



Military Medicine

International Journal of AMSUS

Psychological Health and Traumatic Brain Injury



SPECIAL ISSUE

August 2012

Supplement to Military Medicine, Volume 177, Number 8

Guest Editors

Jay M. Uomoto, Ph.D. | Robert J. Ursano, M.D.

Psychological Health and Traumatic Brain Injury Treatment Resources

Co-occurring Conditions Toolkit: Mild Traumatic Brain Injury and Psychological Health

The “Co-occurring Conditions Toolkit: Mild Traumatic Brain Injury and Psychological Health” offers guidance to primary care providers in the assessment and management of patients with co-occurring mild TBI (also known as concussion) and psychological health disorders. This comprehensive tool kit is based on the Department of Defense and Department of Veterans Affairs clinical practice guidelines on mild TBI, post-traumatic stress, depression, chronic opioid therapy and substance use disorder. To order hard copies contact the Defense and Veterans Brain Injury Center at 800-870-9244 or send your request to info@dvhic.org. You can download a copy at: [www.dvhic.org/Providers/TBI-Clinical-Tools-\(1\).aspx](http://www.dvhic.org/Providers/TBI-Clinical-Tools-(1).aspx)

Mobile application also available at: www.t2health.org/apps/cct



Mild Traumatic Brain Injury Web-based Case Studies

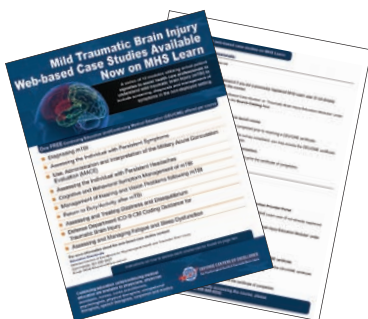
This two-part training is designed for health care providers who care for patients with mild traumatic brain injury (mTBI). Part 1 includes 12 modules that present vignettes of patients with mTBI. These vignettes are designed to provide a basic understanding of mTBI screening, diagnosis and symptom management. Part 2 includes modules that present vignettes of patients with a myriad of psychological health disorders that co-occur with mTBI. These vignettes are designed to provide health care providers with additional information on how these complicated patients present in a clinical setting. The mTBI Web-based case studies are now available through DCoE and MHS Learn.

DCoE website:

www.dcoe.health.mil/Content/navigation/documents/Mild%20TBI%20Web-Based%20Case%20Studies.pdf

MHS Learn: mhslearn.csd.disa.mil

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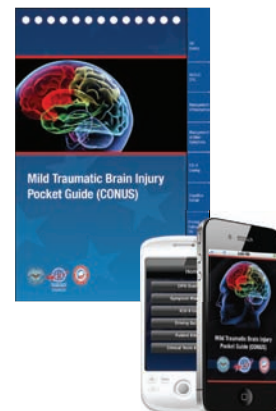


Mild Traumatic Brain Injury Pocket Guide

The Mild Traumatic Brain Injury (mTBI) Pocket Guide is an abbreviated version of the VA/DoD Clinical Practice Guideline for the Management of Concussion/Mild TBI (2009) and updated DoD mTBI guidance. Designed as a brief reference resource for health care providers, the mTBI pocket guide provides information related to the assessment, treatment and management of patients with mTBI and related symptoms. The mTBI pocket guide was developed by the Defense and Veterans Brain Injury Center, in collaboration with the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury. To order hard copies, contact DVVIC at info@dvhic.org or call 1-800-870-9244. While the mTBI Pocket Guide is a hard copy on-the-job reference, an electronic version is also available for download at:

www.dcoe.health.mil/ForHealthPros/TBIInformation.aspx.

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Military Medicine

International Journal of AMSUS

1891-2012

ISSN 0026-4075

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MILITARY MEDICINE is available on the Internet via the AMSUS website (www.amsus.org) to members and subscribers who purchase online access.

MILITARY MEDICINE is indexed by the United States National Library of Medicine (NLM) and is included in the MEDLARS system, ISSN 0026-4075. *MILITARY MEDICINE* is also available online through IngentaSelect web site: www.ingenta.com/activate.htm.

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www.amsus.org

MILITARY MEDICINE (ISSN 0026-4075) is published monthly by the Association of Military Surgeons of the U.S., 9320 Old Georgetown Rd., Bethesda, MD 20814-1653. Periodicals postage paid at Bethesda, MD, and additional mailing offices. POSTMASTER: Send address changes to Military Medicine AMSUS, 9320 Old Georgetown Rd., Bethesda, MD 20814-1653.

MILITARY MEDICINE

VOLUME 177

AUGUST 2012

SUPPLEMENT

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Foreword

In 2005, Steve Jobs, co-founder and former CEO of Apple Inc., delivered a now well-known commencement address at Stanford University. Within that memorable speech was an analogy that reminds me of the journey we are on in military medicine with respect to psychological health and traumatic brain injury (TBI). Jobs said, “You can’t connect the dots looking forward; you can only connect them looking backwards. So you have to trust that the dots will somehow connect in [the] future.” His point was that we do not always realize how valuable our experiences are until we can see the connections looking back. This observation will resonate with most clinicians and researchers but to me it seems particularly apt in light of recent military medical history.

In the fall of 2004, I was deployed as a Combat Stress Control Team Psychiatrist in Al Anbar Province, Iraq. I had just arrived at Camp Fallujah as Operation Al Fajr was about to begin and would bring us casualties from some of the most intense fighting of the war. I was relatively well prepared to treat intense reactions to combat, but I struggled with how to effectively and appropriately treat the numerous concussions from blast exposure we were beginning to see. That experience, combined with seeing colleagues struggle in a similar way with the long-term sequelae of TBI and stress injuries after returning stateside, compelled us to look at psychological health and TBIs across the spectrum of care from prevention and surveillance, to diagnosis and treatment, and to recovery and rehabilitation. We have been challenged, not only in the acute management of concussion but to treat chronic and co-occurring conditions that often come with the experience of combat including post-traumatic stress disorder (PTSD), depression, and substance-use disorders along with TBI and the endless variations in our service members’ ability to recover from the wounds of war.

Now, as the Director of the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE) and serving as the leader for advancing excellence in psychological health and TBI prevention and care, I am reminded that significant progress has been made in military medicine over the last several years. In the fall of 2011, I visited Afghanistan and was thrilled to see concussion care centers, combat stress restoration centers, clear TBI management guidance, innovative treatment practices, and vastly improved clinical data collection. Our recent wartime experience put the Department of Defense in a unique position to lead changes in clinical practice and research, and it drives a deep commitment to finding the answers to address these problems.

This special issue of *Military Medicine* highlights the recent progress we have made in the epidemiology, prevention, screening, diagnosis, treatment, and research on PTSD, depression, substance use disorders, and TBI. I am grateful to have the opportunity to have DCoE sponsor this issue of *Military Medicine* and have it serve as a benchmark of the progress made in military medicine after a decade of unconventional warfare—but the journey is not complete. I encourage you to read the articles in this issue with a focus on where we have been, where we are, and where we are headed in the field of TBI and psychological health, to “connect the dots,” to gain insights and lessons from looking back and use that wisdom to move forward.

