available through the VA health-care system since 2007 including baseline screening and follow-up assessment and evaluation.
- **STRENGTHEN RESEARCH:** Continue research into the consequences of deployment-related TBI, including prospective investigation of the impact of single or multiple insults to the brain

and risk for cognitive decline or other health conditions later in life, which might occur among SMs and veterans. Share findings with civilian health-care providers.

- **FOLLOW EVIDENCE-BASED PREVENTION STRATEGIES:** Continue reducing risk factors, improving quality of protective equipment, and ensuring adherence to evidence-based strategies and guidelines.

Evidence indicates that TBI in the U.S. population, including among those who served in the military, is a public health problem, the magnitude and impact of which are underestimated by current civilian and military surveillance systems. Much research is needed to determine the full magnitude of TBI, identify preventable and modifiable risk factors, develop and test strategies to reduce TBIs in civilian and military life, and improve health and social outcomes and quality of life for those who sustain these injuries. Such research will inform the development of more effective primary prevention strategies and policies, diagnostic tools, and therapeutic interventions and will allow for improved rehabilitation and recovery of TBI survivors.

More details on each of the recommendations, including the rationale and potential benefits, can be found in this document. Imperative in planning for the future is recognizing that the public health and medical communities' understanding of TBI is evolving, with many gaps in knowledge for both military and civilian populations. This report offers recommendations for future TBI-related epidemiologic and clinical research; however, refinement and periodic review of the recommendations and their impact will be necessary.

I. Introduction

In response to public health concerns, Congress passed the *TBI Act of 2008* (*P.L. 110-206; U.S. Government Printing Office 2008*), requiring the Secretary of the U.S. Department of Health and Human Services (DHHS), acting through the Directors of CDC and NIH, in consultation with the Secretary of Defense and the Secretary of Veterans Affairs, to submit a report on TBI to the relevant committees of Congress. It will contain the findings derived from an evaluation of activities and procedures that can be implemented by CDC to improve the collection and dissemination of compatible epidemiologic studies on the incidence and prevalence of TBI in persons who were formerly in the military. This report addresses that mandate and, as requested by Congress, also includes recommendations on the manner in which CDC, NIH, DoD, and the VA can collaborate further on the development and improvement of TBI diagnostic tools and treatments.

Definition of TBI

TBI was recently defined by a consensus panel of experts “as an alteration in brain function, or other evidence of brain pathology, caused by an external force” (*Menon, Schwab, Wright, and Maas, 2010*).

TBI results from blunt or penetrating trauma to the head, or indirect acceleration and deceleration forces or blasts. These forces might temporarily or permanently disrupt the functioning of the brain. The extent and severity of a TBI after an initial mechanical event depends on many factors, including 1) the magnitude of direct or indirect forces applied to the head; 2) the direction of the force; and 3) the subsequent direction, duration and amplitude of angular accelerations to which the brain is subjected (*Gaetz M. 2004*). Other factors influencing the nature and severity of a TBI might include age, sex, body size and weight, comorbidities, alcohol use, genetics, and previous brain injuries, although the evidence on the specific positive or negative effects of each of these is limited. (*Förstl, Haass, Hemmer, Meyer, and Halle., 2010; Coronado et al., 2009; Moppett, 2007; León-Carrión, Dominguez-Morales, Barroso y Martin, and Murillo-Cabezas, 2005; D'Ambrosio and Perucca, 2004; Roof, Duvdevani, and Stein, 1993; Pelligrino, Santizo, Baughman, and Wang, 1998*). The use of protective gear can reduce the occurrence and severity of brain injuries.

The functional consequences of TBI range from transient, reversible alterations in brain function to profound disability or death. Recovery of neurologic functioning after TBI might or might not occur and varies in its time course from a few minutes to many years. More severe injuries require longer recovery periods. However, even in the case of mild TBI, a subset of persons develop post-concussion syndrome, a

syndrome characterized by headaches, depression, irritability, sleep disorder, poor concentration, and fatigue; various studies indicate that 38-80% of those with mild TBI may develop post-concussion syndrome (Hall, Hall, and Chapman, 2005). The effects of a prior TBI on the aging brain are not clear. Multiple severe concussive and sub-concussive injuries, like those reported in boxers who engaged in the sport for several years, are known to cause a delayed dementia syndrome (*dementia pugilistica* or chronic traumatic encephalopathy) (Zetterberg et al., 2006; Zetterberg et al., 2009; McKee et al., 2009; Gavett et al., 2011) that also might be evidenced by a Parkinson-like movement disorder. As described later in this report, case-controlled and cohort studies provide conflicting reports on whether a prior TBI is a risk factor for Alzheimer's disease (Van Den Heuvel C, Thornton, and Vink, 2007; Fleminger S, Oliver, Lovestone, Rabe-Hesketh, and Giora, 2003). Overall, the scope, complexity, and heterogeneity of TBI present challenges for developing precise, sensitive, and accurate diagnostic and prognostic tools and effective medical and other health-related (e.g., rehabilitation) interventions.

II. Pathophysiology and Mechanisms

TBIs can be classified in many ways (*Saatman et al., 2008*). For the purposes of this report, TBI is classified as follows: by physical cause, by functional severity, or by the physical changes associated with TBI. The initial impact to the brain in TBI might result in one or more direct effects. For example, a blow to the head from a fall can cause bleeding and bruising of the brain. The result of the initial impact often gives rise to a number of secondary effects that further worsen the severity of the injury.

Brain injuries also can be characterized as focal (localized) or diffuse (widespread); the localization of injury depends primarily on the initial mechanical trauma. The features of TBI include bleeding around the brain or between the brain and the skull, bruising to the brain that is either localized or diffuse. Other features include decreased blood flow to the brain or swelling of brain tissue, which can contribute to complex secondary outcomes. TBI is sometimes also discussed in the context of primary or immediate injury versus secondary or delayed injury. The physical cause of primary injury can be classified as closed, penetrating, or blast. Classification based on patterns and types of injury is essential for therapy development but is also challenging (*Marshall et al., 1992*).

Primary Injury

Primary injury occurs immediately and as direct result of mechanical trauma. Depending on the injury mechanism and severity, the initial event might cause direct or primary mechanical alterations of the brain tissue (e.g., widespread damage to the axons that provide support and structure to the brain, laceration of the brain, bleeding around the brain or between the brain and the skull, and bruising to the brain).

Autopsy studies following fatal TBI have reported large variability in primary and secondary injuries (*Adams, Mitchell, Graham, and Doyle, 1977; Bigler and Maxwell, 2011*). These types of injuries can occur alone or in combination and are often accompanied by other traumatic injuries to multiple organs or body parts.

Secondary Injury

Secondary brain injuries arise from complications initiated by the primary injury itself and via other mechanisms, including inflammation, cell receptor mediated dysfunction, free radical and oxidative damage, and calcium or other ion-mediated cell damage (*Graham, Gennarelli, and McIntosh, 2002*).

Primary mechanical changes are generally followed by several biologic processes that occur in the minutes to days following TBI (*Scalea, 2005; Gennarelli and Graham, 2005; Granacher RP, 2007*), resulting in secondary brain injuries that can include the build-up of excess fluid in the brain that gives

rise to elevated intracranial pressure (*Granacher, 2007; Porth, 2007; Sullivan et al, 2000; Sauaia et al., 1995*). In turn, these secondary processes modulate gene expression and/or protein regulation that lead either to cell death or repair (*Graham et al., 2002; Luukinen et al, 2005*). Researchers have pursued many of these processes as potential targets for therapies that might limit the extent and severity of injury after TBI.

As in other tissue injuries, an inflammatory reaction to TBI also can occur. Inflammation is involved in the repair of brain tissue after injury, but it can also contribute to secondary brain damage. Secondary injury also might result from other systemic events related to multiple injuries in other organs or body parts; for example, an overall drop in blood pressure might reduce the blood flow to the brain, which contributes to the severity and extent of the initial injury (*Scalea 2005*). Alterations in the regulation of brain blood flow also occur after TBI. Focal constriction of major brain arteries has recently been described after blast TBI (*Bell et al., 2009*). Such large artery vasospasm confined to a small area is considered unusual after non-blast TBI, although it also might be an underappreciated problem (*Shahlaie, Boggan, Latchaw, Ji, and Muizelaar, 2009*). Because the brain is enclosed in the non-expandable skull, brain swelling and hemorrhage added to the intracranial compartment can lead to distortion and compression of brain structures and to raised intracranial pressure (ICP). Elevated ICP after TBI can impede blood flow and thereby cause widespread lack of oxygen to the brain that can result in brain death (*Wijdicks, 1995*).

Focal and Diffuse Injury

TBI can present as a focal (localized) or diffuse (widespread) injury. Some patients may exhibit both focal and diffuse injuries. A focal injury results when bleeding, bruising or a penetrating injury is isolated to a portion of the brain. Focal injury causes neurologic deficits that are related to the functions that take place in the damaged region of the brain. Diffuse brain injury to the axons that connect brain structures is also common, as these “brain wires” provide the major mechanical support to brain tissue and are subject to damaging strain forces upon impact or rapid acceleration/deceleration. Though the neuropathology of blast injury in service members has not been studied systematically, animal studies demonstrate diffuse brain injury after blast trauma (*Cernak, 2005*). Diffuse brain injury also might occur from rapid acceleration and deceleration forces to the head, a common factor in motor vehicle crashes. The neurologic deficits caused by diffuse brain injury also can affect overall brain function.

Closed: Impact and Acceleration/Deceleration

Impact of the head against another object (*Adams, Victor, and Ropper, 1997*) can cause focal brain injury under the skull at the site of impact and sometimes at a site on the opposite side of the head, called contrecoup. These focal impact injuries, termed contusions, are prone to bleeding. Bleeding also can occur into other intracranial spaces, including the space that contains the cerebrospinal fluid that surrounds the brain (known as traumatic subarachnoid hemorrhage) and the space underneath the thick leathery dura that is attached to the undersurface of the skull (known as traumatic subdural hematoma). When a skull fracture disrupts arteries that lie over the dura, bleeding might occur between the dura and the skull (epidural hematomas). Intracranial bleeding can lead to death or permanent disability and might worsen over variable periods (minutes to days) post-TBI. Because the skull is a rigid structure and not expandable, the volume of blood that can be accommodated is limited before pressure inside the skull begins to rise and distortion of brain structures occurs. Evacuation of posttraumatic intracranial blood is one of the most common neurosurgical interventions after TBI (*Bullock et al 2006*).

The most common form of TBI is caused by a combination of impact and acceleration/deceleration forces, such as what occurs in high-speed motor vehicle crashes (*Kotapka et al., 1991; Adams, Graham, Murray, and Scott, 1982*). Acceleration/deceleration creates forces that can damage the brain even if no actual impact of the head against another object occurs, (although the latter is unusual and requires much higher forces; (*Duhaime, 2006*)). Impact combined with acceleration/deceleration injury causes shearing of the connecting fibers in the brain. After death, in brains viewed under a microscope, shearing is visible as disruption and focal swelling of the nerve axons. Visualizing shear injury on standard neuroimaging is difficult (*Hammond and Wasserman, 2002; Gold and Lipton, 2008*). New advanced magnetic resonance imaging (MRI) techniques, might improve imaging of brain lesions, especially those in the mild spectrum and help in the diagnosis of brain injuries. Because these technologies are continuously evolving, they must be refined and validated. (*Kirov et al., 2013*)

Penetrating Injury

Penetrating TBI occurs when an object enters the brain, whether a bullet, shrapnel, knife, bone fragment, or other material. Penetrating injury is focal because of the mechanical disruption of specific brain regions along the track of the object. However, injury also can occur further away from the object's track because of the transmission of kinetic energy from a high-speed projectile to the brain. Penetrating head injury causes a greater risk of posttraumatic seizures and epilepsy than closed head injury (*Temkin, 2009*).

Blast Injury

Blast injury is the result of pressure waves interacting with the body following exposure to a high-order explosion, that is, an explosive event where the blast pressure front moves rapidly, shattering objects in its path. Though studied in the past, blast injury is subject to more intensive scrutiny since the onset of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF). The blast environment presents a high risk for penetrating TBI related to shrapnel and forces that cause rapid head movement or impact against other objects, resulting in shear injury or contusion, respectively. Current evidence from animal studies suggests that brain injury can occur as a result of blast pressure waves—even if the wave is directed at the chest (*Courtney and Courtney, 2009*). Whether lung injury itself contributes to brain injury, or whether the structures of the chest participate in transmitting the blast forces to the brain, is not definitively known. For this reason, body armor might offer some brain protection. Although helmets protect the brain from penetrating injury, skull fracture, and contusion, they might not dampen a blast wave and injury may still occur.

The details of how a blast wave causes brain damage are still poorly defined; standard neuroimaging is generally unrevealing. Major questions remain, including the following: What levels of a single blast intensity or distance from the blast are tolerated without permanent injury? Do repeated prior exposures to blast increase vulnerability? Are any longer term-consequences to blast exposure evident? A major gap in understanding is caused by the lack of information about the pathology of blast injury in humans, which is related to limited research on post-mortem brains. In addition, because of the combination of different mechanisms of TBI in the blast area, differentiating the primary blast pathology from those caused by blunt injury, penetrating objects, or shear injury is difficult. Moreover, biological processes that occur as a result of primary and secondary injuries of any external cause, including blast-related TBIs, are not well understood.

Preliminary data suggest that major differences in symptom etiology and pathophysiology are evident between SMs with blast-related closed TBI and non-blast closed TBI (*Moore et al., 2009; Hoffer, Donaldson, Gottshall, Balaban, and Balough, 2009; Hoffer et al 2010*). Scientists have used a brain-imaging technique called diffuse tensor imaging (DTI) to identify the effects of different injury mechanisms. A DTI study comparing blast and non-blast injury determined that blast injuries resulted in more diffuse damage than non-blast injuries. Blast injuries, but not non-blast injuries, were associated with changes in blood flow or structural brain abnormalities (*Moore, 2009; Huang et al., 2009*). In Landstuhl Regional Medical Center, an MRI study of military personnel with a mild TBI diagnosis after exposure to blast demonstrated subtle abnormalities on diffusion imaging in a subset of patients (18/63)

(MacDonald et al.,2011). Single photon emission CT (SPECT) and positron emission tomography (PET) both demonstrate hypoperfusion (decreased blood flow through an organ) of the frontal lobes, possibly explaining many of the cognitive and behavioral symptoms associated with mild TBI (Nakayama, Okumura, Shinoda, Nakashima, and Iwama, 2006; Gowda et al., 2006).

Research Relevant to Active Duty Personnel and Veterans

Research collaborations among the four participating agencies (CDC, NIH, DoD, VA) is a fundamental starting point to solving the various problems associated with TBI. Current research is the foundation on which further endeavors can build consensus and effort.

Several clinical trials have attempted to slow secondary processes that contribute to additional damage following TBI. Despite potent neuroprotection of certain chemical compounds in rodent models of head injury , no strategy has so far succeeded in humans. Scientists continue to attempt developing an effective neuroprotective treatment to be administered within hours of the initial trauma to improve patient outcome, including a recently launched multi-center study of progesterone, a treatment modality that demonstrated promise in animal models (*U.S. National Institutes of Health, 2012*). NIH also funds research examining brain recovery after injury. In a collaborative effort, NIH and DoD have established the Federal Interagency TBI Research (FITBIR) Informatics database to facilitate comparison among studies and enhance comparative effectiveness research in TBI.

Studies have found that approximately one-third of SMs with mild TBI also have PTSD (Hoge et al, 2008; Brenner et al, 2009). Because of the overlap in symptoms and this common co-occurrence of PTSD and TBI in SMs, studies related to hormonal differences and imaging findings between PTSD and TBI are ongoing. In the interim, several programs, including those at Fort Campbell, Landstuhl Regional Medical Center, Waco Veterans Affairs Medical Center (VAMC), National Intrepid Center of Excellence in Bethesda, and Cincinnati VAMC have developed programs to treat both mild TBI and PTSD simultaneously.

Without published reports of blast neuropathology in soldiers, scientists are unable to compare what they find in animal models to what is actually happening in persons who have suffered from TBI. To help build pathology data, DoD and others have begun postmortem tissue banks. DoD has developed the TBI Brain Bank through the Armed Forces Institute of Pathology (AFIP), with support from DVBIC, where appropriate patient data and brain specimens of deceased SMs can be archived for further clinical and pathological studies. Officially begun in 2009, this DoD program has the potential to be used for the congressionally mandated 15-year longitudinal study of returnees and veterans of OIF and OEF. Study

participants will be invited to consider post-mortem donation of their brains to the DoD TBI Brain Bank as a secondary study arm. In comparison with severe TBI, much less is known about the pathoanatomical or pathophysiological alterations that are produced by mild or concussive injuries, because only in rare cases are these injuries fatal and standard neuroimaging is unrevealing. There may be other opportunities for sharing brain bank resources across agencies to further advance the state of the science.

Research Programs Related to Active Duty Personnel

In the last decade, much work was done to elucidate problems associated with military service-related TBI. A primary focus has been on understanding blast injury (*Lee et al., 2011; MacDonald et al., 2011*) primarily because of the high rate of TBI and blast-related concussion events resulting from combat operations and the limited knowledge about the blast effects on the central nervous system. These blast-related injuries directly affect the health and safety of individual SMs and thereby also affect the level of unit readiness and troop retention (*Defense and Veterans Brain Injury Center [DVBIC], 2012: <http://www.dvbic.org/about/tbi-military>*). In response, on July 5, 2006, DoD issued DoD Directive 6025.21E "Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries" in compliance with Section 256 of Public Law 109–163 (*U.S. Dept. of Defense, 2006*).

This DoD Directive formally established the DoD Blast Injury Research Program that coordinates and manages the medical-research activities and programs of DoD relating to the prevention, mitigation, and treatment of blast injuries. Through this program, increased funding has been made available for projects that will help identify effects of blast on the brain, mitigate risks, and develop diagnostics and interventions to mitigate brain damage and promote recovery. Through a series of delegations of authority, the United States Army Medical Research and Materiel Command (USAMRMC), a subordinate command of the U.S. Army Medical Command (USAMEDCOM), was selected to carry out the Program's day-to-day coordination and management activities because of its unique position and expertise as the Army's total life cycle medical research, development, acquisition, procurement, and logistical support command (*U.S. Dept. of Defense, 2011: <https://blastinjuryresearch.amedd.army.mil/index.cfm?f=application.introduction>*). Under this research program, studies using advanced imaging techniques have demonstrated that structural pathology associated with persistent symptoms in those with blast-related TBI might be evident (*Peskind et al., 2011; Matthews et al., 2011*). The Blast Injury Research Program is focused on filling gaps in the blast-injury knowledge base. Key research topics by program area, for example, include the following:

- **Acute Treatment:** In this area, DoD is working to
 - Develop diagnostics and neuroprotective drugs for TBI.

- Develop hemorrhage control and blood products.
- Develop treatments for psychological trauma.
- **Reset** (a term used in the military to describe a concept that extends beyond rehabilitation to include all activities necessary to return injured SMs to duty or to productive civilian life). In this area, DoD is working to
 - Advance tissue engineering and prosthetics.
 - Improve recovery of physical and mental functioning.
 - Develop return-to-duty standards.

Studies examining the effects of blast injuries are ongoing. Preliminary data suggest that major differences exist in pathophysiology between service members with blast-related TBI and blunt TBI (*Moore et al., 2009*). In a DTI study comparing blast and blunt injury, blast injuries revealed a more diffuse pattern than blunt injuries (*Moore, 2009; Huang et al., 2009*). Blast injuries were associated with abnormalities in the apparent diffusion coefficient, a measure of the movement of water through cell membranes and other parts of the brain, not seen in blunt injuries.

The Breacher Injury Study, conducted by the Defense Advanced Research Projects Agency and the Office of Naval Research (*Applied Research Associates, 2009; Combating Terrorism Technical Support Office, 2008*) examines the physiological effects or the risks of cognitive impairment as a result of repeated, low-level blast exposures. This is the first prospective study with humans to quantify blast-related TBIs. Aspects of this study were conducted in Breacher trainees (personnel trained to use explosives to gain rapid entry into a facility) from the U.S. Marine Corps' Weapons Training Battalion Dynamic Entry School. The study determined that the trainees did not demonstrate any negative effects due to the exposure. However, the trainers who had greater accumulated exposure over time experienced subtle, reversible cognitive changes after training practices. As a result, the Technical Support Working Group (TSWG) recommended various mitigation measures. The personnel-borne data-acquisition systems used in this study were miniaturized, enabling instrumentation of each Breacher during breaching events. Results of this study are being used to direct future research into protective gear for Breachers (*Applied Research Associates, 2009; Combating Terrorism Technical Support Office, 2008*), and findings can be extrapolated to other branches of the U.S. military to prevent injuries. Understanding the effects of the levels of exposure to blasts on the brain might help to improve surveillance by allowing a better diagnosis and case ascertainment, especially in patients with mild TBIs. Findings from efforts like the Breacher Injury Study might result in better follow up, rehabilitation, and provision of services.

Research Programs Related to Veterans

VA has undertaken various activities to understand better the impact of TBI among veterans. Some of the most persistent and disabling consequences include the ability to select and retain goal-relevant information and to use it for decision-making and goal management in daily life (Ry, Cullen, and Bayley, 2010)—skills that persons without TBI take for granted. Common symptoms of these deficits are being easily distracted, and difficulty with concentration, organization, prioritization, and planning. The VA sponsored two special issues of the *Journal of Rehabilitation Research and Development* that focused on TBI and polytrauma in the veteran population (Department of Veterans Affairs [VA], 2007 & 2009). PTSD, auditory, visual, motor impairment, balance, and other clinical concerns were featured, along with polytrauma, rehabilitation, telemedicine for TBI, and research opportunities. More recently, investigators identified a strong relationship between PTSD and post-concussive syndrome (PCS) and determined that evaluation of both factors is important in clinical management (Benge, Pastorek, and Thornton, 2009). VA researchers are focused on a number of veteran-centric TBI research projects that can be searched through the NIH RePORTER system at <http://projectreporter.nih.gov/> (enter “TBI” in the *Text Search* field and select VA in the *Agency/Institute/Center* field and submit query). Selected relevant publications include the following:

- Evaluation of DTI, Magneto Encephalography (MEG), and Computed Tomography (CT) scans to detect mild TBI indicated that MEG might be more sensitive than DTI and CT scans (Huang *et al.*, 2009).
- A study on visual impairment and dysfunction in SM TBI cases suggests that combat troops exposed to a blast with a mild TBI are at increased risk for visual dysfunction such as blurred vision, difficulty reading or squinting (Brahm *et al.*, 2009).
- A randomized trial comparing cognitive and functional rehabilitation approaches documented better short-term cognitive performance among participants receiving cognitive treatment (Vanderploeg *et al.*, 2008).