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ACKNOWLEDGEMENTS

The hosting organizations would like to recognize the invaluable contributions of the following people:

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Epidemiology and Prevention of Combat-Related Post-Traumatic Stress in OEF/OIF/OND Service Members

Barbara A. Hermann, PhD; Brian Shiner, MD, MPH; Matthew J. Friedman, MD, PhD

ABSTRACT This article summarizes information about the prevalence of post-traumatic stress disorder (PTSD) in military personnel and Veterans who have served in the Iraq and Afghanistan conflicts as well as the disorder's impact and efforts to prevent it in this population. We examine prevalence in light of epidemiologic methods and discuss associated outcomes, etiology, and factors affecting risk for PTSD. Prevention strategies are presented both in terms of individual-level interventions and operational strategies designed to mitigate the development of PTSD. Our findings indicate that while research into the prevalence and consequences of PTSD in the Iraq and Afghanistan cohort has been significant, relatively little is known about the effectiveness of approaches designed to prevent it.

INTRODUCTION

Between 2001 and 2011, the first 10 years of the Iraq and Afghanistan conflicts (Operation Enduring Freedom [OEF]; Operation Iraqi Freedom [OIF]; Operation New Dawn [OND]), approximately 2.3 million U.S. troops have served in OEF/OIF/OND.¹ Many experienced combat and are at risk for postdeployment problems, including mental disorders, stress reactions, and readjustment difficulties. Among the most impairing disorders is post-traumatic stress disorder (PTSD), a psychiatric condition that can follow a traumatic event or events. Symptoms of PTSD include re-experiencing of the event, avoidance of reminders of the event, emotional numbing, and physiological hyperarousal.² Understanding who develops PTSD and the determinants that increase risk is critical for informing policy decisions, resource allocation, and any efforts aimed at prevention and treatment.

Effective treatments for PTSD have been developed and disseminated throughout the Department of Veterans Affairs (VA) and Defense Department clinical facilities, whereas efforts at prevention are less advanced. Determining who is at risk for PTSD and developing prevention strategies for service members is complicated by an inadequate scientific understanding of resilience and a lack of evidence-based interventions for PTSD prevention. This article aims to present current knowledge of the epidemiology and prevention of PTSD within the OEF, OIF, and OND cohort. The discussion is contextualized with studies of civilians and of Vietnam and Gulf War service members.

PREVALENCE ESTIMATES OF PTSD IN OEF, OIF, AND OND

Prevalence is the proportion of people in a population that have a given disorder at a given time. Methods employed in epidemiologic studies of PTSD prevalence among service members of the Afghanistan and Iraq conflicts have varied in assessment instruments, the time period since deployment

of the assessment, and the demographic, service-related, or other characteristics of the samples examined. Understanding the meaning of and variation among the widely varying estimates requires seeing them through the lens of these factors.³ We highlight three studies relevant to understanding the prevalence of PTSD, both during the process of returning from combat and during the transition from military to civilian life.

The postdeployment health assessment (PDHA) and post-deployment health reassessment (PDHRA), both of which contain a four-item primary care PTSD screen,⁴ have provided information about the prevalence of PTSD during the process of returning from combat. The PDHA is intended to be administered either in theater at the end of a tour of duty or within 1 to 2 weeks of returning from deployment. The PDHRA is intended to be administered 3 to 6 months after returning from deployment. Two studies examined only Army and Marine personnel. One used data from only the PDHA on those returning from deployment in 2003 and 2004 and found the prevalence of PTSD in OIF service members (4.8%) to be twice that of OEF service members (2.2%).⁵ The other study used both PDHA and PDHRA data from 2005 and 2006 so was able to monitor PTSD prevalence over the 3- to 6-month period. Prevalence from the PDHA was comparable for active duty (6.2%) and reservists (6.6%). Although both cohorts exhibited increased prevalence on the PDHRA, prevalence was significantly higher for reservists (14.3%) than for active duty personnel (9.1%).⁶ It is important to understand that PDHA and PDHRA estimates, based on the brief screening questionnaire, are higher than one would expect from a full diagnostic evaluation.

To investigate the effect of time since deployment, the RAND Corporation conducted a telephone survey targeting large and geographically diverse areas of the United States likely to contain OEF/OIF/OND personnel who had previously been deployed.⁷ Using the PTSD Checklist,⁸ which assesses all 17 symptoms of PTSD found within the DSM criteria,² the overall prevalence of probable PTSD was 13.8%. Interestingly, the number of months since return was

National Center for PTSD, VA Medical Center (116D), 215 North Main Street, White River Junction, VT 05009.

not significantly associated with the development of PTSD. However, the prevalence of PTSD was almost twice as high in those who had separated or retired from the military as in current active duty service members. The study validated other findings and assumptions from the PDHA- and PDHRA-based studies. National Guardsmen and reservists had twice the risk of PTSD as active duty service members. Compared to soldiers, sailors had less than half the risk of PTSD and airmen had less than one-tenth of the risk, whereas Marines had an equivalent risk. To summarize, prevalence estimates for PTSD in OEF/OIF/OND service members ranged widely (2.2%–17.3%). Factors such as time since deployment, service branch and component, and the relative sensitivity and specificity of different assessment instruments employed in these studies account for some of the discrepancies in prevalence estimates.

IMPACT OF PTSD

At the individual level, PTSD negatively impacts quality of life,⁹ as well as physical and psychological health functioning.¹⁰ Adding to the burden are comorbid disorders. Data from the RAND study indicate that PTSD is frequently comorbid with depression or traumatic brain injury (TBI).⁷ One analysis of VA treatment records suggests that among OEF/OIF/OND VA users newly diagnosed with PTSD, nearly half also carried a diagnosis of dysthymic disorder or minor depressive disorder, 21.4% also had major depressive disorder, 18.5% also had an alcohol use disorder, and 12.5% also had a nonalcohol substance use disorder.¹¹ Although the specific effect of PTSD on military attrition has not been examined, the development of mental health problems has been found to increase the likelihood of attrition from the military.⁵ Studies of health care utilization among OEF/OIF/OND VA users indicate that those with PTSD consume nearly twice the general health care of those without a psychological health diagnosis.¹² The 2-year social costs of PTSD and depression in Veterans of OEF/OIF/OND has been estimated at \$3,525 per veteran, with almost two-thirds of the cost because of lost productivity.¹³

ETIOLOGY OF PTSD

Pavlovian fear conditioning has served as a central model for the development of PTSD.¹⁴ Laboratory models in which animals are exposed to inescapable and unpredictable stress have informed human research on PTSD and psychological interventions. The presumed psychobiological circuitry underlying PTSD focuses on excessive activation of the amygdala by stimuli perceived to be threatening.¹⁵ Such activation can be considered the ignition switch that produces outputs to a number of brain areas that mediate memory of emotional events, autonomic and fear reactions, and approach or avoidance behavior. In PTSD, the normal checks and balances by the medial prefrontal cortex on amygdala activation may be impaired.¹⁶ Disinhibition of the amygdala produces a vicious spiral of recurrent fear conditioning in which ambiguous stim-

uli are more likely to be appraised as threatening, sensitizing key limbic areas, and lowering the threshold for fearful reactivity.¹⁷ In the classical conditioning model of PTSD, re-experiencing and arousal symptoms are viewed as conditioned emotional responses in which the traumatic event is the unconditioned stimulus, and associated environmental reminders serve as conditioned stimuli. This model has been elaborated as emotional processing theory.¹⁸ Such a model predicts that improvement can be achieved through extinction of conditioned fear reactions thus reducing trauma-related anxiety and correcting erroneous beliefs associated with the conditioned fear. With extinction of such fears, PTSD escape and avoidance behavior resolves, as well.¹⁹

RISK AND RESILIENCE FACTORS FOR PTSD IN OEF, OIF, AND OND

Although exposure to traumatic events is a necessary prerequisite for the development of PTSD, it is not in itself sufficient. Various factors related to vulnerability versus resilience have been identified, with the OEF/OIF/OND conflicts providing an opportunity for several prospective studies.^{20,21} A comprehensive review of resilience is not possible in the present article. Interested readers are referred to a recent book on resilience, which considers the entire spectrum of factors affecting resilience, from genetic and molecular to social and cultural influences.²²

Predeployment Factors

A number of individual characteristics are modestly associated with the development of PTSD in trauma-exposed individuals. Research specific to service members and Veterans of OEF/OIF/OND suggest that risk of PTSD is heightened by female gender, divorce, exposure to family psychiatric illness, domestic violence, abuse, or violence before military induction, enlisted status, and diminished psychological or physical health before combat.^{10,23–26} Investigations of the genetic factors involved in PTSD have been scarce. The few existing family studies of PTSD, focusing on refugees, physical injury in children and Holocaust survivors, suggest an elevated risk of PTSD among relatives with the disorder but cannot say whether this association is as a result of genetics or environment.²⁷ Twin studies, including the Vietnam era twin registry, compare the degree of similarity within identical or monozygotic (MZ) pairs with the degree of similarity within fraternal or dizygotic (DZ) pairs and indicate that genetic influences account for about one-third of the variance in PTSD risk.^{28,29}

An important current research area is identifying genes that might increase (or reduce) vulnerability to PTSD following exposure to traumatic events (e.g., gene times environment interactions). As might be expected, the current list of candidate genes includes genes involved in the human stress response. These include polymorphisms that modulate

the dopaminergic and serotonergic systems, the hypothalamic–pituitary–adrenocortical axis, corticotropin-releasing factor, neuropeptide Y, and brain-derived neurotrophic factor.^{30–32}

Deployment-Related Factors

Service Experiences

Greater combat exposure, length or number of deployments, or perceived threat of personal danger has been associated with PTSD risk in prospective studies with OEF/OIF/OND service members.^{25,26} In addition, deployment-related physical injuries have been found to prospectively increase the odds of PTSD symptoms postdeployment in the millennium cohort study.²⁶ Interestingly, perceptions of threat have been found to partially or fully mediate the association of combat severity with PTSD in British Veterans of the Iraq and Afghanistan conflicts as well as U.S. combat Veterans from other cohorts.^{33,34} Perceived combat preparedness at pre-deployment has, in turn, been found to moderate the link between combat and perceived threat³⁵ and predict new-onset PTSD prospectively even after accounting for combat exposure.²⁰ Like sense of preparedness, social support may serve a protective function. Specifically, unit member cohesion has been associated with lower odds of developing PTSD in service members serving in OEF/OIF/OND.³⁶

Acute Symptoms

The development of early stress symptoms, particularly those characterized as high arousal, following combat exposure may increase risk of subsequent PTSD.³⁷ A meta-analysis of studies identifying predictors of PTSD found strong evidence for the role of peritraumatic dissociation in determining who develops PTSD in the aftermath of trauma exposure, with an average weighted effect size of $r = 0.35$.³⁸ More recent evidence, from mostly civilian samples, suggests that the persistence of dissociation is a better predictor than its presence.³⁹

Postservice Factors: Life Stressors, Social Support, and Resilience

Postdeployment life stressors, such as economic difficulties, unemployment, and family discord, appear to play a role in PTSD for service members of OIF.^{20,21} Coping with such difficulties may relate to the quality of social supports. A lack of social support after deployment has been associated with worse mental health adjustment in Gulf War veterans⁴⁰ and in National Guard service members of OIF.²⁰ Cross-sectional studies indicate that social support relates to psychological resilience, the capacity to successfully adapt in the face of challenge, in veterans of OEF/OIF/OND.³⁶ The construct of resilience itself has been linked to lower rates of PTSD³⁶ and particularly for those service members who experience high combat exposure.⁴¹ Thus, social resources during and post-deployment may buffer against poor adjustment and may enhance resilience.

PREVENTION STRATEGIES

Early Intervention

Pharmacological

Based on evidence that excessive noradrenergic activity is associated with PTSD, the beta-adrenergic antagonist propranolol has been examined as a prophylactic agent. In the only randomized trial, the medication resulted in some suppression of adrenergic arousal, in comparison with a nontreated group when administered to emergency room accident victims within 6 to 12 hours of the event. However, there was no significant reduction in PTSD symptoms 1 and 3 months later.⁴² Based on findings of low cortisol levels among individuals with PTSD, hydrocortisone administered acutely in intensive care or cardiac care hospital wards yielded promising results, but trials are needed in emergency room or combat settings.⁴³ The most exciting field-based finding is that acute (usually within 1–3 hours) administration of narcotic agents to U.S. Navy and Marine service members wounded in Iraq appeared to result in significantly lower rates of PTSD several months later than compared with nonadministration.⁴⁴ However, the trial was not randomized and did not determine whether the effect was as a result of rapid pain reduction, antagonism of noradrenergic activity, or both.

Psychological

Psychological debriefing (PD), in its most common form of critical incident stress debriefing (CISD), was developed for rescue workers in the acute aftermath of potentially traumatic events. PD typically involves a single session of open sharing and discussion within a unit after a potentially traumatic event. Past reviews of the literature concluded that PD does not prevent subsequent psychopathology.⁴⁵ A recent trial with 1,004 U.S. Army soldiers randomly assigned by platoon to CISD, a stress management class, or no intervention during the final phase of a 6-month peacekeeping mission to Kosovo yielded no clear advantages for CISD.⁴⁶ Although not focused on military samples or combat-related trauma, several randomized controlled trials indicate that brief Cognitive Behavioral Therapy (CBT) may ameliorate Acute Stress Disorder (ASD) and lessen the subsequent development of PTSD.^{47,48,49} Furthermore, a randomized controlled trial of patients admitted to an emergency room suggests that CBT, initiated within a mean of 30 days after the trauma, may prevent chronic PTSD. Specifically, prolonged exposure and cognitive therapy each significantly and similarly reduced the odds of PTSD at 5 and 9 months postintervention, relative to a selective serotonin reuptake inhibitor, a placebo, or wait-list.

Operational Approaches

The U.S. Army established the Comprehensive Soldier Fitness program in 2008, based in part of concepts of sport and positive psychology and with the aim to increase resilience of soldiers and their families both during and after deployment

through enhanced physical, emotional, social, spiritual, and family skills. Confidential online assessment is coupled with self-paced online training modules. Organizationally, Army career schools have been infused with resilience awareness training, and master resilience trainers serve as mentors to Army leaders in order to promote resilience within units. To date, the efficacy of this approach has not been evaluated systematically.