III. Diagnosis

Screening for symptoms possibly associated with TBI involves a quick evaluation of possible exposure to an injury event to determine if an alteration of consciousness (AOC) was evident, if it was associated with the event, or if the event resulted in any neurologic changes or symptoms (*Department of Defense, 2007*). The majority of cases of TBI in the U.S. military are mild TBI and although mild TBIs are often difficult to detect, TBI in persons with multiple trauma—major injuries to the chest, abdomen, pelvis, or extremities—also might be overlooked as other more life-threatening injuries are addressed. Positive TBI screening results should be followed up with a comprehensive evaluation from which a diagnosis is made. This comprehensive TBI evaluation should include identifying the external cause of the patient’s injury, assessment for neurobehavioral symptoms, a targeted physical examination, and a follow-up treatment plan.

Pre-Deployment Neurocognitive Baseline Testing

On May 28, 2008, the Assistant Secretary of Defense for Health Affairs (ASD/HA) issued an interim policy letter calling for the Services to “begin implementing baseline pre-deployment neurocognitive assessments for deploying SMs.” The DVBIC was designated the Office of Responsibility for this DoD program known as the Neurocognitive Assessment Tool (NCAT) Program. ASD/HA selected the Automated Neuro-psychological Assessment Metric (ANAM) as the neurocognitive assessment tool; this instrument allows acquiring a baseline assessment of cognitive performance areas most likely affected by mild TBI, including attention, judgment, and memory.

Baseline pre-deployment neurocognitive assessments are administered to all SMs 4–6 months before deployment and sequenced with the pre-deployment training plan (PTP). This sequencing allows the respective commander and command surgeon the timely opportunity to evaluate SMs who might screen positive. This window also provides the greatest opportunity for the unit’s medical assets to evaluate, re-evaluate, refer, and begin a medical regimen based upon local treatment protocols. This timeliness allows commanders and medical treatment facilities the opportunity to better manage manpower resources to meet mission requirements.

The goal of this pre-deployment testing is to have the capability to compare assessment results before and after an SM is exposed to a blast event, to improve the detection and treatment of mild TBI. This practice will ultimately affect return-to-duty decisions. From June 2007 through March 2012, 743,309 SMs (35.3% of all who deployed during that period) had completed pre-deployment baseline cognitive testing.

The NCAT is used in conjunction with clinical practice guidelines for managing concussion in deployed and non-deployed settings.

The pre-deployment testing program also includes a self-report historical questionnaire screen to determine if TBI or concussion occurred in the past. If an affirmative answer is given in the initial question, additional information is sought regarding loss of consciousness or alteration in consciousness and post-concussive symptoms immediately following the injury and experienced in the 2-year period before testing. The presence of this self-report historical screen and modules other than cognitive evaluation on pre-deployment testing are under review by the Defense Health Board.

In-Theater Screening

In-theater screening occurs immediately following an injury event or as soon as operationally feasible, using the Military Acute Concussion Evaluation (MACE) developed by DVBIC in 2006 (*McCrea, Jaffee, Guskiewicz, and Doncevic, 2009*). MACE allows medics, corpsmen and frontline providers to assess quickly the history of what happened during the event, current symptoms that the SM might experience, a focused neurological exam, and measurement of four cognitive domains: orientation, immediate memory, concentration, and memory recall. The cognitive exam is the Standardized Assessment of Concussion (*McCrea, Kelly, and Randolph, 2000*), which is commonly used as a sideline assessment of sports-related TBI. When combined with other clinical information, this tool helps reveal the presence of any red flags that should prompt an immediate referral because of concerns of a more severe brain injury or to further evaluation and treatment. The currently deployed MACE has been revised substantially (May 2012) and has been validated in combat environments.

In terms of clinical care, before 2010, screening was customarily self-initiated by SMs with potential injury. As a result of an evaluation of in-theater TBI care by both medical and line leadership, concerns were addressed regarding whether this process likely under-evaluated many of those at risk.

Subsequently, policy changes now require that every deployed SM involved in a traumatic event, such as motor vehicle collision, and/or within 50 meters of a blast, undergo mandatory medical screening and a 24-hour period of rest (*Department of Defense Instruction 6490.11, 2012*). This practice ensures that all SMs who are involved in a potentially concussive event are screened in a timely fashion to promote early detection of concussion, which will lead to prompt treatment.

SMs with injuries or medical conditions that require evacuation from theater to Landstuhl Regional Medical Center (LRMC) in Germany undergo further evaluation, including screening for concussion or mild TBI using MACE. This process also identifies any history of prior combat or non-combat TBI and

assesses for the presence of concussion or mild TBI-related signs and symptoms. Patients with ongoing symptoms are triaged to a stateside medical facility for further evaluation and, if necessary, treatment.

Post-Deployment

Because concussion or mild TBI is not always recognized in theater, screening also occurs through post-deployment health assessments (PDHA). Four questions, adapted from the Brief TBI Survey (BTBIS) (*Schwab et al., 2007*), currently appear on the PDHA; positive responses to all four questions prompt a clinical interview to evaluate fully for mild TBI. Although this criterion is more specific than the DoD definition (positive response to questions 1 and 2 only), it allows identification of those with ongoing symptoms who are likely in need of medical services. The Institute of Medicine (IOM) recommended continued use of MACE and BTBIS for screening of combat-related TBI (*Institute of Medicine, 2008*). Some military treatment facilities perform additional screening. For example, Ft. Carson uses the Warrior Administered Retrospective Casualty Assessment Tool (WARCAT) to fully assess possible injuries (*Terrio et al., 2009*).

VA Clinical Screening and Diagnosis Tools

Since April 14, 2007, all VA health-care facilities screen all veterans from OEF/OIF for possible TBI upon initial contact with the VA health system (*England and Mansfield, 2008; U.S. Dept. of Veterans Affairs VHA Directive 2007-013*). Those who screen positive are referred for follow-up evaluations that include a history of the veteran's injury, a physical examination targeted to the veteran's symptoms, and administration of the 22-item Neurobehavioral Symptom Inventory, an inventory that has been adapted by the VA for use in their Comprehensive TBI Evaluation. Veterans Health Administration (VHA) staff received training in administering the screening tool and follow-up evaluation, and the computerized medical record system was modified to include a TBI screening clinical reminder that 1) identifies who needs screening, 2) presents the screening tool to the provider, and 3) enters results into progress notes and into the electronic health record. VA policy requires that a veteran who screens positive be offered a follow-up evaluation with a specialty provider who can determine whether the patient has a TBI and then develop a treatment plan. The evaluation process includes a standardized evaluation template of common problems following brain injury, including a complete TBI-specific eye examination (*Schwab et al., 2007*).

Civilian Clinical Screening and Diagnosis Tools

The clinical diagnosis of acute TBI in the civilian population is usually based on a history of multiple signs and symptoms, including acute alterations in alertness or consciousness or memory problems that occur immediately after the event. If the traumatic event is witnessed, confirmation of a change in consciousness by an observer (in the context of the mechanical injury) makes the diagnosis.

Unconsciousness is usually easy to identify, except if brief, whereas alterations in consciousness might require confirmation through an interview conducted by a medical expert. Most often the witnesses note abnormal behavior, such as disorientation for place or time, poor ability to attend or make new memories, or impaired balance and gait. Sports coaches use standardized tests applied shortly after the injury to diagnose less marked alteration in consciousness in athletes (*Lovell, 2009*).

In moderate and severe TBI, memory impairment during the period of depressed consciousness results in retrograde amnesia, lack of memory extending back in time, and impaired memory for details of the injury itself and extending for some time after the injury or anterograde amnesia (*Sigurdardottir Sigurdardottir, Andelic, Roe, and Schanke, 2009*). If unwitnessed, the clinical diagnosis of TBI can be made in the context of a mechanical event involving the head (scalp wound, hematoma, skull fracture, blood behind the tympanic membrane of the ear, or other evidence of a head injury) in someone who has amnesia for the time around the event. Persons with isolated head trauma with minimal alteration in consciousness might not seek medical attention, making unbiased ascertainment of these cases of mild TBI challenging.

Diagnosis is further complicated by other conditions that might cause alteration or loss in consciousness. Alcohol or drug intoxication, hypoglycemia, cardiac arrhythmia, stroke, and seizures can cause rapid change in consciousness and might contribute to falls and other mechanisms of injury that can result in TBI. Although alcohol can contribute to these injuries, including TBIs, the effect of its role after a TBI has occurred is unclear. A study of 38,019 patients with moderate to severe head injuries documented that patients who tested positive for alcohol were less likely to die than patients who had no alcohol in their bloodstream. These patients had more medical complications during their hospital stay and were younger and had less severe injuries (*Salim et al., 2009*). Additional research indicated that high admission blood-alcohol level in patients with isolated moderate to severe TBI was independently associated with improved survival (*Berry et al. 2010; Berry et al., 2011*). These findings suggest that additional research is needed to investigate the potential therapeutic use of alcohol in the management of TBI (*Salim et al., 2009; Berry et al. 2010; Berry et al., 2011*).

The diagnosis of TBI is usually made clinically, and no well-accepted diagnostic tests (e.g., biomarkers or imaging) are available for use in standard medical practice to diagnose mild and even some moderate TBI. However, neuroimaging is commonly used to detect bleeding inside the skull in persons with TBI because posttraumatic bleeding is associated with worse prognosis and can be life threatening. On occasion, such evidence of TBI is discovered on neuroimaging in persons in which the clinical suspicion of TBI was low. Although not all neuroimaging modalities are able to identify all TBIs, some techniques, for example MRI, are better able to identify patients with some potentially critical injuries such as diffuse axonal injury (DAI) (*Belanger, Vanderploeg, Curtiss, and Warden, 2007; Levine et al., 2006*).

Clinical Presentation/Symptoms

Diagnosis of acute TBI is based on several criteria, including history of the event, clinical and functional assessment, and CT scanning and other neuroimaging. Some of the pathoanatomical features of TBI can be diagnosed with neuroimaging. However, standard neuroimaging does not enable comprehensive quantitative assessment of the brain injury, so a substantial discrepancy between the degree of clinical impairment and the degree of injury is often seen on neuroimaging. This is a major clinical concern, especially when trying to understand the neurological mechanisms associated with PCS. Major research advances in neurotraumaproteomics (a study of protein complexes that make up the nervous system) have identified several candidate markers that are under evaluation as TBI biomarkers. Early research has uncovered several candidates that have shown some preclinical potential; these include lactate dehydrogenase (LDH), glial fibrillary acid protein (GFAP), neuron specific enolase (NSE), and S-100 β . Unfortunately these proteins lack either the necessary sensitivity or brain specificity or both to be used effectively alone (*Pineda, Wang, and Hayes. 2004; Pelsers, Hermens, and Glatz, 2005; Ingebrigtsen and Romner, 2003; Bandyopadhyay, Hennes, Gorelick, Wells, and Walsh-Kelly, 2005; Siman et al., 2004*). More recently, new candidate biomarkers have been discovered; these include: UCH-L1, MAP-2, and TAU proteins (*Kobeissy et al., 2006; Zmlan et al., 1999; Folkerts, Berman, Muizelaar, and Rafols, 1998*), and the II-spectrin protein breakdown products (SBDPs) (*Pike et al., 2004; Pike et al., 2001; Pike et al., 2000; Ringger et al., 2004; Pineda et al., 2007*). These findings highlight the need for biomarker development and validation.

Clinical signs and symptoms can occur alone or in combinations and might result in functional impairment. These signs and symptoms appear to be independent of pre-existing conditions except in cases of exacerbation of pre-existing conditions. They usually can be defined by one or more of the three following categories:

Physical: headache, nausea, vomiting, dizziness, blurred vision, sleep disturbance, weakness, paralysis, sensory loss, spasticity, disorders of speech or language, swallowing disorders, balance disorders, disorders of coordination, seizure disorder;

Cognitive: attention, concentration, memory, speed of processing, new learning, planning, reasoning, judgment, executive control, self-awareness, language, abstract thinking;

Behavioral/emotional: depression, anxiety, agitation, irritability, impulsivity, aggression and violence, acting out, noncompliance, social inappropriateness, emotional outbursts, childish behavior, impaired self-control, impaired self-awareness, inability to take responsibility or accept criticism, or alcohol or drug abuse/addiction. Additional neuropsychiatric problems associated with TBI include apathy, paranoia, confusion, frustration, agitation, sleep problems, or mood swings (*American Psychiatric Association 2000*).

The signs and symptoms listed above are typical of each category but are not an exhaustive list of all possible signs and symptoms.

Severity

TBI is often characterized by severity that is usually based on various clinical factors, including duration or length of LOC, coma scaling, or imaging. Clinicians and investigators have classified TBI as mild, moderate, or severe by scores on the Glasgow Coma Scale (GCS), a widely used scoring system to assess coma and impaired consciousness (*Teasdale and Jennett, 1974; Rimel, Giordani, Barth, Boll, and Jane, 1981; Rimel, Giordani, Barth, and Jane, 1982*). The GCS is an algebraic scale consisting of three components: eye opening, verbal response, and motor response (Table 1). Patients with scores of 8 or less are classified as “severe”; scores of 9 to 12 are “moderate”; and scores of 13 to 15 are “mild” (*National Center for Injury Prevention and Control 2003*).

Ability	Score
Eye Opening (E)	
Spontaneous	4
To voice	3
To pain	2
None	1
Motor Response (M)	
Normal	6
Localized to pain	5

Withdraws to pain	4
Flexion-abnormal (<i>an abnormal posture that can include rigidity, clenched fists, legs held straight out, and arms bent inward toward the body with the wrists and fingers bent and held on the chest</i>)	3
Extension (<i>an abnormal posture that can include rigidity, arms and legs held straight out, toes pointed downward, head and neck arched backwards</i>)	2
None	1
Verbal Response (V)	
Normal conversation	5
Disoriented conversation	4
Words, but not coherent	3
No words, only sounds	2
None	1
Score: Eye Score (E) + Motor Score (M) + Verbal Score (V)= 3 to 15	
Teasdale & Jennett, 1974	

Although not intended or designed as a severity classification, the LOC duration is often used as an approximation of TBI severity by certain users, including CDC. In addition to brief LOC, mild TBI also might be characterized by confusion or disorientation or loss of memory for events immediately before or after the injury. In contrast, more severe TBI is associated with extended periods of unconsciousness of more than 30 minutes, or prolonged post-traumatic amnesia of more than 24 hours. Although the distinction between mild TBI and more severe TBI seems straightforward, establishing definitive, measurable criteria to identify and quantify the occurrence of mild TBI is challenging because clinicians and investigators have been using different diagnostic criteria and methodologies to study this condition (*Ruff and Jurica, 1999; American Congress of Rehabilitation Medicine, 1993; National Center for Injury Prevention and Control, 2003*).

The DoD and VA classify severity for non-penetrating TBI (Table 2) as mild TBI if the length of time of LOC was 0 to 30 minutes, provided that the patient does not have a clinical or imaging diagnosis indicative of more severe TBI (e.g., a patient with an abnormal imaging who had a LOC of 5 seconds). This LOC-related criterion for mild TBI is consistent with the corresponding CDC criterion and ICD-9-CM classification for concussion (850 series) (*National Center for Injury Prevention and Control, 2003*). DoD and VA also classify TBI as a moderate TBI if the patient has a LOC greater than 30 minutes and less than 24 hours; and severe TBI if the patient has a LOC greater than 24 hours. If a patient meets criteria in more than one severity category, the higher severity level of severity is assigned. CDC concurs with DoD and VA criteria.

Current DoD surveillance methods capture penetrating injury as a separate category, regardless of injury severity because this injury pattern might have more substantial long-term consequences than non-penetrating injury. TBI severity for non-penetrating injuries was determined using standard DoD/VA severity algorithms.

If not clinically possible to determine the brain injury level of severity because of medical complications (e.g., medically induced coma), other severity markers are required to determine the severity of the brain injury. For example, one or more of the following may be useful: imaging studies; monitoring intracranial pressure; electroencephalography that may demonstrate absence of electrical brain activity; and, transcranial doppler that may detect the absence of blood flow in the brain.

Table 2. DoD/VA Severity Stratification for Non-penetrating TBI

	Mild	Moderate	Severe
Structure Imaging	Normal	Normal or abnormal	Normal or abnormal
Length of Time of Loss of Consciousness	0-30 mins	>30 mins and < 24 hours	> 24 hrs
Alternation of Consciousness/Mental State	A moment up to 24 hrs	>24 hrs Severity based on other criteria	
Post-Traumatic Amnesia	0-1 day	>1 and <7 days	> 7 days
Glasgow Coma Scale*	13-15	9-12	3-8

*For purposes of injury stratification, the Glasgow Coma Scale (GCS) is measured at or after 24 hours (*Malec et al. 2007; Esselman and Uomoto 1995; American Congress of Rehabilitation Medicine, 1993; Saatman et al. 2008; Model System*).

Source: Department of Defense and Department of Veterans Affairs.

Note: Although the initial severity level might have some prognostic value, it does not necessarily reflect the patient's ultimate level of functioning. This requires serial assessments of the patient's cognitive, emotional, behavioral, and social functioning.

IV. Treatment

Various TBI-related activities are being pursued in the areas of medical care, research, and interagency collaboration.

Persons with isolated mild TBI are usually treated and released from emergency departments. These patients might receive guidance upon discharge regarding when to seek medical care if symptoms persist or worsen and when to return to work, school or sports play (*CDC Heads Up to Clinicians available at <http://www.cdc.gov/concussion/clinician.html>*). In contrast, TBI survivors with moderate to severe injuries are likely to receive treatment in intensive care units and neurosurgical units (*U.S. National Institutes of Health, February 2002*). Treatment depends on the recovery stage of the patient and other factors (e.g., concurrent injuries, comorbid conditions). In the acute stage, the primary aim is to stabilize the patient and to prevent secondary injuries (*U.S. National Institutes of Health February, 2002*). Rehabilitation is the primary treatment for the sub-acute and chronic stages of recovery (*U.S. National Institutes of Health, February 2002*).

Acute Care

TBI care in the Military Health Service (MHS) varies by TBI severity, interval from injury to presentation, and physical location where the injury occurs. In 2005, the Brain Trauma Foundation (BTF), in collaboration with DVBIC and the Uniformed Services University of the Health Sciences (USUHS), published the *Guidelines for the Field Management of Combat-related Head Trauma* (*Knuth et al., 2005*). These guidelines relied on extrapolated data from civilian trauma settings and recognized that tactical operations might alter the care that is provided in the combat setting. A decision-tree included in the document gives frontline providers triage decision-making assistance.

Severe and penetrating TBIs are recognized and triaged at the time of injury. Acute care for conditions such as intracranial pressure management, nutrition, and general critical care are consistent with civilian best practices (*Bullock and Povlishock, 2007*). DVBIC, in conjunction with the American Association of Neuroscience Nurses, supported recommendations for the Nursing Care of Patients with Severe TBI (*Mcilvoy and Meyer 2008*). Military data suggest that patients with combat-related severe and penetrating TBI are at higher risk than patients with less severe or non-penetrating injuries for the development of cerebral vasospasm and vascular injury (*Armonda et al., 2006*).

To assist with management of acute injury in theater, civilian and military experts developed clinical practice guidelines, Evaluation and Management of Mild TBI/Concussion in the Deployed Setting

(*Defense and Veterans Brain Injury Center, 2008*). These guidelines incorporate consideration of the limited resources available in an austere environment, and the co-morbid psychological health (PH) conditions that might be present. The Guidelines provide indications for urgent CT scanning, strategies for symptom management, and instructions for return to duty evaluations. In most cases, patients with mild TBI can be evaluated and treated at the Forward Operating Base for up to 7 days, or up to 30 days at more sophisticated recovery centers.

In late 2009, Concussion Care Centers were established in Afghanistan to provide supervised rest, education, treatment, and recovery for SMs with concussion. Using this model of primary care decreases the stigma of TBI care, any association with PH, and the development of perceptions of chronic illness. For patients not improving in primary care, specialty referrals and management in a dedicated TBI clinic are indicated. Neurocognitive testing done in theater can be compared with the patient's baseline, thereby better informing return to duty decisions. Since 2010, current DoD guidelines have mandated that deployed service members who are in specific, potentially concussive events will undergo standardized evaluation with MACE, which avoids reliance on self-reporting and broadens in-theater screening from symptom-based to incident-based and includes recommendations for a more detailed evaluation of those sustaining recurrent concussions.

To advance care with best practices, a VA/DoD evidence-based workgroup performed a rigorous literature review and developed a Clinical Practice Guideline for the Management of Concussion/Mild TBI (*Defense and Veterans Brain Injury Center & Defense Centers of Excellence, 2008*). These guidelines focus on the management of those with sub-acute to chronic injury and include an educational component regarding the natural history of concussion and the expectation of recovery.

Clinical and surgical guidelines have been proposed to guide decisions in TBI treatment, as defined by an authoritative examination of current evidence (*Maas, Stocchetti, and Bullock, 2008; Brain Trauma Foundation, 2011*). Surgical interventions, such as those for subdural and epidural hematomas, are effective (*Bullock et al., 2006*). Although some consistency is evident in the clinical management of patients with moderate or severe TBI, which is based upon the best available evidence, few of these management guidelines are based on large, well-controlled clinical trials (*Maas et al., 2012*). Difficulty in conducting rigorous studies arises because the pathophysiology of TBI is complex and the disruption in brain function rarely occurs in isolation. Additionally, heterogeneity in neuropathology occurs from person to person (*Jennett, Adams, Murray, and Graham, 2001; Adams, Graham, and Jennett, 2001; Maxwell et al., 2004*). For example, despite success in preclinical or smaller clinical studies, more than 20 drugs or other therapies for moderate or severe TBI have not demonstrated a positive effect on outcome in

large, multi-center phase III clinical trials. Numerous explanations for explaining this discordance exist, but the heterogeneity of the patient population is one of the most noteworthy contributing factors (Narayan *et al.*, 2002; Saatman *et al.*, 2008). Therefore, nearly all of the treatment guidelines are based on smaller studies and case reports, including medical and surgical interventions to attenuate some types of acute neurotraumatic injuries. A neurosurgical intervention to reduce intracranial pressure, decompressive craniectomy, is one example, although this procedure also remains controversial (Bullock *et al.*, 2006). The Brain Trauma Foundation (BTF) has developed guidelines for the management of severe TBI based on the best available evidence (Brain Trauma Foundation, 2007); improvements in outcomes have been reported in an international study when these guidelines were followed (Arabi *et al.*, 2010). Similarly, definitive studies to demonstrate the effectiveness of cognitive therapy and other types of rehabilitation are lacking, but numerous smaller studies have provided a basis for rehabilitation guidelines for TBI (Fadyl and McPherson, 2009; Lane-Brown and Tate, 2009; Cicerone *et al.*, 2008; Borg *et al.*, 2004). Large-scale comparative effectiveness research that leverages the variability in practice patterns also has been proposed as a means of identifying those treatments associated with better outcome (Maas *et al.*, 2011). Despite the lack of class I clinical trials, implementation of guidelines (e.g., the BTF's guidelines) has resulted in improved TBI outcomes (Bulger *et al.*, 2002; Clayton, Nelson, and Manara, 2004; Elf, Nilsson, and Enblad, 2002; Fakhry, Trask, Waller, and Watts, 2004; Patel *et al.*, 2002; Stein Georgoff, Meghan, Mirza, and El Falaky, 2010; Suarez *et al.*, 2004; Varelas *et al.*, 2006).

Long-Term Care

Improving continuity of quality care and service delivery along with inter-service, interagency, intergovernmental, and public and private collaboration for care are all critical to the success of long-term care. In addition, management, transition, and associated training, tracking, and accountability for this care are essential for administering such programs. Work in this area includes establishing multiple reforms (e.g., implementing uniform training for recovery coordinators and medical and non-medical care/case managers, establishing a single tracking system, and providing a comprehensive recovery plan for the seriously injured).

The joint Federal Recovery Coordination Program (FRCP) trains and deploys Federal Recovery Coordinators (FRCs) to support medical and non-medical care/case managers in the care, management, and transition of seriously wounded and ill SMs, veterans, and their families.

For veterans and active duty personnel with any loss of vision, blurred vision, or difficulty reading or squinting, VA provides comprehensive vision rehabilitation services—often while the injured SM is still a patient at a military treatment facility. One hundred and sixty four Visual Impairment Service Team

(VIST) Coordinators provide lifetime case management for all legally blind veterans and all OEF/OIF patients with visual impairments. Additionally, 75 Blind Rehabilitation Outpatient Specialists (BROS) with the VA provide blind rehabilitation training to patients who are unable to travel to a center for the blind. These BROS are certified in low-vision rehabilitation and orientation and mobility training and work closely with neuro-ophthalmologists and optometrists who specialize in low vision problems.

VA's Vet Centers

VA's Vet Centers, operated by the Readjustment Counseling Service in the VHA, provide community outreach and professional readjustment counseling services for war-related psychological readjustment problems (*England and Mansfield, 2008*). Vet Centers treat and address PTSD, family relationship problems, lack of adequate employment, lack of educational achievement, social alienation and lack of career goals, homelessness and lack of adequate resources, and other psychological problems such as depression or substance use disorder. They are community-based facilities, located outside of the larger VA medical centers in convenient easy-to-access settings; they embrace a mission that goes beyond medical care in providing a holistic mix of services. Vet Centers offer an alternative to traditional mental health care that helps many combat veterans overcome the stigma and fear related to accessing professional assistance for military-related problems. Eligibility for Vet Center services is based on military service in a combat theater and does not require a veteran to complete the enrollment process.

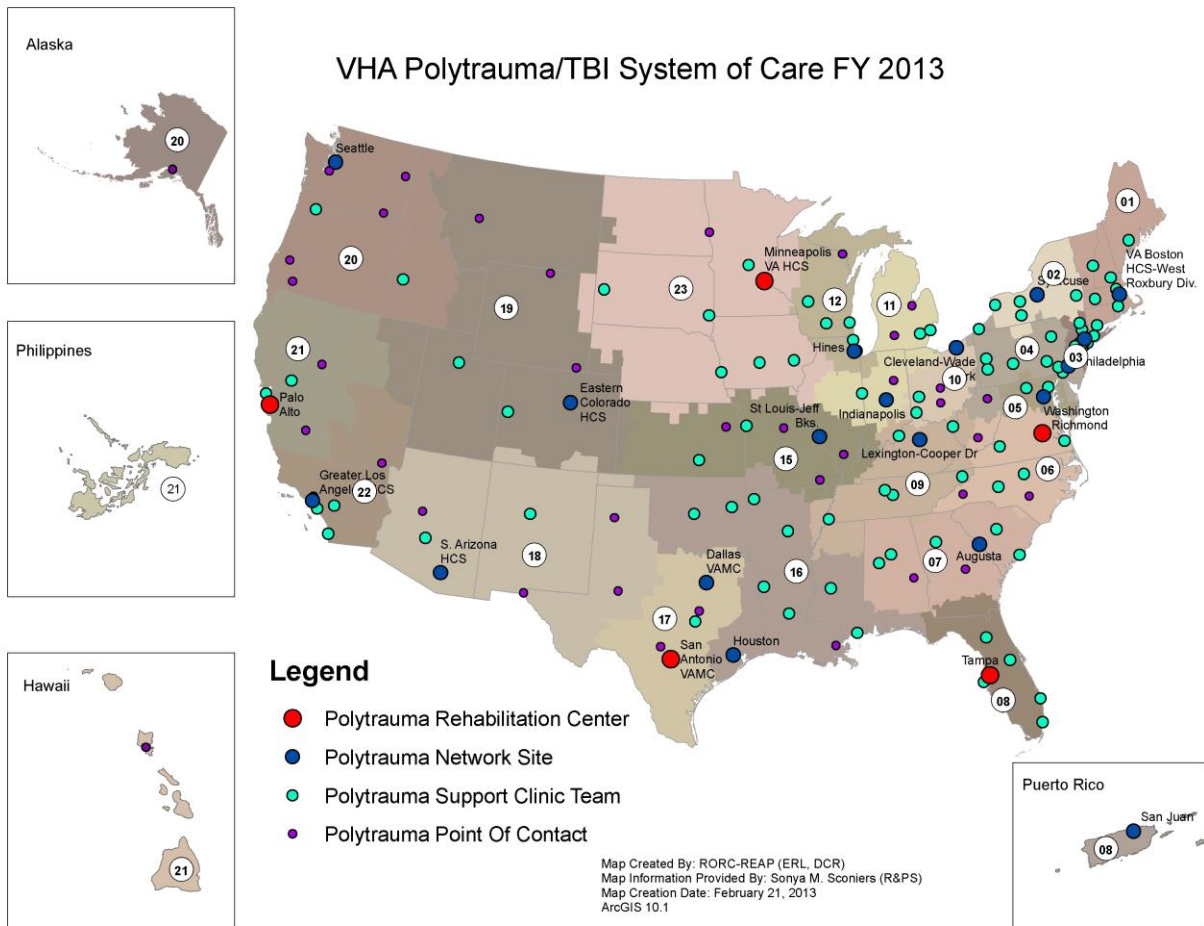
VA expanded the number of its Vet Centers nationally from 209 in 2007 to 300 facilities and 70 mobile units in 2012.

Since the beginning of OEF/OIF, the focus of the Vet Center program has been on outreach at military demobilization, at National Guard and Reserve sites, and at community locations that feature high concentrations of veterans and family members. To promote early intervention, the Vet Center program hired 100 OEF and OIF veteran returnees to provide outreach services to their fellow combatants. These fellow veteran outreach specialists are effective in mitigating veterans' stigma and establishing immediate rapport. For example, from early in FY 2003 through the end of FY 2007, Vet Centers have provided readjustment services to approximately 268,987 veteran returnees from OEF and OIF. Of this total, more than 205,481 veterans were provided outreach services, and 63,506 were provided clinical readjustment services by mental health providers in Vet Centers such as individual and group counseling for veterans and their families, substance abuse assessment and referral, and screening and referral for medical issues.

VA's Polytrauma System of Care

In its polytrauma system of care (that is, treatment for multiple complex injuries from the same event—for example, amputations, burns, hearing loss, and PTSD), the VA offers comprehensive primary and specialty health care to veterans and seriously injured active-duty service members and is an acknowledged national leader in providing specialty care in the treatment and rehabilitation of TBI and polytrauma (*Feeley 2007*). Since 1992, the VA has maintained four specialized TBI Centers that have served as the primary VHA receiving facilities for military treatment facilities seeking specialized care for brain injuries and complex polytrauma. In 2005, the VA established its Polytrauma System of Care, leveraging and enhancing the existing expertise at these TBI centers to meet the needs of seriously injured veterans and active duty service members from operations in Iraq, Afghanistan, and elsewhere.

The mission of the Polytrauma System of Care is to provide the highest quality of medical, rehabilitation, and support services for veterans and active duty service members injured in the service. This integrated nationwide system of care has been designed to provide access to life-long rehabilitation care for veterans and active duty service members recovering from polytrauma and TBI. The polytrauma system of care is composed of four component layers as described below and shown on this map.



Component 1: Regional. The five flagship facilities of the Polytrauma System of Care are Polytrauma/TBI Rehabilitation Centers (PRC) in Minneapolis, MN; Palo Alto, CA; Richmond, VA; Tampa, FL, and San Antonio, TX. These centers serve as hubs for acute medical and rehabilitation care, research, and education related to polytrauma and TBI. The specialized services provided at each PRC include comprehensive acute rehabilitation care for complex and severe polytraumatic injuries, emerging consciousness programs, outpatient programs, and residential transitional rehabilitation programs. Clinical care specific to TBI is provided by a staff of rehabilitation specialists and medical consultants in such fields as psychiatry (doctors who specialize in physical medicine and rehabilitation), rehabilitation nursing, neuropsychology, psychology, speech-language pathology, occupational therapy, physical therapy, social work, therapeutic recreation, prosthetics, and rehabilitation for blind SMs.

One of the newest programs within the PRCs is the treatment program for patients with severe disorders of consciousness. Provision of rehabilitation services for patients who are minimally conscious or

minimally responsive is based on expert opinion rather than scientific evidence. Cornerstones of treatment for patients with severe disorders of consciousness include aggressive medical care to treat potential reversible causes of impaired consciousness (infection, sedation, hormone imbalance); prevention of complications (contracture, pressure sores, malnutrition); family support and education. Additional interventions often include structured sensory stimulation and trials with medications to increase responsiveness. The Disorders of Consciousness Scale is used to monitor response to treatment.

In 2007, staffing for the PRC teams was increased at each center in response to increased demands of patient workload, coordination of care, and support for family caregivers. The PRCs have affiliations and collaborative relationships with academic medical centers, enabling a substantial number of PRC's clinical providers to share VA and affiliated positions in training and medical rehabilitation. The inpatient rehabilitation programs at the PRCs maintain accreditation by the Commission on Accreditation of Rehabilitation Facilities (CARF) for both Traumatic Brain Injury and Comprehensive Rehabilitation.

Component 2: Network. The Polytrauma/TBI Network Sites (PNS), designated in December 2005, represent the second echelon within the Polytrauma System of Care, with one PNS located within each of VA's 21 Veterans Integrated Service Networks (VISN). The PNS provides key components of post-acute rehabilitation care for persons with polytrauma/TBI, including, but not limited to inpatient and outpatient rehabilitation and day treatment programs. The PNS is responsible for coordinating access to VA and non-VA services across the VISN to meet the needs of patients recovering from polytrauma and TBI and their families. The PNS consults, whenever necessary, with the PRC.

Components 3 and 4: Facility. In March 2007, the Polytrauma System of Care network was expanded to include two new components of care: Polytrauma Support Clinic Teams (PSCT) and Polytrauma Points of Contact. With their geographical distribution across the VA, 85 PSCTs facilitate access to specialized rehabilitation services for veterans and active duty SMs at locations closer to their home communities. These interdisciplinary teams manage the care of patients with stable treatment plans, provide regular follow-up visits, respond to new medical and psychosocial problems as they emerge, and consult with their affiliated PNS or PRC when more specialized services are required.

The remaining 40 VA medical centers have an identified Polytrauma Point of Contact who manages consultations for patients with polytrauma and TBI and assists with referrals. The Polytrauma Telehealth Network links the PRC and PNS through state-of-the-art multipoint videoconferencing capabilities. This Network also ensures that polytrauma and TBI expertise are available throughout the system, that care is provided at locations and times most accessible to patients, and that clinical activities include remote consultations and evaluations of patients and education for providers and families.

Another model for using telehealth technology and the sharing of electronic health information along the continuum of care is the rural networks of non-VA health facilities currently funded by the Health Resources and Services Administration's (HRSA's) Rural Veteran's Health Access Program (RVHAP). A key feature of these networks is collaboration between rural healthcare providers and the Department of Veteran's Affairs. These networks are intended to help eligible entities coordinate innovative approaches, collaborative networks, and virtual linkages to increase the delivery of mental health and other healthcare services to meet the needs of veterans of Operation Iraqi Freedom and Operation Enduring Freedom that reside in remote rural areas.

Coordination and Transition of Care. Care management across the entire continuum is a critical function in the Polytrauma System of Care to ensure lifelong coordination of services for patients recovering from polytrauma and TBI. Consistent, comprehensive procedures and processes have been put in place to ensure transition of patients from military treatment facilities to VA care at the appropriate time, under optimal conditions of safety and convenience for patients and their families. At the direction of the VA's Secretary, 100 Transition Patient Advocates have been recruited nationwide. In addition, the VA assigns a care manager to every admitted patient to coordinate services, address emerging medical, psychosocial, or rehabilitation needs, and provide patient and family advocacy.

To facilitate the continuity of medical care, the PRC receives advanced notice of potential admissions, initiates a pre-transfer review, and follows the clinical progress until the patient is ready for transfer. In addition to record review, clinician-to-clinician communication occurs to allow additional transfer of information and resolution of any outstanding questions.

The DoD and VA also have made substantial progress sharing available electronic health information to further coordinate care. DoD is currently transferring DoD medical digital images and electronically scanned inpatient health records to the VA polytrauma centers from Walter Reed National Military Medical Center, and Brooke Army Medical Center. VA hopes to add the capability to provide this data bi-directionally to support any patients returning to DoD for further care. Additionally, VA and DoD are supporting the secure direct connection of authorized providers at VA polytrauma centers into the health-information systems at Walter Reed National Military Medical Center.

In addition, the Department of Health and Human Services Office of the National Coordinator and the Under Secretary for Health of the Veteran's Health Administration (VHA) have established a Memorandum of Understanding to examine ways to leverage existing resources to develop potential pilot sites for Health Information Exchange between rural providers and the VHA. The VHA Office of Rural

Health continues to partner with stakeholders to identify and improve technology adoption in order to expand services to the 3.4 million Veterans that live in highly rural areas.

Psychosocial support for families of injured service members is paramount as decisions are made to transition from the acute care setting of a military treatment facility to a rehabilitation setting. This encompasses psychological support, education about rehabilitation, the next setting of care, and information about benefits and military processes and procedures. VA social worker or nurse liaisons are located at 10 military treatment facilities, including Walter Reed National Military Medical Center. In addition, a Certified Rehabilitation Registered Nurse is available to provide education to the family on TBI, the rehabilitation process, and the PRCs. The Admission Case Manager from the PRC maintains personal contact with the family before transfer to provide additional support and further information about the expected care plan. VA also has benefit liaisons located at military treatment facilities that refer large numbers of patients to the VA to provide an early briefing on the VA services and benefits available to patients and families.

Lastly, the transition from the PRC to the VA Medical Center in or near the home community must ensure that the treatment plan is maintained. Records for VA medical care are readily available through remote access across the VA system. Follow-up appointments are made before discharge, and the transferring practitioners are readily available for personal contact with the receiving provider to ensure full communication. Care managers at the PNS and the home VA medical center provide ongoing support and problem resolution in the home community, while continually assessing for new and emerging concerns. Finally, each PRC team assesses the expected needs at discharge for transportation, equipment, home modifications, other such needs, and makes arrangements for assessed needs.

Recent studies indicate that the number of medical, physical and psychological injuries that are occurring as a result of combat injury are resulting in a greater functional burden on SM's with the need for integrated, interdisciplinary care, longer acute and inpatient rehabilitation stays and greater health care costs (*Sayer et al., 2008; Schneiderman, Braver, and Kang, 2008*). One of these studies examined long-term treatment in four VA acute PRCs for polytrauma and other combat injuries acquired during the first 4 years of the Global War on Terror (i.e., between October 2001 and January 2006) (*Sayer et al., 2008*). In this study of 188 persons, 56% had blast-related combat injuries; 53% had closed head injuries and 44% had penetrating head injuries; and 56% had craniectomy or craniotomy before PRC admission. Additionally, those with TBI-related blast injury had a significantly greater number of multiple injuries. After rehabilitation, 64% were discharged to home or military bases, 27% to other inpatient service or military treatment facilities, 6% to residential day programs, and 3% to nursing homes. The other was a

recent cross-sectional study of veterans following deployment to OEF/OIF examined prevalence of mild TBI and PTSD. In the population surveyed, approximately 12% of 2,235 respondents reported history consistent with mild TBI, and 11% for PTSD (*Schneiderman et al., 2008*).

Care in the Civilian Health System

Transporting severely injured patients directly to the highest level of trauma care (Level I or II trauma centers) has been shown to lower mortality (*Sampalis et al, 1997; Nirula, Maier, Moore, Sperry, and Gentilello, 2010*). Trauma centers demonstrate better adherence to the American Association of Neurologic Surgeons Guidelines for the Management of Severe Traumatic Brain Injury, including immediately available CT scanning, prompt neurosurgical care, and the ability to monitor intracranial pressure (ICP), and treatment of intracranial hypertension (*Hesdorffer and Ghajar, 2007; Fakhry et al, 2004*).

CT scanning is used emergently to identify intracranial bleeding, contusion, or consequences of penetrating injury. These patients might be unconscious on arrival and require stabilization, mechanical ventilation, and intensive care services. In addition, management of co-occurring injuries and meticulous medical care is required to prevent deterioration and the many potential complications, such as infections, acute respiratory distress syndrome, disseminated intravascular coagulation, brain swelling, and multi-organ failure. Monitoring of intracranial pressure is common, and algorithms are in use for lowering raised intracranial pressure to preserve cerebral blood flow and prevent pressure-related distortion of the brain (herniation syndromes). Intracranial bleeding or hematoma might also require neurosurgical intervention.

Guidelines and Best Practices in Civilian Healthcare Systems

Professional medical societies developed detailed best practice guidelines for the management of severe TBI as shown in Table 3.

Table 3. Guidelines for the Management of TBI

Guideline	Source
<i>Guidelines for prehospital management of severe TBI second edition</i>	<i>Badjatia et al., 2006</i>
<i>Guidelines for the management of severe TBI third edition</i>	<i>Brain Trauma Foundation., 2007</i>

<i>Guidelines for the surgical management of severe TBI</i>	<i>Bullock et al., 2006</i>
<i>Guidelines for the acute medical management of severe TBI in infants, children and adolescents second edition</i>	<i>Kochanek et al., 2012</i>
<i>Guidelines for field management of combat-related head trauma 2005</i>	<i>Knuth et al., 2005</i>
<i>The Clinical Policy on Neuroimaging and Decision making in Adult Mild Traumatic Brain Injury in the Acute Setting</i>	American College of Emergency Physicians and CDC (<i>Jagoda et al., 2008</i>)

Although guidelines for neuroimaging and decision making in adult mild TBI exist (Jagoda et al., 2008), there is variability in the use of neuroimaging, decision to admit to hospital or discharge to home, and any follow-up planning (Miele and Bailes, 2009; Timmons and Winestone, 2009; Heller and Mass, 2009). Focus is usually on identifying those who are at risk for deterioration, usually caused by post-traumatic intracranial hemorrhage. Many patients with mild TBI are discharged from emergency departments to their home with instructions to return should symptoms worsen. If all goes well, follow-up is usually first suggested with the patient's primary physician but often this follow-up does not occur (Sosin et al., 1996). U.S federal agencies, international agencies, and professional organizations have developed best practice guidelines for the management of TBI. For example, the VA and DoD have developed joint clinical practice guidelines for the management of concussion/mild TBI (U.S. Dept. of Veterans Affairs & U.S. Dept. of Defense, 2009); the American Academy of Neurology has developed guidelines for neurologists regarding the management of concussion in sports (American Academy of Neurology, 1997); the CDC, convening an expert panel, developed guidelines for coaches on how reduce the numbers of mild TBI and how to recognize cases of mild TBI (http://www.cdc.gov/concussion/HeadsUp/online_training.htm); and an expert consensus group from Canada has developed clinical guidelines for mild TBI and persistent symptoms (Marshall, Bayley, McCullagh, Velikonja, and Berrigan, 2012). Certain states also have enacted legislation requiring student athletes who sustain a concussion to be seen by a medical expert before they can return to play (National Conference of State Legislatures, 2013).

Rehabilitation

A 1998 NIH Consensus Conference on TBI concluded that some evidence supported the use of rehabilitation strategies for TBI, but definitive evidence from large well-controlled clinical trials was lacking. Despite more than 10 years of effort, clinical practice for the rehabilitation of patients with TBI has not advanced substantially. Only limited interventions have demonstrated effectiveness in improving

outcomes for patients in rigorous controlled studies (*Vanderploeg et al., 2008; Cicerone et al., 2005; Levine et al., 2000*). One study actually reported that the overall benefit of inpatient cognitive rehabilitation for patients with moderate to severe TBI was similar to that of in-home rehabilitation (*Salazar et al., 2000*). Thus, the translation to wide-scale clinical adoption is still premature. In the absence of strong evidence, and faced with pressing clinical needs, providers have adopted practices based upon consensus and clinical experience (*Fadyl and McPherson, 2009; Lane-Brown and Tate, 2009; Cicerone et al., 2008*). The challenge to develop effective rehabilitation strategies for TBI patients overlaps with those described earlier in this report regarding acute treatment. At the same time, the progress in contemporary neuroscience, imaging, and cell biology is noteworthy—it will ultimately provide the foundation for effective remediation of TBI.