Another U.S. Army strength-based program is the Battlemind stress management training (now also known as Military Resilience Training). The term Battlemind is used as an acronym for 10 combat-related skills that may cause problems postdeployment if not reframed in the context of civilian life.⁵⁰ A preliminary evaluation of the effectiveness of predeployment Battlemind training was conducted by the Army's fifth Mental Health Advisory Teams in 2008. The evaluation used a convenience sample of 2,195 Army soldiers deployed to Iraq and found that, after adjusting for rank, gender, months deployed, and levels of combat exposure, 12.0% of the soldiers who reported receiving the training screened positive for PTSD, depression, and anxiety versus 20.5% of soldiers who denied undergoing the training.⁵¹ The authors noted that significant differences existed between the groups that may influence these outcomes, but they did not specify these variables or analyze their effects.

The Battlemind training has been modified and now includes a postdeployment intervention, Battlemind Debriefing. This is a single session form of PD administered within 2 weeks of returning from deployment and aimed at providing education, normalizing transition challenges, and encouraging social support. Battlemind Debriefing was evaluated in one group-randomized trial of 2,297 soldiers returning from a year-long deployment in Iraq. It was associated with modest improvements at 4-month follow-up on PTSD, depression, and sleep ($d = 0.21, 0.26, \text{ and } 0.50$, respectively) when compared to a stress education class, but only for soldiers who scored in the top third for combat exposure.⁵⁰ The active components within the Battlemind approach driving these effects have not yet been determined.

Prevention interventions within the Marine Corps and Navy have been guided by the Stress Continuum Model, which organizes all possible stress states into one of four color-coded stress zones.⁵² This model forms the foundation for the Navy and Marines Combat and Operational Stress Control doctrine, which is a set of five core leader functions aimed at promoting psychological health and preventing stress disorders. Several career schools and deployment-cycle training modules have been developed for service members, leaders, and families based on these functions. Line operational leaders use the framework and tools to better recognize when units may be at increased risk for problems in order to target preventative strategies at service members with pre-clinical symptoms. Specific procedures to promote recovery are described in a toolkit called Combat and Operational Stress First Aid. This approach is based on the evidence-

informed Psychological First Aid, a modular approach for assisting people in the immediate aftermath of disaster and terrorism developed jointly by the VA National Center for PTSD and the National Child Traumatic Stress Network. The aim of Psychological First Aid is to reduce initial distress and to foster short- and long-term adaptive functioning following exposure to potentially traumatic events, such as natural disasters. Combat and Operational Stress First Aid encompasses seven steps that serve to assess difficulties, coordinate safety and care, reduce arousal, encourage family and peer support, and restore self-confidence and competence. Combat and Operational Stress First Aid and its tools have not yet undergone empirical evaluation, but studies are reportedly underway.⁵³

CONCLUSIONS

It is clear that deployment to combat zones in Iraq and Afghanistan is associated with the development of stress reactions and PTSD. There is evidence that individual differences in risk and protective factors influence the development of PTSD. To enhance understanding of the etiological pathways of PTSD, additional research that identifies modifiable risk factors involved in PTSD development and moderators of their effects is needed.

Although there are evidence-based psychotherapies and pharmacotherapies for PTSD, the major challenge is to prevent PTSD by increasing resilience and preparation as well as the provision of effective early interventions for traumatized service members in the military theater. Extrapolating from civilian and disaster research, the best candidates to date are cognitive behavioral interventions in the immediate weeks after trauma exposure and approaches, such as Psychological First Aid, that are evidence-informed but require rigorous evaluation. Additional preventative and early intervention strategies have been proposed and are in various stages of implementation and evaluation.

The costs of PTSD for the individual, military, and society are significant. The OEF/OIF/OND cohort has offered an unprecedented opportunity to study the epidemiology and risk and resilience factors related to combat PTSD. It is imperative that this knowledge is translated into novel preventative strategies and that work to evaluate existing prevention efforts continues.

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Screening, Diagnosis, and Treatment of Post-Traumatic Stress Disorder

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ABSTRACT Post-traumatic stress disorder (PTSD) is a prevalent problem among military personnel and veterans. Identification of effective screening tools, diagnostic technologies, and treatments for PTSD is essential to ensure that all individuals in need of treatment are offered interventions with proven efficacy. Well-validated methods for screening and diagnosing PTSD are now available, and effective pharmacological and psychological treatments can be offered. Despite these advances, many military personnel and veterans do not receive evidence-based care. We review the literature on screening, diagnosis, and treatment of PTSD in military populations, and discuss the challenges to implementing the best evidence-based practices in clinical settings.

INTRODUCTION

Post-traumatic stress disorder (PTSD) is a topic of particular relevance for military personnel and veterans. Evidence-based screening, diagnosis, and treatment methods are essential to ensure that individuals with PTSD are identified and offered effective treatment options. In this article, we describe the evidence supporting screening tools, diagnostic technologies, and treatments for PTSD. We then discuss the barriers to accessing evidence-based assessment and treatment and describe important targets of future research. This article is not an exhaustive review of all available assessment or treatment options, but rather an overview of the methods with the best evidence base for military and veteran populations.

SCREENING

Screening for PTSD can serve multiple purposes. The first is to identify individuals at high risk for developing PTSD, but who have not yet manifested its symptoms (risk assessment). Individuals who are identified as high risk for the future development of PTSD would be eligible for prevention efforts. Risk factors for the development of PTSD following a traumatic event include pretrauma (e.g., prior trauma history and childhood conduct problems), peritrauma (e.g., perceived threat, heightened arousal, and dissociation) and post-trauma factors (e.g., hardiness and social support¹⁻³). Recently, researchers have developed screening measures, known collectively as statistical prediction instruments (SPIs), that quantify these risk and resilience factors for the purpose of identifying individuals who may be vulnerable to PTSD following trauma exposure before symptoms actually develop. In a recent example of such an approach, O'Donnell et al⁴ developed and validated a screening instrument that prospectively identifies, during hospitalization, civilian adults at high risk for developing PTSD and/or major depression. Results showed that the

screening instrument had a sensitivity of 0.82 and a specificity of 0.84 when predicting PTSD and a sensitivity of 0.72 and a specificity of 0.75 in predicting Major Depression. Marx et al⁵ tested a similar screening instrument for combat-related PTSD among Vietnam veterans using previously collected cross-sectional data. Drawing on the findings of King et al,² Marx et al⁵ focused on those risk-resilience factors that were found to have the strongest relations with combat-related PTSD status. The resulting instrument, the PTSD SPI, displayed excellent sensitivity (0.90) and good specificity (0.80). These results suggest that it is feasible to develop instruments that could identify veterans and service members who might be prone to develop PTSD following trauma exposure. However, before this instrument or others like it are used for this purpose, it is necessary to conduct additional research using a longitudinal research design with a heterogeneous sample of active duty military personnel and/or veterans. Once such instruments have been validated with new data collected in subsequent studies, they will be of tremendous value to local and national level screening programs conducted by the Departments of Defense (DoD) and Veterans Affairs (VA) in the identification of at-risk individuals for outreach, thorough evaluation, and early intervention efforts.

In addition to risk assessment, screening provides an opportunity for early detection or identification of acute PTSD cases and individuals who are experiencing some PTSD symptoms but do not meet full criteria. Screening also affords the possibility of discovering previously unidentified cases of more chronic and severe PTSD. Such individuals would be candidates for currently available evidence-based interventions. Historically, the field has relied upon a variety of PTSD screening tools. Many of the early screening instruments, such as the PTSD—Keane scale of the Minnesota Multiphasic Personality Inventory-2,⁶ the Impact of Events Scale,⁷ and the Mississippi Scale for Combat-related PTSD⁸ contained items that did not necessarily correspond to PTSD diagnostic criteria. Today, the most widely used screening tools have items that directly correspond to PTSD diagnostic criteria in the fourth edition of the Diagnostic and Statistical Manual of Mental

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Disorders (DSM-IV). One such scale is the Post-traumatic Diagnostic Scale (PDS). The PDS has well-documented reliability and validity, but has generally been tested with civilian rather than military or veteran samples.⁹ The PTSD Checklist (PCL) has been used extensively with military, veteran and civilian samples and has excellent reliability and validity.^{10,11} Recent research has validated the PCL with soldiers returning from combat; these data provide evidence for the utility of this screening measure in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) soldiers.¹² The PCL presents 17 items corresponding to the core diagnostic symptoms of PTSD. Respondents rate how much each symptom bothers them on a 5-point scale from 1 (“not at all”) to 5 (“extremely”), and the sum of the items provides an index of PTSD symptom severity. Population-specific cutoffs are recommended, with cutoffs for returning soldiers and OEF/OIF veterans generally lower than those for veterans of the Vietnam war (e.g., 30 to 34 for OEF/OIF veterans¹²; compared with 50 for Vietnam veterans¹³). Bliese et al¹² developed a shortened version of the PCL, the 4-item Primary Care PTSD Screen (PC-PTSD), for use in primary care settings or other settings in which more extensive screening is not feasible. In a validation study assessing returning soldiers in a primary care setting, the PC-PTSD compared favorably with the PCL.¹² Both older and newer screening tools have potential utility, with newer measures more appropriate for screening of DSM-IV-TR criteria and older measures more suited to assessment of key content areas, making these older instruments valuable as the diagnostic criteria for PTSD change across iterations of the DSM. A limitation of all of the previously described screening tools is that they solely depend upon the individual’s self-report of symptom status. Self-report measures require patients to have sufficient insight into the extent and impact of their symptoms and to provide accurate information to clinicians and researchers. A number of factors can influence self-report, including the desire to appear more or less symptomatic than one is in reality. With the exception of the Minnesota Multiphasic Personality Inventory-2, the measures described previously do not assess the individual’s response bias. For these reasons, among others, there has been great interest in identifying biomarkers that could be used to identify individuals at-risk for the development of PTSD in the wake of trauma exposure. Such tools or procedures would take advantage of information about the genetic,^{14,15} neuroanatomical and neurocognitive,^{16,17} and psychophysiological^{18,19} correlates and precursors of PTSD already gleaned from prior research. Research with military and veteran samples is needed to determine the feasibility and utility of using biomarkers for PTSD screening purposes.

DIAGNOSIS

Multimethod assessment is the preferred means of establishing psychiatric diagnoses such as PTSD. Because any individual assessment method has limitations, converging evidence from different methods of assessment offers the

highest degree of confidence when making a diagnosis. An ideal assessment of PTSD would include self-report measures of symptom severity, such as the questionnaires described above, an interviewer-administered semistructured clinical interview, and measurement of biological indices. A comprehensive assessment should include evaluation of possible comorbid diagnoses and careful consideration of differential diagnosis, and should include measures of psychosocial functioning and response bias as well as symptom severity. A comprehensive discussion of a multimethod assessment for PTSD is beyond the scope of this article. See Weathers et al²⁰ for a thorough review.

Semistructured Diagnostic Interviews

Semistructured diagnostic interviews are the gold standard for diagnosing psychiatric disorders including PTSD. Interviewer-administered measures are preferable to self-report measures because interviewers can clarify items and ask follow-up questions as necessary. Factors such as misinterpretation of questions, attempts to exaggerate or minimize symptoms, or random responding to questions may be more likely to influence self-report questionnaires than interviews.²¹ Semistructured interviews are preferable to unstructured clinical interviews because they provide more accurate diagnoses.²²

The Clinician-Administered PTSD Scale²³ (CAPS) is one of the most widely used semistructured clinical interviews for the assessment of PTSD. A trained interviewer reads questions corresponding to each of the DSM-IV PTSD symptoms and asks follow-up questions using specific behavioral markers to rate the frequency and intensity of each symptom on separate 5-point scales (0–4). Typically, symptoms that receive a frequency score of “1” or higher and an intensity score of “2” or higher are counted as present, and a diagnosis of PTSD is given if at least one re-experiencing, three avoidance, and two hyperarousal symptoms are present (also see Weathers et al²¹ for a detailed comparison of different scoring rules). The sum of the frequency and intensity scores for all symptoms also gives a measure of symptom severity. The CAPS has well-established reliability and validity and has been tested extensively in veterans.²¹

Other semistructured clinical interviews include the PTSD Symptom Scale—Interview Version⁹ (PSS-I) and the Structured Clinical Interview for DSM-IV²⁴ (SCID). The PSS-I includes 17 questions corresponding to the DSM-IV PTSD symptoms, and trained interviewers rate the severity of each symptom from 0 (not at all) to 3 (five or more times a week/very much). Unlike the CAPS, interviewers do not rate frequency and intensity separately and only one question assesses each symptom. In a validation study using a civilian sample, the PSS-I compared favorably to the CAPS.²⁵ The PSS-I has the potential advantage of being faster to administer than the CAPS; however, the PSS-I has not been well-tested in military samples. If a more comprehensive diagnostic tool is necessary, the SCID is another useful alternative. The

SCID assesses anxiety disorders including PTSD, as well as mood, substance use, and eating disorders, offering a broader diagnostic picture of Axis I pathology. In the PTSD module of the SCID, the interviewer asks questions corresponding to each of the DSM-IV PTSD symptoms and rates each symptom as absent, subthreshold, or threshold. Symptoms rated as “threshold” are considered present. However, the SCID does not offer an index of PTSD symptom severity (it is in general considered a dichotomous rating scale) and therefore is less sensitive to changes in symptoms over time. Moreover, the use of a dichotomous scale of symptom expression may not map onto symptom presentation in patient care settings thus limiting the viability of the SCID for certain types of programs and projects.

Biomarkers

Although preferable to self-report measures, semistructured interviews still rely on patients to report their symptoms accurately. Ideally, biological indices of PTSD could be identified as assessment tools that are completely independent of patient report. Psychophysiological measures have been the subject of a great deal of research in recent years, and several physiological indices are reliably associated with PTSD.^{18,26,27} Several different measures of physiological arousal and reactivity are widely viewed as potential markers, to include heart rate, skin conductance (sweat gland activity), blood pressure, and facial electromyography (a measure of muscle contractions in the face). Heart rate and skin conductance have emerged as particularly reliable markers of PTSD status.^{26,27} Physiological differences distinguish between individuals with and without PTSD when participants are (a) at rest, (b) perceiving standardized trauma cues (e.g., Vietnam veterans viewing general images of Vietnam), or (c) perceiving idiographic trauma cues (e.g., hearing a script describing the individual participant’s traumatic experience). Although these findings are encouraging, physiological measures are not perfectly accurate, with a large multisite study indicating that physiological indices correctly identified approximately 2/3 of PTSD cases,²⁷ and have limited specificity. Additionally, there has been little research replicating these physiological findings in OEF/OIF personnel and veterans. More recently, there has been increasing interest in identifying genetic, neuroanatomical, and neurocognitive biomarkers related to PTSD.^{14–17,28} The possible utility of neuroimaging technology for identification of biomarkers is an area of particular enthusiasm.²⁹ However, this area of research is in its nascent stages.