V. Prognosis and Recovery

Proper identification of the long-term and lifelong medical signs and symptoms of TBI are critical to the study of the epidemiology of TBI-related disability, including the identification of cases of TBI; this however, poses some challenges. Recovery after severe TBI can be protracted. Patients might partially or completely improve after spending weeks, months, or years in states devoid of purposeful behavior; patients might recover their ability to speak, walk, and make new memories. The ability to predict which TBI survivors will recover functional independence in society is poor (*Mushkudiani et al., 2007*).

Moreover, what prompts recovery and the speed, duration, and extent of recovery is not well understood. Predicting the future ability of the severe TBI survivor to return to the workforce is even more difficult. Meticulous medical care in the rehabilitation setting enables recovery, but the role of specific rehabilitation strategies in accelerating recovery after the various forms of TBI is unknown. The majority of scientific investigations of recovery after brain injury focus on focal brain injury, especially stroke. Whether or not the lessons learned from these studies can be extrapolated to TBI is not clear. Intense study of the biology that underlies the recovery processes associated with functional recovery after TBI is warranted.

Gaps in knowledge severely complicate surveillance methodologies and processes to define the burden of illness related to previous TBI. Most difficult is identifying those persons who develop a post-concussive syndrome after a mild TBI. This is further complicated in persons with comorbidities, such as depression, personality disorder, or substance abuse, which can cause some of the symptoms seen in post-concussive syndrome. Another challenge for surveillance of TBI is the lack of a working definition of “full recovery” vs. “persistent disability,” which can occur in persons following TBI.

Recovery from TBI

Recovery after TBI is highly variable (*Moppett, 2007*) and depends on many factors. Outcomes and recovery can be measured in several forms and aspects. The 25 most common measures used in the field of brain-injury rehabilitation and assessment have been compiled by the Center for Outcome Measurement in Brain Injury (COMBI). COMBI is a collaborative project of 16 brain-injury facilities or centers, most of them Traumatic Brain Injury Model Systems (TBIMS) through grants funded by the Department of Education’s National Institute on Disability and Rehabilitation Research (*U.S. Dept. of Education, 2012*). The most important factor appears to be the severity of the injury (*Schretlen and Shapiro, 2003*). Milder injuries, which are present in 80% – 90% of TBI survivors, are associated with better outcomes than those with more severe injuries. Many people classified as having a mild TBI might

experience complete resolution of symptoms and return to work and other pre-injury activities. Return to work is considered an important metric of recovery, although it is inadequate for children and retired adults and it is important to recognize that many adults with disabilities successfully participate in the workplace. Estimates indicate that 10% –50% of persons with a mild TBI experience long-term health issues such as persistent headache, difficulty with memory or concentration, or mood changes (*Moppett, 2007; Thornhill et al., 2000*). Persons who sustain more severe injuries have worse outcomes, with only 20% making a good recovery, as assessed by the Glasgow Outcome Scale (*Thornhill et al., 2000*). The course of recovery is also faster following mild TBI, occurring largely within 1 – 3 months, compared with 2 or more years in more severely injured groups. In rare cases, and for unknown physiological reasons, recovery from a persistent vegetative state or minimally conscious state can occur years after the TBI (*Schiff et al., 2007; Berube et al., 2006*). The ability to predict which severe TBI survivors will recover functional independence is poor (*Mushkudiani et al., 2007*).

A retrospective analysis of data from clinical trials that tested treatments in adults with severe TBI revealed that increasing age was strongly predictive of worse outcomes (*Mushkudiani et al., 2007*). Race and education also might affect outcomes. Studies have determined that African Americans and Asians with a history of TBI have lower odds of being employed up to 5 years post injury compared with whites who have a history of TBI. (*Gary et al., 2009; Berry, Ley, Mirocha, and Salim, 2010*). In 1998, another report indicated that persons who were employed at the time of injury, had higher educational levels, and less disability from their injuries were most likely to be employed at 1–3 years after their injury (*Gollaher 1998*). The reasons for these findings need to be explored further. Some studies suggest that women have worse outcomes following TBI (*Slewa-Younan van den Berg, Baguley, Nott, and Cameron, 2009*), whereas others report no gender difference (*Mushkudiani et al., 2007*). Further complicating this picture are animal studies that have demonstrated better recovery in females (*Stein, 2004*).

Research has demonstrated that the type of injury and certain complications might influence the acute and long-term consequences of TBI. Penetrating injuries have worse outcomes than closed injuries (*Wertheimer, Hanks, and Hasenau, 2008*). Comorbidities and secondary injuries, such as low blood pressure that might result from severe blood and fluid loss from other injuries, negatively affect outcomes after TBI (*Butcher et al., 2007*). Genetic factors also might play a role. Certain reports indicate that those persons who have a gene variant associated with Alzheimer’s disease, apolipoprotein E4, also are more likely to have poorer outcomes following TBI (*Nathoo Chetty, van Dellen, and Barnett, 2003; Wilson and Montgomery, 2007*). The majority of experimental preclinical investigations of recovery after brain injury use models of focal brain injury. Clarifying whether this information can be extrapolated to diffuse forms

of TBI such as diffuse axonal injury and edema is critical. Intense study of the biology that underlies the recovery processes associated with functional recovery after TBI is warranted.

Post-Concussive syndrome (PCS)

PCS is a term used to describe disabling symptoms following a neurotraumatic event even when no intracranial pathology is detected with imaging (*Bigler, 2008*). At least two major hypotheses exist regarding the neural substrate for PCS. One is that PCS is caused by diffuse axonal injury, which results in a loss of connectivity between regions of the brain and subsequent behavioral alterations (*Smith, Meaney, and Shull, 2003; Bazarian et al., 2007; Gold and Lipton, 2008*). Diffuse axonal injury is not yet reliably detected with CT scans or other neuroimaging tools, but rapid progress is being made in this area. DTI appears to be a promising diagnostic tool for diffuse axonal injury (*Inglese et al., 2005; Sharp and Ham, 2011*).

A second hypothesis is that persistent metabolic alterations in injured, but not lethally injured, brain cells result in neuronal dysfunction and subsequent behavioral impairments (*Marcoux et al., 2008*). Metabolic alterations following TBI have been reported using sophisticated imaging tools, such as SPECT, PET, and functional MRI, but these methods lack accepted validation for routine clinical use. These hypotheses might both be correct, occurring in separate subsets of persons with TBI. These processes also might both be linked to one underlying mechanism of injury. For example, that metabolic alterations in grey matter are caused by reduced neuronal activity secondary to a loss of connectivity from diffuse axonal injury might be possible.

A better understanding of the pathophysiology of PCS and mild TBI and the development and validation of more sensitive imaging tools is a priority for TBI research. Although many persons seek medical attention immediately or shortly after a TBI, diagnosis can occur at later points in time. Other potential (not yet validated) diagnostic tools for TBI include electroencephalography (EEG); near infrared spectroscopy (NIRS); sensory tests for vision, hearing, and balance, and cognitive and motor assessments (*Suchoff et al., 2008; Arenth, Ricker, and Schultheis, 2007; Pickett, Radfar-Baublitz, McDonald, Walker, and Cifu, 2007*).

Posttraumatic Stress Disorder (PTSD)

PTSD is defined by the DSM-IV criteria as a syndrome occurring in response to a stressor that was a serious threat and the person's response to that threat includes intense fear, helplessness, or horror (*American Psychiatric Association, 2000*). Although PTSD symptoms have been reported in patients with moderate and severe TBI, preliminary data from DoD suggests that TBI patients who have lost

consciousness tend not to acquire this condition. Persons with LOC resulting from TBI and no memory for the traumatic event might not experience the PTSD-like response to the trauma. Similarly, persons with PCS infrequently recall the event or have persistent avoidance of stimuli associated with the trauma. The symptoms of PCS and the PTSD symptom cluster, called hyper-arousal symptoms, tend to overlap. Symptoms such as irritability or outbursts of anger, concentration difficulties, and sleep disturbances occur in both PCS and PTSD and are included in the DSM-IV criteria for PTSD (*American Psychiatric Association, 2000*). They also occur in various physical and psychological disorders. Hypervigilance and excessive startle response are included in the hyper-arousal symptom cluster for PTSD but are not common in PCS. Symptoms common to PTSD appear to occur in greater proportions in those with mild TBI compared with other injuries (*Hoge et al., 2008*). In a study of 2,525 soldiers returning from OEF/OIF, headache was found to be the only symptom with strong association to mild TBI alone (*Hoge et al., 2008*). The approximately one-third of SMs with mild TBI who are also diagnosed with PTSD fare worse on neurocognitive tests of executive functioning and processing speeds than those diagnosed only with mild TBI (*Nelson, Yoash-Gantz, Pickett, and Campbell, 2009; Hoge et al., 2008; Brenner et al, 2009*).

Long-term Health Outcomes or Disability

The list of neurologic and other problems associated with TBI is long. Cognitive deficits, such as memory impairments, are hallmarks of TBI. Tasks involving complex cognition, including executive function requiring attention, judgment and insight, are particularly problematic for people with TBI, whereas simpler cognitive tasks such as keeping track of daily responsibilities or appointments might not reveal deficits (*Silver, McAllister, and Arciniegas, 2009*).

Neuropsychiatric disorders, including depression, anxiety, PTSD, suicidal tendencies, disinhibition, and substance abuse, have been reported following TBI (*Silver et al., 2009; Belanger et al., 2011*). These neuropsychiatric and emotional disorders might create the most serious challenges to returning to work or other pre-injury activities and to community reintegration. Posttraumatic seizures are common after penetrating head injury or traumatic intracranial hemorrhage; TBI is the largest known risk factor for epilepsy (*Temkin, 2009*).

TBI also can produce movement and sensory disorders that disturb balance, vision, perception, and hearing (*Katz, Zasler, and Zafonte, 2007*). Headaches, pain, sleep disturbances, and fatigue are other frequent symptoms following TBI (*Formisano, Bivona, Catani, D'Ippolito, and Buzzi, 2009; Nampiaparampil, 2008; Rao et al., 2008*). The association of TBI with later development of Alzheimer's disease or chronic traumatic encephalopathy is the subject of continued study.

On December 10, 2012, VA published a proposed rule to amend its adjudication regulations concerning service connection for secondary illnesses associated with TBI. The proposed amendment is in response to a report of the National Academy of Sciences, Institute of Medicine (IOM), Gulf War and Health, Volume 7: Long-Term Consequences of Traumatic Brain Injury. The effect of this proposal would be to establish that if a veteran who has a service-connected TBI also has one of five diagnosable illnesses, then that illness will be considered service connected as secondary to the TBI, which may provide additional benefits to the veteran.

Specifically, VA's proposed regulation states:

(d) Traumatic brain injury. (1) In a veteran who has a service-connected traumatic brain injury, the following shall be held to be the proximate result of the service-connected traumatic brain injury (TBI), in the absence of clear evidence to the contrary:

- (i) Parkinsonism following moderate or severe TBI;
- (ii) Unprovoked seizures following moderate or severe TBI;
- (iii) Dementias (presenile dementia of the Alzheimer type and post-traumatic dementia) if manifest within 15 years following moderate or severe TBI;
- (iv) Depression, if manifest within 3 years of moderate or severe TBI, or within 12 months of mild TBI; or
- (v) Diseases of hormone deficiency that result from hypothalamo-pituitary changes if manifest within 12 months of moderate or severe TBI.

VA received over 200 public comments on the proposed rule and is now preparing the final rule for publication.

Risk of Neurodegenerative Disease Following TBI

Epidemiologic evidence indicates that synergy exists between TBI and permanent neurodegeneration. Longitudinal MRI-based studies have demonstrated brain atrophy occurring in the months to years after TBI (*Ross, 2011*). Contradictory findings regarding the relationship between TBI and Alzheimer's disease exist (*Van Den Heuvel et al. 2007*). Evidence suggests that risk for dementia is increased two to four fold after moderate or severe TBI, but risk following mild TBI is unclear (*Shively, Scher, Perl, and Diaz-Arrastia, 2012*).

Additionally, evidence indicates that repetitive TBI can cause a unique neurodegenerative disorder first reported in boxers and called *dementia pugilistica* (*Martland, 1928*). Now termed chronic traumatic encephalopathy (CTE), this disorder is characterized by the aggregation of the microtubule-associated

protein called tau in nerve cells. This is the same protein that aggregates inside dying neurons in Alzheimer's disease and in the brains of persons with a tau gene variant that causes fronto-temporal dementia. Some studies demonstrate that tau aggregation, once started, has the ability to spread from one nerve cell to another; this could explain how an initial focal injury could lead to widespread damage over time (*de Calignon et al. 2012*). The genetic variant apolipoprotein E4, a known risk factor for Alzheimer's disease, has been associated with poorer outcomes after head injury (*Nathoo et al., 2003*) and in some studies with increased risk for the later development of Alzheimer's disease (*Graham et al., 2002; Luukinen et al., 2005; Rabadi and Jordan, 2001; Jordan et al., 1997*). However, this association has not been found in all studies (*Jellinger, 2004*). More recently, CTE has been described in athletes who participated in contact sports and in 21 veterans (86% of whom were also athletes) (*Goldstein et al. 2012; McKee et al., 2009*). Sharing symptoms with PTSD, patients who died with CTE have been described to present with poor concentration and memory, irritability, depression, and suicidality. The extent of the burden of CTE in service members exposed to TBI is unknown.

VI. Surveillance

Case Definition Background

Public health surveillance is the ongoing, systematic collection, analysis, interpretation, and dissemination of data on a health-related event, such as TBI, for use in reducing morbidity and mortality and to improve health (CDC, 2001). Surveillance is a labor-intensive process and requires adequate funding, manpower, and, very frequently, a solid public health infrastructure to be successful and sustainable (CDC, 2001). For the purposes of this report and based on accepted requirements for identifying cases for surveillance purposes, CDC and NIH, in consultation with the Secretary of Defense and the Secretary of Veterans Affairs, have defined a case of “traumatic brain injury (TBI) in people formerly in the military” as any combat or non-combat TBI that occurred in a person while serving in the U.S. military (from now on termed *military service-related TBI*) since the beginning of military operations in the first Gulf war on January 17, 1990 (Atkinson, 1993). This time-linked case inclusion criterion can be modified if additional resources become available (i.e., supplementing or changing existing systems).

Surveillance data can be used to estimate the magnitude of a public health problem, understand the natural history of a condition, detect epidemics, document the distribution and spread of a health event, test hypotheses about etiologies, evaluate control measures and develop and implement prevention interventions (Teutsch, 2000).

Standard clinical and surveillance case definitions assist in identifying new cases of TBI and cases with persistent symptoms, impairments, functional limitations, or disabilities resulting from this condition. Historically, each of the departments and agencies involved in this report has used agency/department-specific standard TBI definitions to meet their mandates and needs, but for public health surveillance, the definition described above is used. TBI definitions used by clinicians and investigators may vary, especially for cases of mild TBI (National Center for Injury Prevention and Control, 2003; Culotta, Sementilli, Gerold, and Watts, 1996). The WHO Collaborative Center Task Force on mild TBI published a comprehensive review of definitions. They found that 62% of the definitions reviewed incorporated GCS scores, but differing ranges of scores (13–15, 14–15, or only 15) was evident. LOC or amnesia was required in some definitions, but the duration of LOC varied. The WHO task force concluded that surveillance would benefit from a common definition and collaborated with CDC and other agencies and groups to develop one (Carroll, Cassidy, Holm, Kraus, and Coronado, 2004).

In 2009, TBI researchers from CDC/NCIPC, NIH, DoD, VA, and other federal and nonfederal partners recommended standardized clinical and surveillance case definitions and data elements for TBI research

(National Institute for Neurological Disorders and Stroke, 2013). Although certain evidence-based definitions are still under revision due to the paucity of research, their use by all federal agencies and partners might allow better TBI-related research and comparability of data collected in the United States.

Although CDC, NIH, DoD, and VA agree on a common clinical definition for TBI, different perspectives are evident among CDC, Centers for Medicare and Medicaid Services (CMS), NIH, VA, and DoD, and other stakeholder groups, on how to code multiple clinical manifestations of this condition with codes of the International Classification of Diseases (ICD). CDC, NIH, DoD, and VA believe that ongoing interaction and discussion is foundational to advancing TBI-related epidemiologic and clinical research. As more is learned about the natural course of TBI, CDC, NIH, DoD, and VA have committed to continue their collaborations and to extend that to other public and private sector stakeholders and partners to improve and standardize TBI-related definitions (for clinical and epidemiologic purposes), which will be used in all federally funded TBI research. As such, codes of the ICD-9-CM (to identify TBI survivors), ICD-10 (to identify TBI deaths) and the future ICD-10-CM (to identify TBI survivors) classifications will be evaluated continuously. This evaluation process will improve identification of cases of TBI when analyzing ICD-coded administrative or vital statistics databases in the United States. The agencies and partners are committed to this collaborative work that will improve TBI coding and classification, while adhering to structure and conventions of the ICD.

Conceptual and Operational Definitions

To properly and accurately identify patients with TBI, clinicians, researchers, and investigators use conceptual and operational definitions.

A **conceptual case definition** provides criteria to identify a case of TBI for surveillance purposes based on selected clinical signs, symptoms, and neuroimaging. This definition is necessary as a reference standard for the evaluation of operational or working definitions of mild TBI used by surveillance systems.

An **operational case definition** provides quantifiable criteria to consistently identify cases of TBI for surveillance purposes when reviewing ICD-coded health-care administrative or vital statistics databases, when abstracting information from medical records, or when analyzing data from surveys and personal interviews. Operational definitions should be designed to approximate the conceptual definition as closely as possible. Operational definitions might be based on clinical symptoms, clinical records (clinical definition) or based on existing diagnostic coding (e.g., those found in death certificates or administrative hospital data bases).

Clinical Case Definition

CDC issued the following clinical case definition for TBI regardless of injury severity in its 1995 publication, *Guidelines for Surveillance of Central Nervous System Injury* (Thurman et al., 1995).

Clinical Case Definition

For surveillance systems using data from clinical records, a case of TBI (craniocerebral trauma) is defined as an occurrence of injury to the head that is documented in a medical record, with one or more of the following conditions attributed to head injury:*

- observed or self-reported decreased level of consciousness,[†]
- amnesia,[‡]
- skull fracture,
- objective neurological or neuropsychological abnormality,[§] or
- diagnosed intracranial lesion**

* Injuries to the head might arise from blunt or penetrating trauma or from acceleration-deceleration forces.

† Decreased level of consciousness refers to partial or complete loss of consciousness. This includes states described as less than full mental capacity, stupor, or coma.

‡ Amnesia might include loss of memory for events immediately preceding the injury (retrograde amnesia), for the injury event itself, and for events subsequent to the injury (posttraumatic amnesia).

§ Neurological abnormalities are determined from neurological examination. Examples include abnormalities of motor function, sensory function, or reflexes; abnormalities of speech (aphasia or dysphasia); or seizures acutely following head trauma. Neuropsychological abnormalities are determined from mental status and neuropsychological examinations. Examples include disorders of mental status (such as disorientation, agitation, or confusion) and other changes in cognition, behavior, or personality.

**Examples of diagnosed intracranial lesions include traumatic intracranial hematomas or hemorrhage (epidural, subdural, subarachnoid, or intracerebral), cerebral contusions or lacerations, or penetrating

cerebral injuries (e.g., gunshot wounds). The diagnosis of such intracranial lesions is usually confirmed with a CT or MRI brain scan or by other neurodiagnostic procedures.

The clinical definition of TBI excludes the following:

- lacerations or contusions of the face, eye, ear, or scalp, without other criteria listed above
- fractures of facial bones, without other criteria listed above
- birth trauma
- primary anoxic, inflammatory, infectious, toxic, or metabolic encephalopathies that are not complications of head trauma
- neoplasms
- brain infarction (ischemic stroke) and intracranial hemorrhage (hemorrhagic stroke) without associated trauma

Definition of TBI based on ICD Diagnostic Coding

The ICD has been used worldwide to code and classify morbidity and mortality data enabling health-care providers to code specific diagnoses. In the United States, some versions of the ICD are used to code and classify mortality data only; since 1999, the tenth version of WHO's ICD-10 (*World Health Organization 1992*) is used to code and classify such data from death certificates.

Clinical modifications (CM) of the ICD have been produced with authorization from WHO to classify morbidity (as opposed to classify mortality). A clinical modification of the WHO ninth revision of ICD (ICD-9-CM; *Centers for Disease Control and Prevention, 2009*) is being used in the United States to code diagnoses, including those of TBI. To replace ICD-9-CM, a clinical modification of the ICD-10, known as ICD-10-CM, has been developed by CDC/National Center for Health Statistics (NCHS) with input from health-care industry stakeholders; this version will be implemented on October 1, 2014.

TBI Morbidity

Morbidity codes currently in use were last updated in 2001. The ICD-9-CM codes recommended for inclusion in the definition of TBI at this time include the following:

800.0 – 801.9 Fracture of the vault or base of the skull

803.0 – 804.9	Other and unqualified and multiple fractures of the skull
850.0 – 854.1	Intracranial injury, including concussion, contusion, laceration, and hemorrhage
950.1 – 950.3	Injury to the optic chiasm, optic pathways; and visual cortex
959.01	Head injury, unspecified (beginning 10/1/97)
995.55	Shaken Infant Syndrome

Since 2001, additions have been made to ICD-9-CM codes to address emotional and behavioral symptoms of TBI. VA and DoD proposed these additions in response to a request from Congress to address concerns by SMs and veterans who are receiving mental health diagnoses for symptoms of TBI. This is particularly important due to the stigma related to mental health issues as compared to physical injuries. Some of these changes were consistent with ICD and accepted by NCHS. These changes resulted in the inclusion of TBI as a clinical term in ICD-9-CM. VA and DoD also proposed a new code for history of traumatic brain injury (V15.52) and a new code section for signs and symptoms involving emotional state. These new codes allow emotional and behavioral symptoms of TBI and other conditions to be coded without assigning a mental health diagnosis. In addition, VA and DoD have proposed including these codes for several TBI-associated cognitive symptoms.