TREATMENT

Several effective pharmacological and psychological treatments for PTSD are available, offering patients and therapists a choice of different treatment options. However, most treatments have not yet been tested in OEF/OIF veteran samples with PTSD.

Pharmacological Treatment

Selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) are effective in the treatment of PTSD, with several large randomized controlled trials (RCTs) supporting their use in both civilian and veteran populations.³⁰ Treatment responders should be continued on maintenance doses of these medications following symptom reduction because relapse is likely following discontinuation of these medications.³¹ Although atypical antipsychotics initially showed promise as adjunctive treatment to SSRIs for treatment-refractory patients,³² a large multisite RCT found no benefit of risperidone for treatment-resistant military service-related PTSD.³³ As a result of these equivocal results and potentially harmful side effects, the most recent VA/DoD clinical practice guidelines for PTSD recommend against the use of risperidone and indicate that the benefit of other atypical antipsychotics is unknown.^{30,34} The current practice guidelines also recommend against using benzodiazepines to treat PTSD because of their addictive potential, in terms of both tolerance and substance dependence.³⁴ Other pharmacological treatments are also available for PTSD; see Friedman³⁰ for a comprehensive review.

Psychotherapy

Evidence-based psychotherapies for PTSD include cognitive behavioral therapies and eye movement desensitization and reprocessing treatment (EMDR). Two forms of cognitive behavioral therapy, Cognitive Processing Therapy (CPT)³⁵ and Prolonged Exposure (PE),³⁶ have received consistent research support. The “national rollout” is currently disseminating these treatments throughout the Department of VA Healthcare System in order to improve access by training and certifying mental health clinicians in specified empirically supported treatments.³⁷

CPT is a manualized 12-session cognitive behavioral treatment for PTSD originally developed for treatment of sexual assault victims.³⁵ CPT includes cognitive restructuring and exposure/emotional processing elements. Cognitive restructuring interventions are designed to teach patients how to challenge maladaptive thoughts (“stuck points”) about the trauma. Specific interventions include asking patients to write an “impact statement” describing the meaning of the traumatic event, Socratic questioning by the therapist, written homework assignments, and a specific focus on beliefs about the self and other in five domains (safety, trust, power/control, esteem, and intimacy). The emotional processing component of CPT involves having the patient complete “written accounts” or detailed descriptions of the traumatic event designed to elicit the natural emotions experienced during the trauma. At least four RCTs have provided evidence supporting the efficacy of CPT in the treatment of PTSD.³⁸ In a RCT examining veterans with military-related PTSD, veterans receiving CPT improved significantly compared to a wait-list control group, and 40% of veterans receiving CPT no longer met criteria for PTSD at the end of treatment.³⁹ In addition to CPT, other forms of cognitive

therapy have been shown to be effective in the treatment of PTSD in civilian samples.³⁸

Exposure therapy is another evidence-based psychotherapy for PTSD. It was first tested in veterans and shown to possess efficacy for treatment of combat-related PTSD.^{40,41} Since that time, a manualized form of exposure treatment, PE, has received a great deal of attention in the literature. PE includes two core components: in vivo and imaginal exposure. In vivo exposure involves creating a hierarchy of feared situations that the patient currently avoids because of trauma-related fears and repeated exposure to those situations outside of session. Imaginal exposure involves describing trauma memories during session and listening to a recording of the descriptions at home between sessions. PE also includes education about common reactions to trauma, breathing retraining, and discussion of thoughts and feelings elicited by the exposure assignments. A large body of research supports the efficacy of PE, with at least 13 RCTs published in the literature and a recent meta-analysis reporting large effects of PE relative to wait-list or psychological placebo comparison groups.⁴² Similar to CPT, PE was first applied to the treatment of sexual assault victims, and much of the research supporting PE has been conducted in civilian samples. However, at least one RCT provided evidence for the efficacy of PE for female veterans,⁴³ and a case series examining 10 veterans, including eight men and five OEF/OIF veterans, showed significant reductions in PTSD and depressive symptoms after a course of PE.⁴⁴

EMDR is another treatment for PTSD that possesses a modest evidence base for treating civilian forms of PTSD. EMDR includes assessment of the trauma memory and associated negative and positive cognitions, desensitization, and reprocessing, which involves holding the trauma memory in mind while making alternating eye movements, and installation of positive cognition, which involves holding positive cognitions in mind while making alternating eye movements. Meta-analyses have shown EMDR to be effective in treating the core symptoms of PTSD, but some studies suggest that EMDR is less efficacious in military samples.^{45,46} Although eye movements were theorized to be an essential component of this treatment approach, more recent research has shown that eye movements or other alternating movements do not add to the benefit of EMDR, which is comparable to other exposure-based treatments.⁴⁵

Comparative Efficacy and Extension to OEF/OIF Personnel

The pharmacological and psychological treatments described have been well-studied in a variety of different populations with different trauma types. Evidence-based psychotherapies are generally equally effective, with similar effect sizes seen for CPT, PE, and EMDR.⁴² Notably, no RCT has ever compared the relative efficacy of medication versus psychotherapy, making it difficult to directly compare pharmacological and psychological treatment approaches. Moreover, further research is

needed to determine the effectiveness of these treatments for OEF/OIF personnel. Treatment studies focused on returning veterans are ongoing, including RCTs of both CPT and PE as part of the large South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (STRONG STAR) research consortium. Given the high rates of PTSD symptoms in returning veterans, determining the effectiveness of PTSD treatments for this group is vitally important.

Novel Treatment Approaches

Despite the emergence of evidence-based treatments for PTSD, research shows that up to 30% of patients may be unresponsive,³⁹ indicating the need for further research to refine existing treatments and develop new alternatives. Novel approaches to the treatment of PTSD currently under investigation include medications such as prazosin and propranolol, couples and family therapy, acceptance and commitment therapy, mindfulness-based interventions, imagery rehearsal therapy, narrative disclosure, and behavioral activation, among others.⁴⁷ Modifications to increase the effectiveness of existing therapies are also being examined, such as the use of virtual reality technology or the medication d-cycloserine to increase the effectiveness of exposure-based treatments.

BARRIERS TO CARE

Well-validated PTSD screening tools and diagnostic technologies have been developed, as well as effective pharmacological and psychological treatments. However, not all active duty personnel or veterans are receiving evidence-based practices.⁴⁸ In many clinical settings, there are significant barriers to implementing the best evidence-based practices for screening, diagnosing, and treating PTSD.