As the United States starts to replace the current ICD-9-CM coding system with ICD-10-CM, an opportunity exists to improve TBI classification. Federal stakeholders have been concerned regarding the need for a better classification for TBI symptoms using ICD codes as acute or persistent (or chronic) for both epidemiologic and clinical uses. CDC, NIH, DoD, VA, and other federal agencies are reviewing proposed codes of ICD-10-CM classification and making suggestions for changes that would improve TBI reporting in the United States.

Although different perspectives exist among CDC, NIH, DoD, VA and other stakeholders, and because knowledge gaps are apparent regarding the natural course of TBI, these agencies support ongoing interaction and discussion, which is foundational to advancing TBI-related epidemiologic and clinical research. For example, little is known about the pathophysiology and the long-term effects of blast-related TBI. CDC, NIH, DoD, and VA will continue to work together and with other public and private sector stakeholders to 1) standardize all TBI-related definitions to be used in all federally funded TBI research in the United States (*Thurmond et al., 2010; National Institute for Neurological Disorders and Stroke, 2013*) and 2) propose modifications to the ICD-CM that are consistent with the structure and conventions of the classification that will improve identification of cases of TBI in the United States.

TBI Mortality

For TBI Mortality (based on ICD-10 codes). The ICD-10 codes recommended for inclusion in the definition of TBI at this time include the following:

S01.0 – S01.9	Open wound of the head
S02.0, S02.1, S02.3, S02.7 – S02.9	Fracture of skull and facial bones
S04.0	Injury to optic nerve and pathways
S06.0 – S06.9	Intracranial injury
S07.0, S07.1, S07.8, S07.9	Crushing injury of head
S09.7 – S09.9	Other and unspecified injuries of head
T01.0	Open wounds involving head with neck
T02.0	Fractures involving head with neck
T04.0	Crushing injuries involving head with neck
T06.0	Injuries of brain and cranial nerve with injuries of nerves and spinal cord at neck level
T90.1, T90.2, T90.4, T90.5, T90.8, T90.9	Sequelae of injuries of head.

Case Ascertainment by Severity

The use of ICD-9-CM to classify TBI severity is problematic since coding is not consistent with conceptual and clinical definitions for mild, moderate, and severe TBI. This is especially problematic for differentiating mild from moderate TBI. As illustrated by Table 4, persons with LOC 30 minutes to 1 hour would be categorized as mild, rather than moderate since ICD 9-CM, does not differentiate persons with LOC of less than 30 minutes from those with LOC of 30 minutes to 1 hour. Injuries that include brain contusion, hemorrhage, or laceration will be categorized as moderate or severe, depending on LOC and the severity of the focal injury. However, it may not always be possible from ICD-9-CM codes to distinguish between moderate and severe TBI, especially if LOC is not stated. For persons with more than one TBI diagnosis, severity should be consistent with the most severe diagnosis.

Table 4. Stratification of Severity by Length of time of Loss of Consciousness

Classification	Mild	Moderate	Severe
DoD/VA Common Definition	0-30 mins	>30 mins and < 24 hrs	>24 hrs
Classification	Brief LOC	Moderate LOC	Prolonged LOC
ICD-9-CM	No LOC; brief <1 hr (30 mins or less, 31 mins to 59 mins)	1 to 24 hrs	>24 hrs
V15.5 DoD/VA Extenders	< 1 hr	1 to 24 hrs	>24 hrs

Source: Department of Veterans Affairs (VA) and Department of Defense (DoD).

Because of these inconsistencies, VA and DoD previously proposed adding synonyms in ICD-9-CM as follows: “mild TBI” for LOC <30 minutes, “moderate TBI” for LOC >30 minutes to <24 hours, and “severe TBI” for LOC > 24 hours. This proposal was intended to aid clinicians and coders in selecting the correct acute injury code. In the ICD-9-CM review process, the proposals, however, were not supported by stakeholders. VA continues to advocate for a simple revision to ICD-10-CM before the activation in 2014. This revision would eliminate possible coding errors with “concussion” by limiting that section to true concussion (mild TBI, LOC < 30 minutes), and move the remainder of codes in that section to "other intracranial injuries" (S06.89).

DoD V15.5 code-related extenders to stratify TBI severity. DoD uses an additional set of internal codes to stratify injury. A series of extenders appended to ICD-9-CM code V15.5 (i.e., personal history of injury) indicate severity based on LOC and to indicate SM's deployment. These extenders are not valid ICD-9-CM codes and are not recognized by other users of the ICD-9-CM classification in the United States. Therefore, any data collected using these codes will be applicable to military settings only. In addition, new V15.5 codes were proposed and implemented (e.g., code V15.52 - History of TBI, was implemented on October 1, 2009).

Mild TBI

In 2003, a CDC Definitions Subgroup of the CDC Workgroup on mild TBI produced and recommended a definition for mild TBI (CDC, 2003). This definition for mild TBI, however, does not categorize other levels of TBI severity (i.e., moderate or severe) and might not be well suited for surveillance of mild TBI

not treated in hospital or Emergency Department (ED) settings. Based on this definition (*CDC, 2003*), the CDC mild TBI Working Group recommended the following three operational or working definitions for case ascertainment based on 1) interviews and surveys; 2) health-care administrative data sets; and 3) clinical records.

Interview/Survey. Mild TBI is recognized when a person or proxy surveyed or interviewed affirms the occurrence, in the period under surveillance, of a nonfatal injury to the head that is accompanied by the following conditions:

- Criteria consistent with the recommended conceptual case definition (occurrence of injury to the head resulting from blunt trauma or acceleration or deceleration forces that result in any period of observed or self-reported transient confusion, disorientation, impaired consciousness, and amnesia around time of injury; or observed signs of other neurological or neuropsychological dysfunction, such as seizures, headache, irritability, fatigue and poor concentration);
- Loss of consciousness or altered consciousness;
- Loss of memory for events immediately before, during, or after the injury.

Surveys and interviews should ask whether health-care professionals evaluated such injuries and, if so, what level of care was provided. Where possible, analyses of data should distinguish among persons who received no medical care, non-hospital-based care which includes physician office visits, hospital emergency department care, inpatient hospital care up to 24 hours, and inpatient hospital care of greater than 24 hours. Unfortunately, these data have not typically specified whether the TBI or some other injury was the reason for the length of stay, but occurrences of brain injury with inpatient hospital care of greater than 24 hours may be classified as more severe because they do not meet the criteria for mild TBI.

ICD-9-CM based Definition. Mild TBI is recognized among persons treated in health-care facilities and who are assigned the following ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) diagnostic codes:

ICD-9-CM First Four Digits = 800.0, 800.5, 801.0, 801.5, 803.0, 803.5, 804.0, 804.5, 850.0, 850.1, 850.5 or 850.9: 800-804- Skull Fracture; 850-854 Intracranial Injury, excluding those with skull fracture

ICD-9-CM Fifth Digit subclassification is required for categories 851 to 854 to identify loss of consciousness, if any, and the length of time as follows:

- 0, unspecified state of consciousness;
- 1, with no loss of consciousness;
- 2, with brief (less than one hour) loss of consciousness;
- 6, with loss of consciousness of unspecified duration; and
- 9, with concussion, unspecified.

ICD-9-CM First Four Digits = 959.0: Injury, Other and Unspecified

ICD-9-CM Fifth Digit = 1, with no loss of consciousness.

These codes indicate either skull fracture or concussion without evidence of underlying brain hemorrhage or contusion, and no more than brief LOC. It is important to note that although the fifth digit 2 is being used to indicate mild TBI, this ICD-9-CM code is problematic for indicating severity. A fifth digit of 2 indicates loss of consciousness less than 1 hour. As mentioned above (Table 4), the clinical definition used by DoD/VA of mild TBI includes only those patients with loss of consciousness of less than 30 minutes. However, the ICD-9-CM does not differentiate between LOC of less than 30 minutes and 30 minutes to 1 hour. The latter would actually indicate moderate TBI. Thus, use of the fifth digit “2” as mild overestimates the number of persons with mild TBI and underestimates the number of persons with moderate TBI.

Clinical Records Definition. Mild TBI is recognized when the medical records document any one of the following conditions:

- Criteria consistent with the recommended conceptual case definition;
- GCS score between 13 and 15 assigned at the time of first medical evaluation at a health-care facility;
- Abbreviated Injury Severity Scale score of 2 for the head region (*Gennarelli and Wodzin, 2008*).

Exclusions: Injuries accompanied by indicators of neurological deterioration during the course of acute care, such as cases in which subsequent GCS scores fall below 13 are excluded (*NCIPC, 2003*).

TBI-Related Disability

Ascertaining the prevalence of disability attributable to severe TBI relies on medical records, access to supportive services, and school or work status. Persons with severe TBI frequently have residual cognitive or other neurological disability (e.g., weakness, stiffness, slurred speech, incoordination, posttraumatic epilepsy) and commonly require long-term assistance. Patients with severe TBI who survive their injuries frequently require extensive rehabilitation, first as an inpatient and later as an outpatient. Neurological recovery might take place over months or even years; however, many do not recover to independent functioning or enter/re-enter the work place, and carry a diagnosis of chronic brain injury caused by trauma (*Riggio, 2011*).

TBI-related disability is identified over time during the continuum of assessment and management of TBI. Ascertaining the prevalence of disability because of TBI is difficult for mild and moderate TBI. Patients with mild TBI can acquire conditions such as disordered sleep, fatigue, headache, dizziness, poor concentration, anxiety disorder, memory, and depressed mood. While recovery usually occurs during the first few months following injury, 10% – 50% might have symptoms that last more than a year (*Riggio, 2011*). In addition, evidence suggests that persons with repeated events of TBI tend to recover more slowly after each ensuing event and in extreme cases might develop chronic neurodegenerative changes—first seen as *dementia pugilistica* in boxers but now termed chronic traumatic encephalopathy (CTE) (*McKee et al., 2010*).

Specialized survey techniques are necessary to quantify the incidence and duration of post-concussive syndrome. Batteries of standardized neuropsychological testing can determine the level of cognitive function in specific domains: attention, memory, executive function, processing speed, verbal ability, spatial ability, depressed mood, and symptom validity. However, pre-testing is not routinely done for most persons, making these comparisons challenging. Determining pre-injury levels of function is more difficult, but can be estimated based upon previous level of achievement in education or employment. Comparison of scores on pre-injury and post-injury tests of cognitive abilities might be the most reliable means to determine if the effects of TBI are persistent.

Data Sources

Civilian

The primary responsibility for public health surveillance in the civilian system resides at the state level (*Jacobson, Hoffman, and Lopez., 2007; Horan and Mallonee, 2003*). Since the mid-1990s, CDC and at least 30 states have developed injury surveillance systems, including TBI (*CDC State Programs, 2009*);

the capacity of these state systems is variable (*CDC unpublished data*). States must improve their capacity to identify all injuries and yet have the specificity to identify TBI events and use linkages between data systems or other indicators to identify veterans with military service-related TBI in all 50 states and territories. A number of civilian health and injury surveillance systems already exist and could incorporate additional measures to capture or validate information specific to TBI and/or military service (Table 5).

Table 5. Civilian Public Health Surveillance Systems

Name of Surveillance System (in alphabetical order)	Agency	Design and Use
Behavioral Risk Factor Surveillance System (BRFSS)	CDC and health departments in 50 states, District of Columbia, Puerto Rico, Guam, and Virgin Islands	Population based, random-digit dialed telephone survey of adults (aged ≥ 18 years) in the United States; three components: core, optional, state-specific. Used to track health conditions, disability, and risk behaviors and to collect state/territory data on preventive health practices linked to chronic diseases, injuries, and preventable infectious diseases.
CDC Traumatic Brain Injury Surveillance System (CDC TBI SS)	CDC/National Center for Injury Prevention and Control: Core Violence and Injury Prevention Program (VIPP)	Statewide representative ongoing population-based surveillance system. Used to identify, track, and analyze statewide trends in TBI. Information used to inform primary and secondary prevention strategies.
National Ambulatory Medical Care Survey (NAMCS)	CDC/National Center for Health Statistics	Nationally representative multistage probability survey based on a sample of visits to non-federal office-based physicians engaged primarily in direct patient care. Excludes those in anesthesiology, radiology, and pathology. Representative sample used to identify and track ED and outpatient department visits.
National Electronic Injury Surveillance System – All Injury Program (NEISS-AIP)	Consumer Product Safety Commission (CPSC) and CDC/National Center for Injury Prevention and Control	Nationally representative, stratified probability sample of all U.S. hospitals that have at least 6 beds and provide 24 hour ED services. Used to identify, track, and analyze national trends in injury-related ED visits.

National Health Interview Survey (NHIS)	CDC/National Center for Health Statistics	Population-based, nationally representative, face-to-face probability sample survey among civilian, non-institutionalized U.S. population. Used to monitor trends in illness and disability, track progress toward achieving national health objectives, characterize various health problems, determine barriers to access and use of health care, and evaluate federal health programs.
National Hospital Ambulatory Medical Care Survey-Emergency Department and Outpatient Department Modules (NHAMCS)	CDC/National Center for Health Statistics	Nationally representative multistage probability sample of visits to emergency and outpatient departments and to ambulatory surgery facilities in noninstitutional general and short-stay hospitals, excluding Federal, military, and Veterans Administration hospitals, located in the 50 States and the District of Columbia. Used to identify and track ED and outpatient department visits.
National Hospital Discharge Survey (NHDS)	CDC/National Center for Health Statistics	Nationally representative three-stage stratified sample survey of inpatient hospital records acquired from probability sample of ~500 non-federal short-stay hospitals. Provides information on characteristics of patients of all ages that were hospitalized and discharged from hospitals in sample.
Nationwide Inpatient Sample (NIS)	Agency for Healthcare Research and Quality (AHRQ)	Nationally representative multi-state health data system of all hospital discharges from a stratified probability sample of non-federal short-stay hospitals (40 states; 1,044 hospitals in 2007). Used to identify, track, and analyze national trends in health-care utilization access, charges, quality, and outcomes by diagnoses.
State and Local Area Integrated Telephone Survey (SLAITS)	CDC/National Center for Health Statistics	Collection of broad-based ongoing surveillance systems; uses sampling frame of CDC's National Immunization Survey (NIS), following NIS random-digit dialed telephone survey; surveys vary, based on need of sponsors. Tracks and monitors health and well-being of children and adults in 50 states, District

		of Columbia, and 27 urban areas. Contacts more than 1 million households annually.
The National Health and Nutrition Examination Survey (NHANES)	CDC/National Center for Health Statistics	Nationally representative survey of 5,000 persons annually, combining interviews and physical exams; focus on different population groups or health topics. Used to determine prevalence of chronic conditions, risk factors for disease, nutritional status; helps to develop public health policy, direct and design health programs and services, and expand health knowledge.

Department of Defense

Armed Forces Health Surveillance Center (AFHSC)

The Armed Forces Health Surveillance Center (AFHSC) was established in February 2008 by the DoD to be the central epidemiology health resource for the U. S. military. It merges the capabilities and resources of the Army Medical Surveillance Activity (AMSA), the DoD Global Emerging Infections Surveillance and Response System (DoD-GEIS), and the Global Health Surveillance Activity of the Force Health Protection Directorate of the Office of the Assistant Secretary of Defense for Health Affairs. Also, AFHSC assumed responsibility for AMSA's Defense Medical Surveillance System (DMSS) and the DoD Serum Repository (DoDSR). DMSS contains up-to-date and historical data on diseases and medical events (e.g., hospitalizations, laboratory tests, immunizations) affecting SMs throughout their military careers. DMSS contains over two billion records on nine million service members and other beneficiaries of the MHS.

The AFHSC maintains, promotes, and enhances the health of military and military-associated populations through development, refinement, and improvement of surveillance methods; coordinates a global program of militarily relevant infectious disease surveillance.

Defense Medical Surveillance System (DMSS)

In 1997, The Army Medical Surveillance System transitioned to the Defense Medical Surveillance System (DMSS). This is the primary tool used by AFHSC for all its public health surveillance. It combines data from inpatient, outpatient, and purchase care databases maintained by TRICARE

Management Activity and contains personnel data from Defense Manpower Data Center and health assessments completed by SMs. The DMSS contains data from three main sources: Standard Ambulatory Record Data (SADR) and Comprehensive Ambulatory Professional Encounter Record (CAPER); Standard Inpatient Data Records (SIDR); and TRICARE Encounter Data (TED)/Health Care Service Record (HCSR). DMSS data are integrated in a continuously expanding longitudinal surveillance data base for all persons who have served since 1990 and facilitate the efficient analyses of morbidity among SMs.

Theater Medical Data Store (TMDS)

The TMDS receives data from various military and civilian systems, which allows the following: view clinical information; view, track, and manage ill or injured patients through continuum of care; access data on critically injured patients before they arrive a next point of care; access to deployment-specific medical data; access to blood inventory management activity; and, view pre-deployment health information..

Blast Tracker Program (BTP)

The Army National Guard designed the Blast Tracker Program (BTP) as a secure data base accessible to all service branches via defense link website. It will be incorporated into the Combined Information Data Network Exchange of U.S. Central Command data system. The goal is to capture blast and related events and identifies persons in proximity to blasts. Units and individual persons can receive reports and previously deployed units can add past exposure information.

VA

The following systems are implemented by the Veterans Health Administration (VHA) to identify veterans receiving health care within VA who have a possible TBI.

VA TBI Screening and Evaluation Program

The TBI Screening and Evaluation Program is a web-based tracking application that began in 2007 to capture information on veterans who screen positive for mild TBI using a TBI Clinical Reminder tracking system. The system was designed to improve screening for veterans of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) for mild TBI. The program provides information to confirm diagnosis and provide treatment.

VA TBI Health Registry

The TBI Health Registry is a secure web-based portal for VA users to evaluate data, develop policies, assess resource demands, determine incidence/prevalence of TBI and evaluate treatment and outcomes. The system provides prospective longitudinal health surveillance, epidemiologic, and health-care quality analysis for OEF/OIF veterans.

Challenges/Limitations

The identification of veterans who had a military service-related TBI in the immediate or remote past in the civilian systems poses many medical, epidemiologic, methodologic, and administrative challenges. Collecting data, standardizing collection methods, and sharing data among partner agencies is a critical component of an overall plan to improve the outcome of TBI injuries. Furthermore, these data will support future efforts related to the implementation of prevention measures.

Veterans with moderate or severe military service-related TBIs have the potential to be counted easily because their injuries are often self-evident. They frequently have clear clinical signs of brain injury or with imaging results (CT and/or MRI) that are abnormal. Similar to civilians, veterans with less severe TBIs might be more difficult to identify if their signs and symptoms were not evaluated immediately after the injury, not recorded (*National Center for Injury Prevention and Control [NCIPC], 2003*), or not diagnosed (*Andary et al., 1997; Chambers, Cohen, Hemminger, Prall, and Nichols, 1996*). Long-term dysfunction might be related to multiple events of mild TBI, making the number of exposures as important as the severity of any single exposure. Accurate measures of the accumulated number of blast exposures add further complexity to accurate data gathering. Moreover, diagnosing TBIs that occurred years previously, such as during the First Gulf War, might be difficult because of substantial memory loss and inability to recall the initial diagnosis, external causes, or risk factors (*Jekel, Katz and Elmore, 2001; Paterson and Scott-Findlay, 2002*). Survivors also might have comorbidities, such as PTSD, that might mimic or overlap with the signs and symptoms of TBI (*Glaesser, Neuner, Lutgehetmann, Schmidt, and Elbert, 2004; McMillan et al., 2001; Schneiderman, Braver, and Kang, 2008*). In other instances, health-care providers might not be able to detect or diagnose (*Jekel, 2001*) TBIs and/or determine causative factors, especially if they are mild (*Andary et al., 1997; Chambers et al., 1996*). Other medical concerns include malingering (*Halligan, Bass, and Oakley, 2003; Sweet et al., 2000; Bianchini Curtis, and Greve, 2006*) or the inability of the civilian provider to access military medical records documenting the injury event, diagnosis and risk factors.

Identifying veterans who had a military service-related TBI since the beginning of the First Gulf War in the civilian system requires data sharing among interested parties. Such sharing of data might be particularly useful for identifying those veterans who are subsequently receiving care in the civilian health-care system. However, this poses administrative challenges, including the Health Insurance Portability and Accountability Act of 1995 (HIPAA) Privacy Rule (*United States Department of Health and Human Services, 2009*) that regulates uses and disclosures of “protected health information” (PHI) by covered entities (45 CFR 164). The HIPAA Privacy Rule defines covered entities as health-care providers, health plans, and health-care clearinghouses (45 CFR 160.103 (B)(3)). Examples of PHI include information that identifies or can be used to identify a person who is related to any physical or mental health condition, or treatment, or payment for treatment of a person by covered entities.

The HIPAA Privacy Rule permits the disclosure of PHI without the authorization of the individual for specified purposes including disclosures required by law and disclosures to public health authorities who are authorized to collect it. HIPAA generally requires the disclosure of the minimum amount of information necessary to achieve the intended purpose (45 CFR 162.502 (b)). CDC and state health departments, as public health agencies with public health authority, may obtain protected TBI-related health information for public health purposes (under 45 CFR 164.512(b)(2)) from VA and DoD to identify the target population of this report in the civilian system. Various applicable laws regulate the disclosure of identifiable information from CDC and state health departments (e.g., the Privacy Act, HIPAA Privacy Rule, state laws). Development and dissemination of veterans’ TBI-related information in the civilian health-care and public health systems will require high levels of cooperation and collaboration among various federal (CDC, NIH, DoD, and VA), state, local entities, and other stakeholders. Despite these hurdles, the Federal TBI Common Data Elements project is developing standards so that TBI in persons formerly in the military is effectively measured and data shared among interested parties while maintaining appropriate privacy protections. The ongoing activities of this interagency group can go a long way towards further strengthening collaboration and data sharing among organizations responsible for conducting, monitoring, and evaluating current civilian and military TBI-related surveillance systems.

VII. Epidemiology

Epidemiology is the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems (*Last, 1988*).

The epidemiology of a condition, like TBI, can be characterized using data collected via surveillance systems as described in the surveillance section above. Injury surveillance data are useful for several reasons. Even the simplest surveillance programs are designed to identify as many persons as possible who have a particular injury or disease. Other programs, like the CDC Core Violence and Injury Prevention Program surveillance system (*Marr and Coronado, 2004*), might collect additional data about selected demographic and clinical characteristics of the injured population, cause of injury, alcohol use, and use of protective devices, such as seat belts or motorcycle helmets.

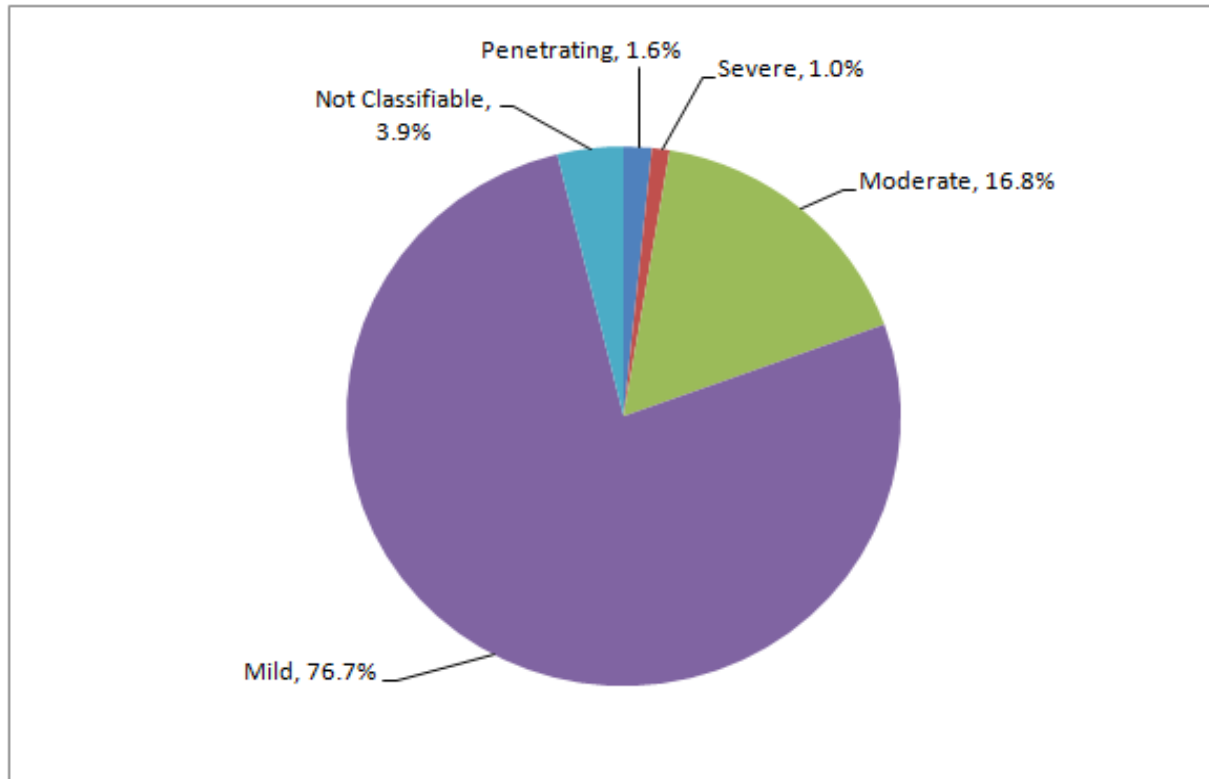
Although surveillance systems typically do not collect data at the same level of detail as research studies, they provide more current data than research data. Furthermore, they can generate data on an ongoing basis, which is useful for studying, for example, trends or the efficacy of preventive interventions (*Coronado et al., 2009*). Obtaining more detailed epidemiologic data requires in-depth and time-consuming studies of specifically defined populations (*Coronado et al., 2009*). In most cases, researchers find it feasible to collect the necessary amount of details from samples of persons drawn from a population of interest rather than study the entire population (*Coronado et al., 2009*). These limitations contribute to the difficulty of extrapolating results from detailed studies to surveillance data. However, data from both approaches are necessary to understand the magnitude and effects of injuries and diseases.

Incidence: Traumatic Brain Injury

Incidence indicates the number of new cases that occur over time. It is usually expressed as a percentage of persons who will be affected during a year, or as a rate calculated as the number of persons who develop the condition during a period divided by the number of person-years at risk.

From 2000 through 2011, a total of 235,046 service members (SMs) (4.2%) of the total 5,603,720 who served in all components of the Army, Air Force, Navy, and Marine Corps were diagnosed with a TBI. Most of these SMs with a TBI (76.7%) had a mild TBI (Figure 1). Less than 3% of SMs with a TBI had severe and penetrating TBIs (Figure 1).

Figure 1. Percentage of U.S. Military Service Members Diagnosed with a TBI, by TBI Severity, 2000-2011 (N=235,046)



Source: Defense and Veterans Brain Injury Center

The overall rate of TBI among active duty service members more than doubled from 720.3 per 100,000 SMs to 1,811.4 per 100,000 SMs from 2000 to 2011 (Table 6 and Figure 2). The TBI rate increased dramatically from 2006 to 2008 followed by slight increases in 2010 and 2011. This may reflect an actual increase in TBI, but may also reflect an increased number of SMs deployed along with increased awareness of the need to seek care and improved recognition and diagnosis. Overall TBI rates increased in every active-duty service branch from 2000 through 2011 (Figure 3). The largest increases were among active-duty Army and Marine Corps members. The rate of TBI in the active-duty Army was 3.3 times higher in 2011 than in 2000 (2,717.9 versus 815.6 per 100,000 service members). The TBI rate among active-duty Marine Corps personnel in 2011 was 2.4 times higher than in 2000 (2,286.3 versus 959.8 per 100,000 SMs).

Table 6. Estimated Annual Rates* of TBI among Active-Duty U.S. Military Service Members by TBI Severity, 2000-2011.

Year	Penetrating	Severe	Moderate	Mild	Not Classifiable†	Overall
2000	17.9	11.6	274.8	413.7	2.3	720.3
2001	19.4	12.6	234.4	506.0	2.3	774.7
2002	13.9	9.2	192.3	553.7	2.4	771.5
2003	16.0	10.4	150.1	563.5	1.8	741.8
2004	17.1	9.0	128.5	614.7	2.1	771.4
2005	13.9	9.8	108.3	581.5	2.3	715.9
2006	19.7	11.1	145.3	835.7	3.4	1015.1
2007	23.9	13.3	216.9	1087.5	13.8	1355.3
2008	27.7	15.1	193.6	1289.5	169.7	1695.6
2009	28.2	18.5	205.0	1279.8	126.6	1658.1
2010	17.1	13.3	236.8	1405.6	90.7	1763.6
2011	15.8	12.3	239.4	1429.1	114.8	1811.4

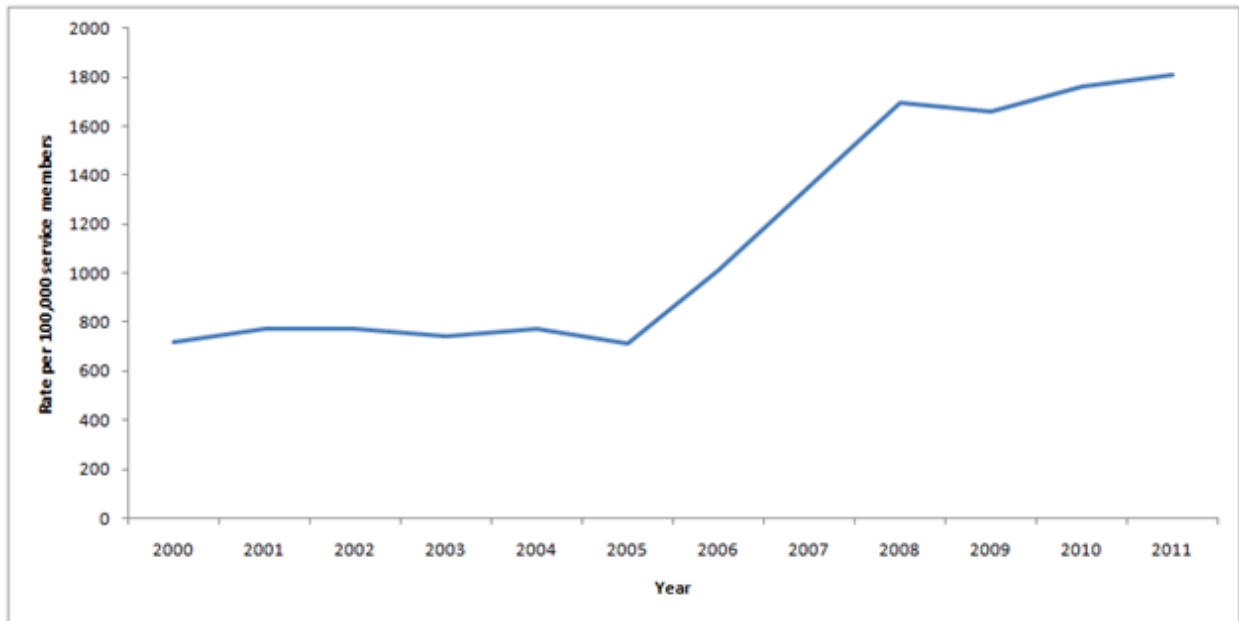
*Incidence Rates per 100,000 service members.

†Changes were made to the DoD TBI case definition in 2008 to include codes that do not provide information about the severity of the TBI.

Source: Defense and Veterans Brain Injury Center.

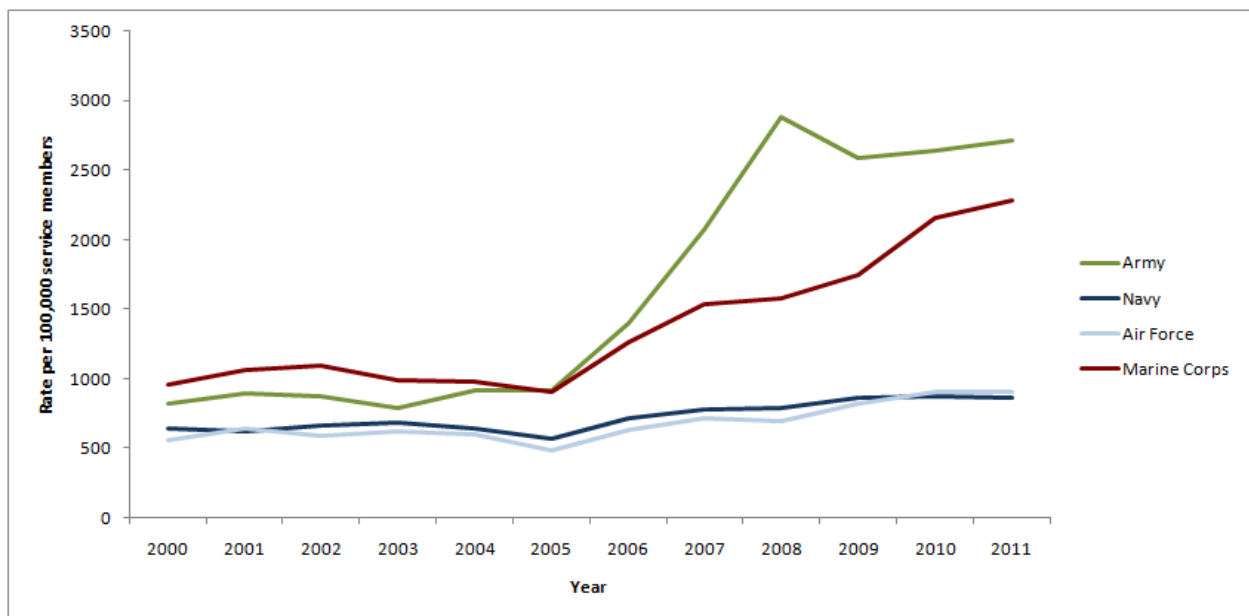
The mild TBI rate among active-duty service members increased from 2000 through 2011 (Table 6 and Figure 4). The increase in the rate of mild TBIs accounted for most of the increase in the overall TBI rate in the active-duty military population. The rate of moderate TBIs in this population decreased from 2000 through 2005 and then increased in 2006 and 2007, followed by a decrease in 2008 and then increased each year through 2011 (Table 6 and Figure 4). The rates of penetrating and severe TBIs among active-duty service members increased dramatically from 2006 through 2009 (Table 6 and Figure 5). However, these rates decreased substantially after 2009 (Table 6 and Figure 5). In 2010 and 2011, the rate of penetrating TBIs among active-duty service members decreased 43.9%. During those 2 years, the rate of severe TBIs decreased 33.4%; this decrease is likely a function of multiple factors including fewer people deployed and improvements to both vehicles and personal protective equipment.

Figure 2. Estimated Overall Annual Incidence Rates of TBI Among Active-Duty U.S. Military Service Members, 2000–2011 Surveillance Systems



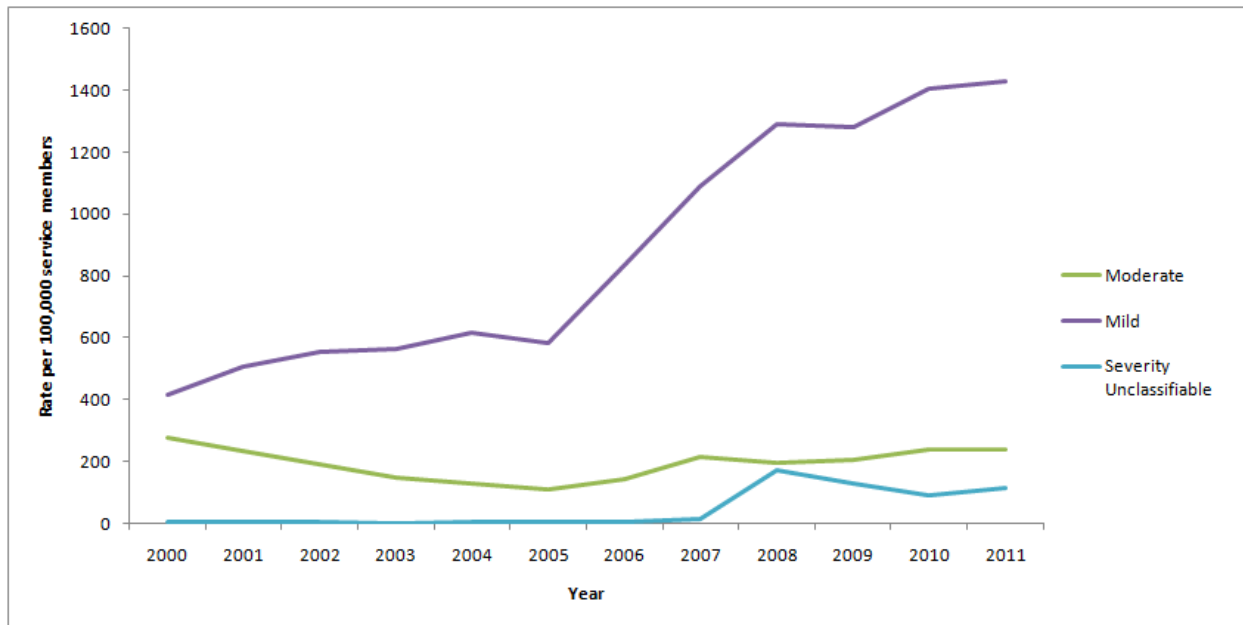
Source: Defense and Veterans Brain Injury Center

Figure 3. Estimated Overall Annual incidence Rates of TBI among Active-Duty U.S. Military Service Members by Service Branch, 2000–2011



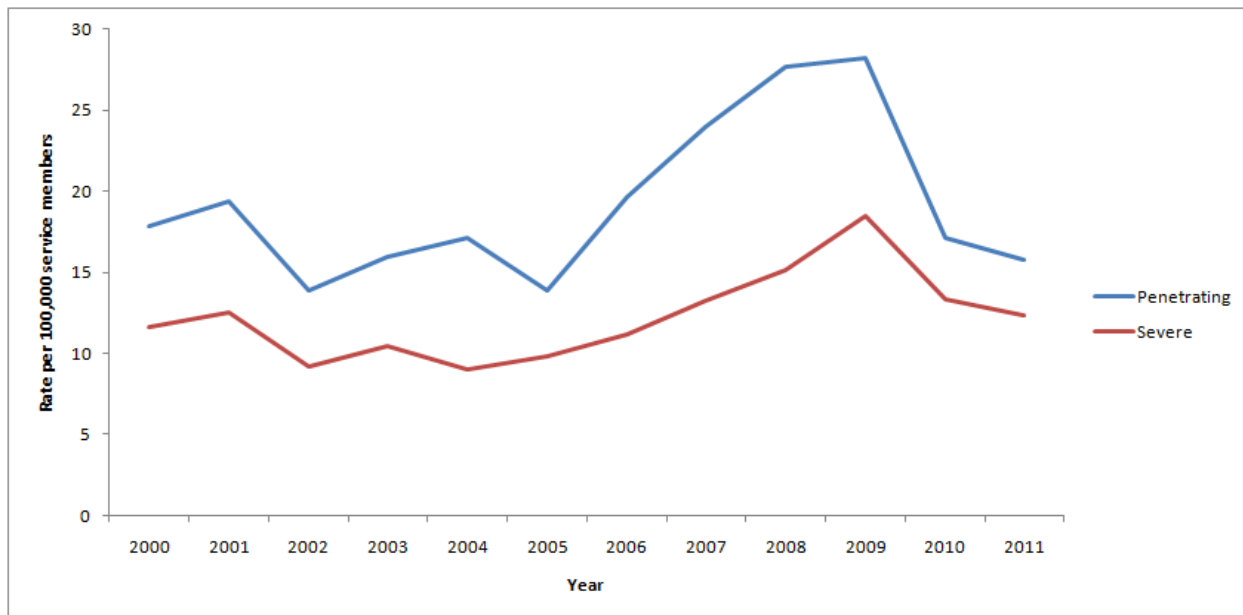
Source: Defense and Veterans Brain Injury Center

Figure 4. Estimated Annual Incidence Rates of Mild and Moderate TBIs and TBIs with Unclassifiable Severity Among Active-Duty U.S. Military Service Members, 2000–2011



Source: Defense and Veterans Brain Injury Center

Figure 5. Estimated Annual Incidence Rates of Penetrating and Severe TBIs Among Active-Duty U.S. Military Service Members, 2000–2011



Source: Defense and Veterans Brain Injury Center

The incidence of blast-induced TBI in U.S. civilian populations is low, with a report of 0.2% of TBI cases in a major urban trauma center (*Bochicchio et al., 2008*); however, civilian blast injuries are becoming an increasing problem worldwide (*Summers et al., 2009*). Data for TBI in the civilian population from 1995 to 2009 show that the rate for emergency department visits increased significantly from 434.1 per 100,000 population in 1995 to 686.0 per 100,000 in 2009. During the late 1990s, the rate of TBI hospitalizations decreased significantly from 95.5 per 100,000 population in 1995 to 77.9 per 100,000 in 2000 but then the rate increased over subsequent years and the rate for 2009 was similar to that reported in 1995. Deaths in which a TBI was listed either as an isolated injury or in conjunction with other injuries decreased significantly from 19.9 per 100,000 in 1995 to 16.6 per 100,000 in 2009 (*Coronado et al., 2012*).

Although additional research is required to understand the specific causes, a number of factors may have contributed to the significant increase in the rate of TBI-related emergency department visits including the increased awareness of head injury through education campaigns (for example, CDC's *Heads Up: Concussion* campaign), the efforts of various sports organizations to reduce TBI among athletes, and the media attention given to TBI among military service members fighting in Iraq and Afghanistan. In addition, a number of states have passed legislation to reduce TBI in youth sports, further raising awareness of the importance of addressing these kinds of injuries among coaches, athletic trainers, parents, and youth. While a number of factors likely contributed to the decline in TBI-related deaths, the largest single contributor is the reduction in the number of transportation related deaths (*Coronado et al., 2012*).

Prevalence: Traumatic Brain Injury

Prevalence is the number of all new and old cases of a disease or occurrences of an event (in this case TBI) during a particular period (*Mosby 2009*).

Active Duty Military Personnel

Determining the prevalence of TBI in the transient military population remains challenging as it might not allow accounting for all those who are living with the consequences of this condition. Other challenges stem from the use of multiple databases and electronic medical records that lead to duplication of cases or inability to locate records and inconsistencies in coding that might contribute to inappropriate symptom attribution.

Another concern that can affect reporting prevalent cases is the lack of chronic TBI codes. Commonly, SMs might be seen and treated for persistent headaches following TBI. The primary diagnostic code is captured as headache. Unless a history of TBI code is also used, this person might not be captured in

reporting. The DoD, CDC, VA, and other federal agencies collaborated to revise the ICD-9 codes that most accurately reflect TBI. These revisions that are already in use incorporated consideration of comorbid conditions and were publicly reviewed, discussed, and adapted by all partners. The addition of cognitive-behavior codes is important because many of the symptoms of mild TBI overlap with psychological comorbidities, in particular PTSD.

Inconsistencies in coding also might affect reporting. To overcome these problems, educational activities are underway to ensure that providers and medical coders consistently use recommended codes that will enhance incidence and prevalence detection. Guidance documents have been developed to assist in improving documentation (*TRICARE 2010; Defense Centers of Excellence, 2010*).

To better estimate the prevalence of TBI in the military, MHS requires continuing the practice of conducting pre-deployment screening to have baseline measures; after a possible TBI, screening all SMs as soon as possible; training all medical personnel in the detection of TBI and coding methods for TBIs; improving and maintaining better medical record keeping and reporting; and expediting the standardization of the multiple and disparate databases in the military. Efforts have been initiated to coordinate databases within the DoD and other federal agencies as mandated by the National Defense Authorization Act (NDAA).

The majority of TBIs are mild (approximately 80%; *Thurman, Alverson, Dunn, Guerrero, Sniezek, 1999; Defense and Veterans Brain Injury Center, unpublished data*) and less likely to yield chronic symptoms. If mild TBI-related symptoms are present, they are often non-specific headaches, dizziness, or cognitive or neuropsychiatric difficulties. According to current coding guidelines, chronic symptoms, such as headache, are recorded but often without information necessary to determine whether and how they may be attributed to a prior TBI. Therefore, the prevalence of mild TBI is difficult to ascertain. SMs who have sustained a moderate, severe, or penetrating TBI and who are represented in the TBI database are more likely to have disability linked to their TBI. However, with the exception of post-traumatic epilepsy, no process is in place for determining and recording long-term consequences.