Practical Barriers

Large-scale screening can be difficult to implement widely. Primary care centers have been targeted as a natural setting for screening¹²; however, primary care clinicians have limited time with patients and need to screen for a number of other medical and psychiatric issues in addition to PTSD. Diagnostic tools can also be difficult to disseminate to a broad range of clinical settings. Semistructured interviews require training to administer reliably and are more time-intensive than self-report measures. Assessment of psychophysiological indices of PTSD requires expensive equipment and training to administer and score accurately. Evidence-based psychotherapies also require extensive training, making them difficult to disseminate widely. The VA has initiated a “national rollout” providing training in CPT and PE to providers across the country to increase patient access to these two therapies. However, the actual implementation of such interventions across large institutions like VA and the DoD can be a substantial challenge.⁴⁹ Another related challenge to accessing these treatments is the significant time commitment that is required, which can be difficult for active duty

personnel, working veterans, and individuals living in rural locations who may have to travel long distances to meet with a therapist. Telehealth and internet-based interventions have been proposed to increase access to care in remote locations, and such treatments are currently under investigation.⁵⁰ Pharmacological treatments are thought to be easier to disseminate, but not all veterans are willing to take psychotropic medications, and pharmacological treatments for PTSD are only modestly effective. Additionally, many pharmacological interventions have undesirable side effects, such as impaired sexual functioning, making compliance difficult.

Comorbidity

Active duty service members and veterans typically present with a number of medical and psychiatric complaints all requiring attention. The existence of comorbid conditions can interfere with both diagnosis and treatment of PTSD. The presence of comorbid mental or physical health conditions can complicate diagnosis if PTSD symptoms are attributed to other causes. Treatment for PTSD may be delayed because of the presence of comorbidities. For example, in the case of comorbid PTSD and substance dependence, the current VA/DOD clinical practice guidelines recommend deferring PTSD treatment until medical detoxification is complete.³⁴ This concern is all the more pressing because patients often do not present with one DSM-IV disorder, but rather are likely to meet criteria for multiple mental health concerns. In one large nationally representative sample, more than 40% of individuals meeting criteria for one disorder had at least one comorbid disorder, and the likelihood of comorbidity increased with symptom severity.⁵¹ Traumatic brain injury (TBI) and PTSD commonly co-occur in civilian, military, and veteran populations and can be difficult to distinguish because both can result from the same traumatic incident.^{52,53} The two conditions also have several overlapping symptoms, including impaired concentration, decreased sleep, psychomotor agitation, and irritability, and there is currently no established method of differentiating the etiology of these common symptoms.⁵³ Depression and substance use are also commonly comorbid with PTSD and co-occur frequently with PTSD symptoms in OEF/OIF personnel and veterans.⁵⁴ When veterans present with multiple mental health concerns, a comprehensive evaluation and treatment plan is essential to ensure all relevant treatment targets are addressed.

Stigma

Another important barrier is the stigma associated with mental illness. Active duty personnel may be concerned that a PTSD diagnosis will interfere with their work or result in a medical discharge from the military, and veterans may be concerned about their ability to return to service in the future. Such service members may not seek treatment or may be motivated to conceal or minimize the severity of their symptoms to clinicians. Research with OEF/OIF samples indi-

cates that concerns about stigmatization are prevalent. In one study of OEF/OIF service members and veterans, over half of respondents who screened positive for a mental health disorder expressed concerns about possible stigmatization associated with seeking mental health treatment (e.g., endorsed items such as “It would harm my career,” “my unit leadership might treat me differently,” or “I would be seen as weak”), highlighting the salience of this concern for returning veterans.⁵⁴ Factors associated with perceived stigma include negative beliefs about mental health treatment and lower levels of perceived unit support.⁵⁵ Unfortunately, perceptions of stigma are highest among service members who most need treatment, with those who screen positive for mental health disorders, including PTSD, reporting greater stigma.^{55,56}

CONCLUSIONS AND FUTURE DIRECTIONS

Screening and diagnosis of PTSD have improved exponentially in recent years. Existing assessment methods are effective in identifying the severity of PTSD symptoms and discriminating PTSD from other psychiatric disorders. Although establishing a PTSD diagnosis is useful, this type of assessment offers little insight into a patient’s social, occupational, physical, and cognitive functioning. Not only is the assessment of functional impairment critical from the standpoint of making a PTSD diagnosis, it is crucial for treatment planning and outcomes monitoring. Similar to PTSD, functional impairment can be assessed using clinical interviews, self-report instruments, and performance-based measures.

Effective treatments for PTSD are available and as a result clinicians, active duty military personnel, and veterans have the choice of several evidence-based pharmacological or psychological treatment options. Although several treatment options are available, not all treatments have a strong evidence base with military samples, and more research is needed with OEF/OIF samples in particular. Furthermore, little is known about which treatment is best for which patient. Identifying genetic factors or demographic or personality variables that discriminate effectiveness of different treatments for particular patient populations is an exciting area of future research.

In summary, several well-validated PTSD screening tools and diagnostic technologies now exist, and effective pharmacological and psychological treatments for PTSD are available. Despite these advances, many active duty personnel and veterans still do not receive these evidence-based assessment and treatment approaches. Future research should focus our efforts on dissemination or how to get these proven methods in the hands of clinicians and delivered effectively to the military personnel and veterans who need them.

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Prevention and Care of Combat-Related PTSD: Directions for Future Explorations

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ABSTRACT In the past decade, military personnel supporting the wars in Iraq and Afghanistan have faced multiple deployments and repeated traumatic stressors. Despite efforts to prevent post-traumatic stress disorder (PTSD) and other combat-related emotional difficulties, a significant number of military personnel experience psychological injuries during and following their deployments. Despite increased attention to prevention and treatment of these problems, it is clear that substantially more work is required to fully understand the emotional impact of combat and to better intervene to prevent potentially chronic problems. In the present article, the authors discuss possible avenues for future research and interventions (clinical and otherwise) to better prevent the development of combat-related PTSD. We discuss screening, assessment, education, and intervention for PTSD throughout the deployment cycle. In this discussion, we attend to both the needs of the current cohort of combat veterans and the potential advances that may mitigate the severity and chronicity of post-traumatic problems arising from future conflicts.

INTRODUCTION

The United States has deployed over two million troops in support of the wars in Afghanistan and Iraq. Many have deployed multiple times and have been repeatedly exposed to traumatic stressors. Despite increased awareness and emphasis placed on minimizing the psychological injuries associated with combat, a significant portion of those deployed to these wars experience emotional difficulties in theater¹ and upon their return home.² Estimates suggest 15% of service members, some 300,000 individuals, returning from combat in Iraq and Afghanistan will be diagnosed with post-traumatic stress disorder (PTSD). The long-term consequences for individuals with PTSD are often complicated by the presence of comorbid problems, including traumatic brain injuries, chronic pain, and additional psychiatric disorders,²⁻⁴ and the reticence of troops to seek care.⁵

Despite theoretical and therapeutic advances, efforts to prevent chronic PTSD (i.e., persisting 3 months or more) continue to fall short. This article presents the authors' speculation on potentially fruitful directions for future research and development efforts. Rather than describing specific studies that could answer each open question, we assume that readers will use appropriate research designs when examining the issues we identify. However, we note the need for longitudinal studies and controlled treatment outcome studies.