Veteran Population

The overall U.S. veteran population is diverse and includes those who served during various eras, including WWII, the Korean conflict, the Vietnam War, the First Gulf War, OEF/OIF, and other conflicts and operations. The number of women veterans has steadily increased; beginning in the First Gulf War, women have played an increasingly important role in the U.S. military. Estimating the TBI prevalence in veteran population should optimally consider services provided by both the VA health-care system and civilian medical facilities outside of that system. Prevalence among OEF/OIF veterans seen by VA is

defined by data from VA's Inpatient (PTF) and Outpatient (OPC) treatment records data and is presented in Table 7.

Table 7. Numbers of OEF/OIF Veterans Reported with ICD-9-CM Codes Indicative of TBI Diagnosis or a Selected TBI Outcome or Other Type of Head Injury Commonly Associated with TBI who were Evaluated or Treated in the VA Health-Care System from October 2001 through December 2011

Diagnosis/Health Outcomes	Number¹ of Veterans (N=59,218)
Postconcussion syndrome	12,367
Fracture of skull ²	113
Fracture of base of skull ²	113
Fracture of face bones ²	3,237
Other and unqualified skull fracture ²	90
Multiple fractures involving skull or face with other bones ²	209
Concussion ³	36,412
Cerebral laceration and contusion ³	392
Subarachnoid, subdural, and extradural hemorrhage following injury ³	243
Other and unspecified intracranial hemorrhage following injury ³	62
Intracranial injury of other and unspecified nature ³	18,509
Injury to optic nerve and pathways ²	257

¹The sum of the number of veterans corresponding to each ICD-9-CM code is more than 59,218 because a patient might have more than one ICD-9-CM code.

²ICD-9-CM codes that are commonly associated with TBI.

³ICD-9-CM codes with specific TBI diagnoses.

Source: Epidemiology Program, Post Deployment Health Group, Office of Public Health, Veterans Health Administration, Department of Veterans Affairs, March 2012.

Epidemiologic studies of the long-term consequences of TBI, including those that focused on veterans who served during WWII, the Korean conflict, and the Vietnam War have been reviewed by the Institute of Medicine (IOM 2009). Many of the early studies of TBI reviewed by IOM focused on moderate or severe TBI or pre-date contemporary improvements in assessment, treatment, and rehabilitation, highlighting the ongoing need for additional research.

Several factors have contributed to current interest in understanding the epidemiology, early detection, treatment, and rehabilitation of not only moderate and severe TBI but also mild TBI. This includes increased use by enemy forces of improvised explosive devices (IEDs) and rocket propelled grenades (RPGs); increased survival of military service men and women who are critically injured on the battlefield; and recognition of the potential for overlap between mild TBI and PTSD. In the last decade studies within the U.S. military and VA systems have addressed the long-term consequences of military service-related TBI. Of these studies, most address the consequences of military service-related mild TBI (*Hoge et al., 2008; Schneiderman et al., 2008, Taber and Hurley 2009; Rona et al, 2012*).

The National Defense Authorization Act of Fiscal Year 2008 (Public Law 110-181, Section 1704 (d) requires the VA Secretary to establish and maintain a TBI Veterans Health Registry (VHR). The registry must include information about each person who served as a member of the Armed Forces in OEF/OIF who exhibits symptoms associated with TBI and who applies for services or files a disability claim. Section 1704 also stipulates that the VA shall collaborate with facilities that conduct research on rehabilitation for persons with TBI, facilities that receive grants for such research from the National Institute on Disability and Rehabilitation Research (NIDRR), DVBC, and other relevant programs of the Federal government, including the Defense Centers of Excellence.

Pursuant to this statutory requirement, VA sought an interagency agreement with NIDRR through which VA can draw upon the expertise of NIDRR's TBI Model Systems (TBIMS) program—the largest longitudinal database for TBI in the country. With NIDRR's assistance, VA is working to develop a TBI VHR housed on secure web-based portal at the TBIMS National Data and Statistical Center in Denver, Colorado. The portal will be accessible to authorized VA users and developed in compliance with VA data security regulations, HIPAA, and Privacy Act considerations. A custom-built web portal will enable authorized VA users to access data to support policy development and evaluation; assess resource usage and health-care needs; determine incidence and prevalence of TBI among OEF/OIF veterans; and evaluate course of treatment and outcomes.

Characterizing the prevalence and long-term consequences of military service-related TBI in the civilian system will require even greater manpower and economic resources to ensure that appropriate linkages

are made between the military, VA, and civilian health care systems. There is also an absence of fully valid and reliable screening instruments to diagnose TBI, especially cases of mild TBI, and the co-occurrence of cases of PTSD and TBI that are not correctly classified. Moreover, the natural history of combat-related TBI, especially its long-term consequences, has not yet been fully explained (*Ramchand et al., 2008*).

Because the VA system provides medical care to a subset of all eligible veterans, conducting studies of the prevalence of military service-related TBI will likely require the use of civilian databases, for example, the TBIMS or the Framingham Study. The Framingham Study has been conducting research on neurological disorders for decades. In 1997, for example, it began a post-mortem Brain Tissue Donation Program that has enrolled more than 600 participants and analyzed approximately 100 brains—yielding substantial information on genetics, the environment, the aging process, stroke, Alzheimer's disease, Parkinson's disease, or other neurological illness. Because the program can also document the extent of a disease, military service-related TBI and civilian TBI could also be studied.

Civilian Population

Certain challenges related to TBI prevalence in military-associated cases also affect civilian populations. An estimated 3.2 million Americans are living with long-term consequences from TBI (*Zaloshnja, Miller, Langlois, and Selassie, 2008*). This estimate reflects the use of updated methodology and is based on the results of statistical modeling and analysis of 2005 TBI hospitalization incidence data from Maryland, Vermont, and New Jersey. A previous CDC estimate indicated that approximately 2% (approximately 5 million) of the U.S. population live with the long-term consequences of TBI (*CDC, 1999*). These estimates, likely underestimate the prevalence of TBI-related disability as they do not include persons with TBI who were treated and released from emergency departments or other health-care settings, those who were treated in a DoD or VA facility, or who did not seek treatment. With current resources and limitations in surveillance methodology, the prevalence of TBI-related impairment and disability in the United States cannot be measured with confidence (*Coronado et al., 2009*).

Interview surveys that attempt to link history of TBI to a disability are prone to underreporting, mainly because of poor or no recall of past injuries (*Walker, Logan, Leukefeld, and Stevenson, 2004*). Population-based prospective cohort studies of persons recently diagnosed with an acute TBI might be more promising. Using this method, two studies examined the occurrence of TBI-related disability in representative samples of persons followed 1 or more years after hospitalization for TBI (*Whiteneck et al., 2004; Pickelsimer et al., 2007*). Since information on annual disability (*Selassie et al., 2008*) does not account for the cumulative prevalence of TBI, statistical methods must be applied to estimate such figures

(Zaloshnja *et al.*, 2008). The true prevalence of military and civilian TBI and TBI-related disability in the general U.S. population will remain elusive without continued investment in sound, long-term, representative follow-up studies or adding questions into existing national surveys, such as, NHIS, NHANES, and SLAITS.

The Economic Costs of TBI

The economic costs of TBI are difficult to estimate in both the military and civilian populations. Some of the reasons include 1) uncertainty about which outcomes can be attributed specifically to TBI, 2) variability in the types of TBI-related outcomes, 3) inability to measure the precision of cost estimates, and 4) limited resources (including data available for research) to conduct more complex and long-term economic studies. Some estimates are more straightforward whereas others can only be derived using a large number of assumptions and complicated econometric and statistical methods that distance the estimates from actual cost data (Coronado *et al.*, 2009).

Because of these difficulties, few attempts to estimate the costs of TBI have been undertaken, especially those costs faced by society as a whole. One recent study estimated the annual economic burden of TBI in the United States in year 2000, including direct medical and rehabilitation costs and societal costs, to be \$60 billion (Finkelstein, Corso, and Miller, 2006). The few studies that have attempted to estimate the cost of TBI injury among military SMs have had major limitations such as including only hospitalized cases of TBI and studies with small sample sizes. Despite these limitations, available data suggest that the total costs might be substantial (Ommaya, Ommaya, Dannenberg, and Salazar, 1996; Wallsten and Kosec, 2005; Eibner, Ringel, Kilmer, Pacula, and Diaz, 2008).

Certain studies have attempted to estimate the costs of TBIs that have resulted from OEF/OIF. One study estimated that the total lifetime cost of severe TBIs sustained in OIF through August 2005 to be \$16 billion (Wallsten and Kosec, 2005), but it has two limitations that must be considered. First, the authors estimated that 20% of all SMs wounded in OIF had a severe TBI, which is high when compared with DoD data. DoD TBI surveillance data indicate that only 1% of all SMs with a TBI during that time sustained a severe TBI (Defense and Veterans Brain Injury Center, unpublished data). Furthermore, the estimated proportion was obtained from a newspaper article rather than actual surveillance data. The second limitation was that the lifetime cost of severe TBI was based on numerous assumptions and estimated costs that might not be applicable to SMs with TBI. For example, the data used to estimate lifetime-treatment costs was derived from civilian sources and might not be applicable to the DoD and VA health systems. A 1996 study of costs for acute treatment of TBI among SMs and their beneficiaries suggests that costs in military hospitals might be lower than costs in private hospitals (Ommaya, 1996).

Furthermore, a highly variable and controversial cost, known as the value of a statistical life (VSL), was used to estimate other aspects of the lifetime cost of severe TBI, such as lost wages. The VSL is the value that a person places on a marginal change in their likelihood of death; it is estimated by looking at the risks that people are voluntarily willing to take and how much they must be paid for taking them (*Viscusi and Aldy, 2003*). A review of literature about VSL indicated that it can vary from \$4 million to \$9 million per life, depending on the assumptions made and methodology used to estimate it (*Viscusi and Aldy, 2003*).

In 2008 the RAND Corporation released a report estimating TBI costs resulting from OEF/OIF (*Eibner et al., 2008*). The report provided cost estimates for acute treatment and rehabilitation, mortality and suicide, and lost income. In the first year following injury, costs were estimated to be \$27,260 to \$32,760 per case for mild TBI and up to \$408,520 for those with moderate to severe injury. The estimated overall cost for acute treatment of deployment-related TBIs in the hospital in 2005 ranged from \$6.9 million to \$14.3 million. The estimated cost of inpatient rehabilitation was \$1.9 million and the estimated cost of outpatient rehabilitation ranged from \$377,000 to \$907,000. The estimated costs associated with mortality from deployment-related TBIs in 2005 ranged from \$67 million to \$89 million, unemployment associated with deployment-related TBI was \$13 million, and reduced wages associated with deployment-related TBI was \$1.2 million.

These estimates have the same serious limitations as those calculated by Wallsten and Kosec in 2005. Treatment cost estimates are derived from civilian cost data that might be different from costs incurred by military hospitals. In addition, estimated costs resulting from the death of a SM are based on the VSL, which can vary substantially. Another serious limitation is that the estimated treatment cost per case of mild TBI in the RAND report is for SMs who required hospitalization. This estimate is likely too high for most SMs with a TBI because most persons with mild TBI only are not hospitalized. More problematic is the lack of evidence regarding the extent of long-term disability resulting from blast exposure and whether other major health effects such as neurodegenerative disorders might arise years later.

Using 1992 data, the Defense and Veterans Head Injury Program, now DVBIC, published estimates of TBI-related costs in the military (*Ommaya et al., 1996*). These costs were estimated from a study of 5,568 SMs and other beneficiaries of the MHS who were hospitalized for TBI in both military and private hospitals in FY 1992. The authors attempted to compare costs from both types of hospitals. Although outdated, these estimates are the only ones known to be published that were derived from actual costs incurred by the MHS. The overall estimated cost of TBI-related hospitalizations in the U.S. military medical system in 1992 was approximately \$42 million (*Ommaya, 1996*).

Current military per-patient hospitalization costs associated with TBI in the military can be estimated by adjusting Ommaya et al.'s estimates for inflation. This method has been used by others to update older cost estimates (*Thurman, 2001*). Table 8 presents Ommaya et al.'s per patient cost estimates adjusted to 2011 dollars. However, these estimates have limited reliability because the inflation factor used for adjustment was not just for hospitalizations, and included all types of health care. Furthermore, the inflation rate for TBI treatment costs might be different from treatment cost inflation for other conditions.

Table 8. Estimated Median Acute Hospitalization Cost per Patient for Military Personnel Hospitalized with TBI (in 2011 Dollars)

TBI Characteristics	Cost/Patient [†]	
	Military Hospital	Private Hospital
TBI with no LOC*	\$1,773	\$5,308
TBI with any LOC*	\$2,299	\$8,216
TBI with LOC of unknown duration	\$2,901	\$6,051
TBI with LOC >1 hour	\$8,237	\$22,744
TBI with other type of injury	\$10,245	\$10,991
TBI with other health condition	\$3,967	\$7,835

* LOC=loss of consciousness.

† Costs presented in this table are medians of actual costs incurred by military hospitals and allowable expenses paid by the MHS to private hospitals in fiscal year 1992 (*Ommaya et al.1996*). These costs have been adjusted to 2011 dollars using the U.S. city average CPI for medical care (*US Bureau of Labor Statistics*). Military and private hospital cost estimates might not be directly comparable because of the different methods used to compute them. However, the military hospital costs include the clinic proportion of total facility expenses including construction, maintenance, staff wages, equipment, and supplies.

Source: Defense and Veterans Brain Injury Center.

Estimating the Cost of TBI

The only way to obtain realistic estimates of TBI-related costs in the military is to perform a comprehensive long-term study that obtains actual cost data at the level of individual patients, based on specific TBI characteristics, treatments, comorbidities, health consequences, rehabilitation needs and long-term disability. Such a study must follow injured SMs and veterans over a long period to collect accurate cost data for services they receive. It must also account for the effects of improvements in technology and treatment on costs to ensure compatibility of cost estimates from different periods. To obtain information about the economic consequences of TBI-related mortality, families of those SMs who died from TBIs also can provide insight. Without continued study of the outcomes of military service-related TBI, estimates of the total costs of TBI to society will continue to rely mostly on assumptions and complex economic modeling techniques that might result in estimates that are imprecise or unreliable.

VIII. Prevention

Preventing TBI

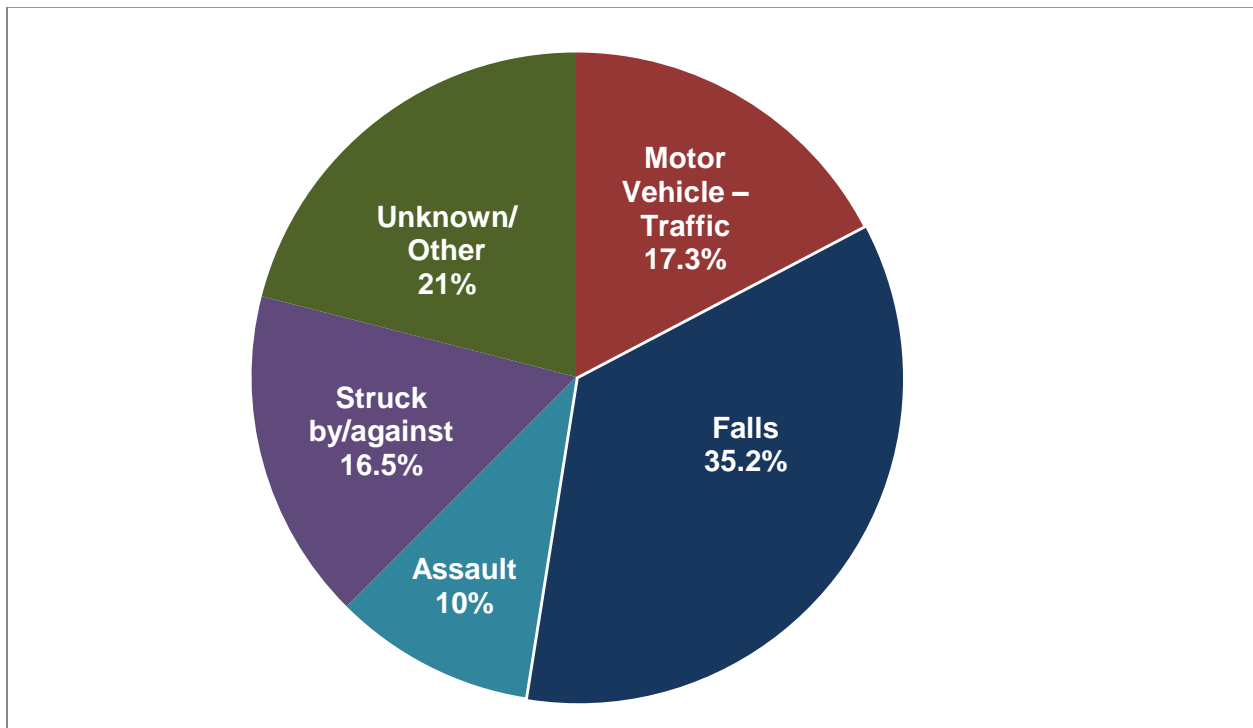
Many potential ways exist to prevent TBI and the poor outcomes that can result when TBIs are sustained. Improving outcomes from TBI includes pre-hospital care and faster transport to medical centers. Early detection with better diagnostic tools also can lead to better outcomes when paired with timely interventions. Reducing risk of injury and preventing further damage after initial injury are essential to ensuring improved outcomes. Protective gear, including helmets, can prevent or reduce the severity of TBI. Helmet use is recommended in many sports and combat situations, and improved helmets with stronger and lighter weight ballistic materials for the helmet's outer shell as well as new helmet pads to provide greater blunt impact protection are under development as part of a developmental program known as the Soldier Protection System (SPS).

The goal of SPS is to do development and testing during FY13 and FY14 with the intention of beginning production in FY15. The use of seatbelts in motor vehicles is required, as are motorcycle helmets for SMs in the non-deployed setting. Although not yet well understood, chest protection also seems to reduce blast TBI severity in rats, possibly by preventing systemic changes in blood pressure (*Long et al., 2009*).

Enhanced forms of hard armor ballistic plates, improved outer tactical vests, pelvic protection systems, ballistic eyewear, and limited numbers of face shields and lower mandible protectors have already been fielded and will be further enhanced through the SPS. All of these improvements to personal protective gear are crucial advances for SMs moving outside of the forward operating bases and especially when dismounted from a vehicle. In addition, improved vehicle armor has also been instituted over the last several years to mitigate blast effects on vehicle occupants. Improvements in protective eyewear not only minimize fragment penetration to the eyes but also penetration to the brain.

Among veterans and SMs returning to the United States who are no longer at risk for deployment-related injuries, the prevention of TBI is similar to the civilian population (Figure 6). The majority of TBIs, either occurring alone or in conjunction to other injuries, are caused by several factors (e.g., falls, motor vehicle traffic crashes, and striking or being struck by an object or person, or acts of violence against oneself and others) (*Faul et al., 2010*).

Figure 6. Fatal and Nonfatal Traumatic Brain Injuries either occurring alone or in conjunction with other injuries by Mechanism - US, 2002-2006.



Source: Faul M, Xu L, Wald MM, Coronado VG, 2010.

Preventing TBI Associated with Motor Vehicle Traffic Crashes

Motor vehicle crashes and resulting injuries are a serious public health problem among civilian and military populations. Implementing prevention strategies to decrease the occurrence of these incidents is a public health priority.

Mortality rates from severe TBI in motor vehicle crashes (a leading cause of severe TBI in civilians and SMs) have declined since the 1970's, but remain unacceptably high. Programs and policies that encourage improvements in vehicle design, the road environment, and reductions in risky behaviors such as speeding, alcohol-impaired and distracted driving can reduce the risk of crashes. Activities that encourage improvements in occupant protection such as appropriate seat belt use and air bags can reduce the risk of injury in the event of a crash. Programs and policies to protect motorcyclists from injury include those that promote the use of helmets. Risks to pedestrians can be reduced through various measures that include vehicle, environmental and behavioral factors. (NHTSA, 2011; Elvik, Høy, Vaa, and Sørensen, 2009)

Preventing TBI Associated with Falls

Causes of falls vary, whether they occur as a result of falls among adults who might slip in their homes or teenagers who fall while engaging in athletic activities. Among older adults, fall-related injuries can be reduced by programs supporting regular weight-bearing and balance exercises; over the counter and prescription medication review to reduce use of those causing dizziness or drowsiness; annual eye exams to optimize vision; and home modifications when prescribed by an occupational therapist (e.g., reducing tripping hazards, adding grab bars inside and outside the tub or shower and next to the toilet, adding stair railings and improving lighting) (*Stevens, 2010; Gillespie et.al., 2009*). Injuries from falls among working-aged adults are most commonly experienced on the same level, on/from stairs or steps, or from a height such as on ladders or scaffolds; fall injuries during work are similar to those that are non-work related, suggesting that programs and policies successful in one arena might be applicable to others (*Smith, Sorock, Wellman, Courtney, and Pransky, 2006*).

Preventing TBI Caused by Striking or Being Struck

Struck by/against events are those in which a person was struck and unintentionally injured by another person or object (e.g., falling debris, a ball in sports) or a person struck against an object, such as a person struck against a wall or a collision between two or more people (*Rutland-Brown et. al., 2006*). Many sports-related TBIs are included in this category. Sports and recreation-related TBIs can be prevented by programs and policies encouraging appropriate use of safety gear (such as helmets), environmental changes (such as padding goal posts and padding or removing other obstacles), strict officiating and enforcement of rules and sportsmanship, and examination of effects of select rule changes (*Gilchrist, Saluja, and Marshall, 2007*).

Rest before returning to play or work after even mild TBI is equally important. Re-injury leading to sudden death (second-impact syndrome) has been reported in some athletes who returned to sports after symptomatic concussions (*Franklin, 2012*). As described in the In-theater Screening section under Diagnosis, the military has implemented required rest periods following TBI.

Preventing TBI Associated with Intentional Injury

In addition to assaults, TBIs can result from self-directed violence, which is included as “other/unknown” in Figure 6. Interpersonal conflicts, relationship problems, and alcohol/drug use are common circumstances preceding homicides and suicides (*Karch, Logan, and Patel, 2011*). Suicide and violence-prevention strategies can reduce the risk of TBI by enhancing social problem solving and coping skills,

improving access and reducing barriers to appropriate mental health care, and providing support and services to those struggling with multiple life stresses, including financial, substance abuse, and family violence-related challenges (*Lubell and Vetter, 2006; Goldsmith, Pellmar, Kleinman, and Bunney, 2002; CSPV, 2012*). In addition to individual and family-level factors, suicide and violence prevention strategies also need to address community-level factors such as norms about violence and help-seeking, access to education and employment opportunities, and the level of connectedness or social bonds among people (*CDC, 2010*).

Prevention of Secondary Brain Injury

Improved Emergency Medical Services (EMS) or pre-hospital care has substantially improved outcomes from TBI. In the prevention of secondary brain injury, pre-hospital care focuses on keeping airways open, maintaining blood and oxygen flow to the brain, and controlling blood pressure and hemorrhage, which can all improve survival and reduce long-term damage. Implementation of other types of early interventions to prevent secondary damage (e.g., hypothermia and administering osmotic agents) might depend on the situation, nearby infrastructure, and availability of experienced emergency teams (*Boer et al, 2012*).

Biomarkers for diagnosis also have the potential to improve early intervention and prevention of secondary injury. Research to identify TBI biomarkers is ongoing (*Schiff, 2012; Papa, 2012*). Some gene variants might have positive or negative effects on TBI outcomes (*Dardiotis et al., 2010; Miller et al., 2010; Al Nimer et al., 2012; Darrah et al., 2012*).

IX. Recommendations

CDC, NIH, DoD and VA acknowledge that the military service-related TBI cases will be difficult to identify in civilian systems because several of these cases occurred in the past (e.g., during the early years of OIF). However, the majority of the incident and prevalent cases of military service-related TBI can be identified through TBI screening and reporting conducted by DoD and VA. Identifying cases of TBI not diagnosed while in service or by the VA system, although more difficult, might be possible by conducting surveys on veteran status; by educating health-care providers to ask their patients with TBI-related signs and symptoms about previous military service and risk factors, and to use, when appropriate, the terrorism and war-related ICD-9-CM external cause of injury (E) codes.

To accomplish the mandates of the *TBI Act of 2008* and to address identified public health concerns, CDC, NIH, DoD, and VA produced general recommendations applicable to all federal agencies and departments. In addition, recommendations specific to each agency and department might be useful for guiding their interactions with stakeholders. Underlying these recommendations is a commitment to using data sources that are accessible, valid, and reliable.

General Recommendations

CDC, NIH, DoD, and VA concur on the following key recommendations:

- **STRENGTHEN COLLABORATION:** Continue to foster and strengthen collaboration related to identifying military service-related TBI among current military SMs and veterans, including those who do not seek care from the military or VA health-care systems. Improving data collection and sources will be emphasized.
- **UTILIZE STANDARD DEFINITIONS:** Improve reporting through federal agencies that use and promote standard clinical and surveillance definitions and severity classification of TBI among U.S. military and civilian health-care providers and researchers.
- **ENHANCE CODING AND CLASSIFICATION:** Continue to foster and strengthen collaboration with each other and other relevant organizations on coding and classification of TBI. All four participating agencies should continue to meet with professional, academic, health care, and coding organizations to discuss improvements in ICD-10-CM, including the classification of TBI and concussion and differentiation of self-limited and persistent symptoms.

Revise the intracranial injury code set in ICD-10-CM to improve the accuracy of disease coding consistent with accepted case definitions before ICD-10-CM implementation on October 1, 2014.

- **IMPROVE DISSEMINATION:** Promote dissemination of information by federal agencies to non-VA facilities regarding TBI services available through the VA health-care system since 2007, including baseline screening and follow-up assessment and evaluation.
- **BUILD EVIDENCE BASE:** Continue research on the neurological consequences of blast events and TBI among SMs and veterans; the research should include 1) systematic neuropathological study in blast-exposed SM's and veterans who have died; 2) correlation of neuropathological and brain imaging findings; 3) prospective investigation of whether blast exposure increases risk for subsequent cognitive decline and neurodegenerative diseases such as chronic traumatic encephalopathy, Alzheimer's, Parkinson's and amyotrophic lateral sclerosis.

Recommendations to Improve TBI Diagnosis and Treatment

Military Health System

Development and validation of helmet-mounted sensor systems (HMSS). The Vice Chief of Staff of the Army (VCSA) directed that soldier combat helmets be fitted with electronic sensors that can record helmet response to dynamic events (blunt impacts, ballistic impacts, and/or exposure to blast events). Sensors that could be able to predict when someone has reached a threshold for exposures are under development (*McAllister et al., 2012; Broglio, Surma, and Ashton-Miller, 2012*). Development of a signal library of carefully controlled blunt, ballistic, and blast signatures will allow indirect identification of mechanical insults (exposure) of HMSS signals from the field. This will allow the development of an injury assessment tool, as the first approximation of a dose-response curve. Expanding the use of these sensors to the USMC and others with these types of exposures will be based on the efficacy of the Army's initial use of them.

Development of therapeutics to improve the outcome of mild, moderate, and severe TBI. Despite advances in basic and clinical research and neurological intensive care in recent years, and despite promising pre-clinical data, most of the clinical trials have failed to yield any significant improvement in TBI outcome. Nevertheless, DoD is currently exploring combination drug therapies, novel drugs, and small-volume resuscitation liquids (i.e., fluids administered to patients in relatively small amounts to restore and maintain adequate blood circulation following severe blood loss) for their ability to improve functional recovery from TBI.

Development of animal/computer model for TBI, most importantly for blast TBI. No validated animal model exists for blast TBI. Development of a clinically and physiologically relevant model is critical for the successful validation of helmet-mounted sensors, SMs' protective armor, and for the evaluation of therapeutic interventions. Through a collaboration among Joint Improvised Explosive Device Defeat Organization (JIEDDO), DVBIC, and the Institute of Soldier Nanotechnology at MIT, the most advanced computer model of the brain and blast effects on the brain has been developed (*Moore et al., 2009*). Work to determine characteristic pathology of human blast injury is underway.

Identification of biomarker(s) to identify mild TBI/assay to discriminate between mild TBI and PTSD. Distinguishing between mild TBI and PTSD is complicated because of partial overlap in symptoms, including irritability, memory and concentration difficulties. The development of rapid, non-invasive, reliable testing is needed to discriminate between the subtle cognitive deficits of mild TBI and PTSD. Serum biomarkers such as S-100 protein show promise, although utility has been limited by its short half-life. Other biomarkers, including lactate dehydrogenase, neuron specific enolase, also might be useful but lack sensitivity and specificity (*Ingebrigtsen and Romner, 2002; Pike et al., 2004; Ringger et al., 2004; Pineda et al., 2007; Papa et al., 2010*). Preliminary results from ongoing serum biomarker studies are more promising. If these injuries could be detected objectively, quickly, and non-invasively, medical personnel would be able to begin early interventions.

VA Health System

The VA Office of Research and Development sponsored a State of the Art Conference in 2009 to identify research priorities for TBI. Representatives from DoD, NIH, DVBIC, and VA attended. A planning committee commissioned background papers for workgroup discussions. The papers examined topics such as the pathology of blast-related brain injury; diagnosis; comorbidities, including mental health issues and sensory deficits; brain imaging; care management; community reintegration; and, the role of veterans' families in TBI care. Six work groups focused on different aspects of TBI (i.e., basic science, neuroimaging, sensory deficits, comorbidities, rehabilitation and community reintegration, and care management) and then presented summaries of their findings and research recommendations for discussion with the entire group. An issue of the *Journal of Rehabilitation and Development* was dedicated to this meeting (Volume 46, Issue 6) and the research recommendations of the work groups were grouped into three main categories: (1) Diagnosing TBI (e.g., screening and imaging), (2) understanding short- and long-term effects of TBI (e.g., co-occurring conditions, severity, neurodegenerative disease), (3) understanding existing treatment approaches and developing new treatments (e.g., neurotrophins, neuroplasticity, case-management, community re-integration).

Civilian Health System

Although many opportunities exist to advance opportunities for TBI research and improve diagnosis and treatment in the civilian health system—that is, the organization of people, institutions, and resources to deliver health care services for the general population, a few strategic future directions for the field, with leadership from CDC, NIH, DoD, and the VA, include the following:

Developing a pathoanatomical classification system for TBI. During the past two decades much has been learned about TBI at a cellular and molecular level. Applying this knowledge to develop effective therapies for specific subtypes of injury, rather than for the entire constellation of injuries, is likely the key to developing successful interventions. Characterizing the pathophysiology and temporal evolution of these subtypes of injury would provide a foundation for identifying therapeutic targets and the window of opportunity for using them. It would provide the necessary scientific rationale for testing single and combined agents to hit these targets to attenuate injury or promote repair processes. A new classification system based on the pathoanatomy, rather than on the Glasgow Coma Scale also would inform chemical biomarker development and correlation of pathology with neuroimaging for these subtypes of injury. Surrogate markers would make it possible to identify people who have these subtypes of injury and also to monitor the biological effects of experimental interventions during clinical trials. Overall, breaking down the complex problem that TBI presents into smaller, more manageable parts should make it a more tractable problem.

Discovering the biological basis of mild TBI. This builds upon the previous recommendation because the milder injuries are often less complex than more severe injuries. Current research should be further enhanced to identify the biological mechanisms responsible for persistent deficits such as PCS and concurrent conditions including PTSD and to develop diagnostic tools for persons currently classified as having a mild TBI. Because a subset of persons described as having a mild TBI experience persistent disabilities, the term “mild” is often misleading.

Developing more effective and efficient approaches for preclinical drug development.

Approximately 130 agents with proven preclinical efficacy for TBI are available, and more are under development and testing (*Marklund, Bakshi, Castelbuono, Conte, and McIntosh, 2006*). An efficient testing system for optimizing the dose and timing and for comparing effectiveness of interventions, alone and in combination, is needed to accelerate therapy development.

Facilitating data sharing. To date, much of the research on TBI has been small studies across agencies and centers, without definitively answering important research questions. A federal interagency project

developed standardized terminology and a data dictionary for TBI to enable data sharing and secondary analysis and meta-analysis. In addition, the Federal Interagency TBI Research Informatics, a DoD and NIH collaboration, is available for aggregating and sharing data. Use across federal agencies is encouraged. Ongoing and new research on biomarkers would be accelerated by sharing data and supporting larger, multicenter projects to rapidly obtain greater numbers of samples and subjects. This is also true for advancing the development of neuroimaging and other diagnostic tools and biomarkers and for the validation of outcome measurement tools for clinical trials.

Coordinating and collaborating on clinical studies for TBI. A large, prospective observational comparative effectiveness research study is an efficient way to address some of the major gaps in knowledge regarding the validity of diagnostic tools and biomarkers and the effectiveness of various medical and surgical interventions for TBI. A coordinated and collaborative effort would enhance trial designs, increase the rate of subject enrollment and data collection, and optimize statistical analysis and data interpretation. Studies would be completed more quickly, and if successful, this collaborative approach would also facilitate implementation of these valid diagnostic tools, biomarkers, and proven interventions into clinical practice. TBI clinical studies should include subjects across the spectrum of injury severity, across the lifespan, during acute and chronic stages of injury, and should evaluate pharmacologic and non-pharmacologic interventions.

Methodological Concerns and Research Priorities

Evidence indicates that continued research is needed to 1) determine the magnitude and socioeconomic and medical impact of military service-related TBI; 2) identify preventable and modifiable risk factors to reduce injury; 3) reduce impairment and disability; and 4) develop and evaluate evidence-based interventions.

CDC, NIH, DoD, and VA recommend that studies of the incidence and prevalence of military service-related TBI must include the following:

- Designed with clear and relevant research questions and methodology;
- Involve statistically representative populations;
- Allow determination of risk factors and the socioeconomic and demographic characteristics of these populations; and
- Allow characterization of the acute and long-term outcomes for TBI.

Such studies could assist in developing primary, secondary, or tertiary prevention programs, especially if modifiable risk factors are identified. Moreover, prevalence studies have the potential to identify gaps and guide resource allocation.

CDC, NIH, DoD, and VA also recommend continued evaluation and improvement of screening tools for TBI, especially tools used to identify milder forms of TBI. These studies are important to assess the incidence, prevalence, and long-term consequences of TBI, and the availability of and access to TBI-related support and rehabilitation services.

Finally, the four agencies also recognize that the recommendations in this report and all TBI-related management and treatment guidelines used by CDC, NIH, DoD, and VA need to be updated every 3 to 5 years to incorporate findings of epidemiologic, clinical, social, and behavioral research. The agencies are already working together through the Common Data Elements project and this provides one useful forum for regular reviews of important issues.

Morbidity and mortality associated with TBI affect civilian, military, and veteran populations. The leading causes of these injuries vary according to age and sex of injured persons. Therefore, these recommendations, prepared by the four participating agencies, will ensure that present practices in diagnosis of TBI and treatment for those persons affected by it will be sustained and improved. Additional progress to improve structural changes in defining TBI, improving surveillance systems, and recording epidemiologic data will assist in forming an achievable plan for the future.

Recommendations to Improve TBI Surveillance

Military Health System

To better estimate the incidence and prevalence of TBI in the MHS, DoD recommends:

- Screening all SMs as soon as possible following a possible TBI-causing event,
- Using the MACE or other appropriate screening tools; and
- Training all medical personnel (from theater through the VA system) in the detection and correct coding of TBI.
- Improving record keeping and standardizing multiple and disparate databases in the U.S. military using standardized common, streamlined questionnaires with variable complexity, depending on the level of care provided by the reporting medical facility (e.g., uncomplicated questionnaires for medics in theater to complex questionnaires for tertiary care facilities.) Coordination of databases has been initiated among DoD, VA, and NIDRR model systems.

Veterans Health System

Recommendations to better estimate the incidence and prevalence of TBI in the VA include:

- Continue screening all OEF/ OIF veterans upon contact with the VA health system;
- Training of all medical personnel in the detection of TBI and in the methods to correctly code for TBI; and,
- Timely and comprehensive follow-up evaluation of all veterans who screen positive for possible TBI.

Civilian Health System

Recommendations to improve surveillance of TBI in the civilian health system include:

- Expand surveillance activities by ensuring that TBI surveillance is part of comprehensive state injury surveillance systems,
- Continue to collaborate with DoD and VA to identify strategies for improving surveillance of TBI among veterans.

Methods for Detecting TBI Incidence and Prevalence

Military Health System

Key areas have been identified to improve measuring the incidence and prevalence of TBI in the military system, including case ascertainment; case documentation and reporting; follow-up; and, data dissemination. Specifically:

- Continue to use the established guidelines and strategies for identifying and treating TBI as described in this report; evaluate and update such guidelines every 3 years to reflect the advances in methods and technology.
- Produce portable data collection instruments to capture TBI data in the military, the VA, and civilian systems. These instruments should be specific to the level of care (e.g., a standard instrument to be used in theater only).
- Use TBI-specific diagnostic and external cause ICD-10 and ICD-9-CM codes to identify new cases (incidence) and history codes to ensure capturing prevalence data, recognizing the challenges of current coding and classification of TBI.
- Expand current care coordination and case management programs within DoD and VA to facilitate follow-up care and to document patients with persistent symptoms.

- Coordinate and exchange aggregated-level data (excluding personal identifiers) with CDC/NCIPC to produce a yearly report on TBI in the military by race/ethnicity, sex, age group, and risk factors. This report also should include information on the clinical characteristics, comorbidities, and concurrent injuries in persons with acute and chronic TBI.

VA Health System

Key areas have been identified to improve measuring the incidence and prevalence of TBI in the VA including:

- VA health-care system facilities should screen for TBI among eligible OEF/OIF veterans upon contact with the VA health system and further evaluate those who screen positive.
- Timely and comprehensive follow-up evaluation should be offered to veterans who screen positive for possible TBI.
- Medical personnel should be trained in TBI and in the methods to correctly code for TBI, recognizing the challenges with regard to current coding and classification of TBI.

Civilian Health System

Key areas have been identified to improve measuring the incidence and prevalence of TBI in the civilian health system including:

- Enhance capabilities to conduct surveillance at the state level; using national surveys, including public and private telephone and internet-based systems; and encouraging civilian and military health-care providers to document and report war and terrorism-related external cause-of-injury codes (E-codes).
- For all federally funded TBI research, use the newly recommended common operational clinical and surveillance definitions described earlier in this report, including all TBI-related ICD-10 and ICD-9-CM diagnostic, external cause of injury, terrorism, and war-related codes.
- Reporting incident cases of military service-related TBI while SMs are in the military. Collaborate with DoD, VA, and Defense Medical Surveillance System to share aggregated level data via CDC, and through peer and non-peer reviewed publications, periodicals, mass media, and books. Aggregate DoD TBI surveillance data is currently available at <http://www.dvbic.org/dod-worldwide-numbers-tbi>.

- Identification, surveillance, and burden of cases of military service-related TBI in veterans seeking care outside the VA system, which might include those who have not sought medical care or were not diagnosed while SMs in the military or VA health-care systems.
- Initiate research that examines disability, quality of life, and long-term outcomes associated with all severity levels of TBI.
- Add questions to federal or state sponsored population-based follow-up studies to determine the occurrence and the epidemiologic and clinical characteristics of the long-term consequences of TBI among eligible persons.
- Use existing civilian and military-related TBI surveillance systems and registries to develop prospective follow-up studies to determine the long-term epidemiologic, clinical, cognitive, and socioeconomic characteristics among eligible persons; and to determine if these persons have access to and receive appropriate social and rehabilitation services.
- Share TBI systems and registries available in the civilian, DoD, and VA Health Systems to determine the occurrence and the long-term medical and socioeconomic characteristics of TBI among eligible persons.
- Assess the burden of military service-related TBI in veterans receiving care outside the VA system. Routinely use the recommended federal TBI definitions when analyzing data from large national surveys and surveillance systems conducted by CDC/NCHS and other federal agencies (see Data Sources in Chapter VI).

Recommendations to Improve TBI Prevention

Ultimately the goal is to prevent the occurrence of TBI for SMs on- and off-duty. During off-duty hours and those retired from active duty, the risks are similar to the civilian population, with falls and motor-vehicle crashes among the major causes. Active-duty SMs face additional risk from blast and penetrating injuries. Further research is needed to ensure these risks are reduced. Where evidence-based strategies exist, it is imperative that there is strict adherence to those practices. The recommendations below focus on continued research to reduce risk factors, improve the quality of protective equipment, and ensure that current guidelines and evidence-based strategies are adhered.

- Enhance research to reduce the risk of TBI from blast injury.

- Research to promote adherence to current guidelines on returning to active-duty following TBI.
- Conduct more research to improve the quality of protective equipment such as helmets.
- Strengthen evidence on the risk and protective factors associated with a TBI or the prevention of a TBI. Research may include but is not limited to reducing use of alcohol, ensuring adherence to use of seatbelts, motorcycle helmets and other protective equipment.
- Provide meaningful education to veterans who have sustained a TBI, their families and their clinicians about the elevated risk for subsequent TBI and actions that can be undertaken to mitigate this risk.

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List of Acronyms

AFIP: Armed Forces Institute of Pathology

AMS: Army Medical Surveillance Activity

BRFSS: Behavioral Risk Factor Surveillance System

BROS: Blind Rehabilitation Outpatient Specialists

BTBIS: Brief TBI Survey

BTF: Brain Trauma Foundation

BTP: Blast Tracker Program

CDC: Centers for Disease Control and Prevention

CDMRP: Congressionally Directed Medical Research Program

CIDNE: Combined Information Data Network Exchange

CNRM: Center for Neuroscience and Regenerative Medicine

DHHS: Department of Health and Human Services

DHMIS: Defense Health Information Management System

DoD: Department of Defense

DMDC: Defense Manpower Data Center

DVBIC: Defense and Veterans Brain Injury Center

FRCP: Federal Recovery Coordination Center

FRC: Federal Recovery Coordinator

FIRP: Federal Individual Recovery Plan

GCS: Glasgow Coma Scale

HRSA: Health Resources and Services Administration

IOM: Institute of Medicine

JIEDDO: Joint Improvised Explosive Device Defeat Organization

LOC: Loss of consciousness

LRMC: Landstuhl Regional Medical Center

MACE: Military Acute Concussion Evaluation

MCS: Millennium Cohort Study

MHS: Military Health System

NCAT: Neurocognitive Assessment Tool

NCHS: National Center for Health Statistics

NCIPC: National Center for Injury Prevention and Control

NCMRR: National Center on Medical Rehabilitation Research

NDAA: National Defense Authorization Act

NDSC: National Data and Statistical Center

NHANES: National Health and Nutrition Examination Survey

NHIS: National Health Interview Survey

NHLBI: National Heart, Lung, and Blood Institute

NIA: National Institute of Aging

NIAAA: National Institute on Alcohol Abuse and Alcoholism

NICHD: Eunice Kennedy Shriver National Institute of Child Health and Human Development

NIDA: National Institute on Drug Abuse

NIDRR: National Institute on Disability and Rehabilitation Research

NIH: National Institutes of Health

NIMH: National Institute of Mental Health

NINDS: National Institute of Neurological Disorders and Stroke

NINR: National Institute on Nursing Research

OAFME: Office of The Armed Forces Medical Examiner

OEF: Operation Enduring Freedom

OIF: Operation Iraq Freedom

OPD: Outpatient department

PCS: Post-concussive syndrome

PDHA: Post-deployment health assessments

PH: Psychological health

PHI: Protected health information

PRC: Polytrauma Rehabilitation Center

PTSD: Posttraumatic stress disorder

QUERI: Quality Enhancement Research Initiative

SLAITS: State and Local Area Integrated Telephone Survey

SM: Service member

SME: Subject matter expert

SMs: Service members

TBI: Traumatic brain injury

TBIMS: TBI Model Systems

TMDS: Theater Medical Data Store

TSWG: Technical Support Working Group

USAMRMC: U.S. Army Medical Research and Materiel Command

USUHS: Uniformed Services University of the Health Sciences

VA: Department of Veterans Affairs

VCSA: Vice Chief of Staff of the Army

VHA: Veterans Health Administration

VHR: Veterans Health Registry

VIST: Visual Impairment Service Team

WARCAT: Warrior Administered Retrospective Casualty Assessment Tool