We will use the deployment cycle as a framework for this article. As a rough schematic, the deployment cycle can be broken into three phases: (1) predeployment (including accession and basic military training) during which individuals, families, and units prepare to deploy; (2) deployment during which the service member or unit is actually deployed into theater; and (3) postdeployment when the service member returns from theater and must adjust to life at home. The stress

and requirements placed on individuals differ throughout the cycle. Thus, the factors that allow an individual to function without PTSD during a combat deployment may not be the same skills required for successful reintegration upon return. For example, unit cohesion may help mitigate the effects of combat during deployment, but may also complicate reintegration into the family and community. Importantly, in the current operational environment, service members returning from combat may already be preparing for their next deployment, effectively merging the postdeployment phase of one deployment with the predeployment phase of the next one.

FUTURE DIRECTIONS: SMALL STEPS AND GIANT LEAPS

Our goal is not to thoroughly review the existing literature on combat and PTSD. Rather, we will use that literature to inform directions for future research and clinical efforts to address the problem of PTSD. Some suggestions are small steps forward in refining or adapting existing technologies to meet identified needs, others represent giant leaps from the existing literature. We do not assume that all the ideas suggested here will result in meaningful findings or effective treatments, merely that there are open questions that may reveal interesting answers.

Advances in predicting, preventing, or treating PTSD do not come without potential negative consequences. To use an unrelated example, the development of a genetic test for Huntington's disease has provided significant relief to some who are at risk. It has also led to significant ethical, emotional, and economic issues that must be considered. It is important for the reader to consider both positive and negative consequences of new developments. For example, if we are able to identify persons genetically at risk for PTSD before entry into the military, would they be prevented from enlisting? If we eliminate those with a genetic predisposition for PTSD from military service, might we end up with too

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few military personnel to meet mission requirements? Lastly, what will be the impact on society if some may serve and others may not based on their genes?

PREDEPLOYMENT

There are three basic strategies to limiting PTSD during the period before combat deployment, each may benefit from significant research. The first approach would screen personnel for risk markers or risk factors associated with PTSD. The second approach involves intervention before combat deployments, providing information or skills that would mitigate the effects of combat trauma. The third approach changes how personnel are assigned to units and how those units and individuals are deployed to reduce risk. It would also be possible to combine risk identification with changes to training, education, or duty assignments to reduce risk.

Screening and Assessment

In theory, screening for PTSD risk is straightforward. Risk markers must be identified, appropriate tests administered and results properly read and interpreted. In practice, screening for PTSD risk is complicated and requires substantial research and development. Although many variables differentiate persons with and without PTSD, few have been tested as “predictors” of future PTSD. Also, it is clear that PTSD is multiply determined and that individual pretrauma characteristics explain little of the variation in the presence of PTSD.^{6,7} Therefore, any effective screening effort will need to assess multiple factors and develop an algorithm that takes into account the results of multiple tests or indicators.

Candidates for predeployment screening include biologically based factors, such as genetic,⁸ epigenetic,⁹ neurophysiological (e.g., hippocampal volume),¹⁰ endocrinological (e.g., cortisol),¹¹ and physiological factors (e.g., psychophysiological reactivity).¹² Other candidates are psychological health characteristics, such as previous psychiatric diagnoses,⁶ a tendency to dissociate,^{13,14} negative self view,¹³ and persistent avoidance.¹⁵ A third category involves individual and family history factors, such as aversive childhood experiences and family history of psychopathology.⁶ It should be noted that few existing studies that have identified factors related to PTSD have incorporated prospective designs that would allow a clear determination of causal relations.

To develop a useful screening tool, the prospective predictive power of potential screening targets needs to be determined. Also, assuming multiple predictors are necessary for effective screening, the algorithm combining those predictors needs to be developed. Research should examine predictive models specifically relative to combat trauma. There is general consistency in PTSD across trauma types; however, specific aspects of combat trauma (e.g., taking a human life) and military training may change the relative risk associated with specific indicators. One must also consider military-specific factors that may impact the utility of

the test. The desire to deploy (or to avoid deployment) can contribute to error as can variation in testing situations. In addition, tests must be able to be administered on a large scale to screen all military personnel.

Education and Intervention

It is possible that one could provide individuals some skill or knowledge that would help protect them, effectively inoculating them to PTSD, following future trauma. The PTSD literature offers a few clues as to what might be taught. Two potential targets evident in the PTSD risk literature are increasing the use of social support systems and normalizing post-trauma responses. The presence of a supportive social environment is one of the strongest predictors of recovery following trauma,⁶ and individuals critical of their own emotional responses to a trauma are also most likely to see those responses persist over time.¹⁶ These ideas are incorporated in existing programs including the Army’s Battlemind program¹⁷ and the Marine Corps’ Combat Operational Stress Control (COSC) program. However, research examining the efficacy of such resilience or prevention programs is needed.

Additional targets for resilience training are suggested by the PTSD treatment research. For example, the effectiveness of exposure-based therapies has led some to suggest that exposure to potentially traumatic stimuli in a controlled situation (e.g., training) might inoculate individuals to later trauma. Alternatively, educating personnel about the potential negative consequences of avoidance may decrease problems in the aftermath of trauma. Cognitive therapy treatments for PTSD suggest that predeployment training could strengthen cognitive processes incompatible with PTSD. Similarly, the utility of stress or anxiety management skills training for people with PTSD suggests potential targets for increasing resilience. Research is needed to determine whether training in these skills before combat exposure would reduce the occurrence of PTSD.

Research outside of the PTSD arena may offer potential targets for predeployment training. For example, the field of applied sports psychology has identified techniques that can improve performance in high-stress situations including improved attentional focus, physiological control, increased confidence, and imaginal rehearsal. The field of positive psychology provides potential interventions to increase optimism and promote positive adjustment. Although research is still needed to establish the effectiveness of these techniques in promoting resilience and adjustment following combat, they form the basis for existing military efforts including the Army’s comprehensive soldier fitness program and the Marine Corps’ COSC program.

Considerable research and development is required for any resilience or prevention program. Basic questions about what should be trained and how it is best trained within the larger military training regimen must be addressed. More detailed questions such as who should conduct the training

(e.g., military trainers or behavioral health experts), how it should be delivered (e.g., live training or online), and when, relative to a combat deployment (or deployments), should the training occur need to be answered. Added research will need to examine how best to match personnel to the type of PTSD prevention program that will be most effective for them. This may involve using screening tools discussed earlier to target individuals with specific skills training that will be most helpful. A similar model is being used currently in the Army's comprehensive soldier fitness program (described below) to target specific areas of need for training.

Modified Military Training

Data collected in deployed settings¹ suggest that characteristics of the military environment such as strong leadership and unit cohesion can help mitigate the emotional impact of combat trauma on individuals. These findings have been understood in the context of the positive effect of social support following trauma. However, the specific mechanisms through which leadership and unit cohesion reduce the impact of combat trauma are not well understood. Research is needed to better understand the effects of these and other unit-level variables on the psychological impact of combat and risk for PTSD. Further, constructs such as leadership and unit cohesion incorporate a variety of skills and characteristics. To capitalize on the role that these and other unit-level variables play in the adjustment of unit members, we must study which aspects of these constructs are most important.

Tremendous effort has been put forward to develop military training that produces an effective fighting force.^{18,19} However, no research that we know of has examined how military training may impact risk for PTSD. Specific questions of how military training could be leveraged or modified to reduce the risk of PTSD must also be studied. Given the apparent importance of leadership and cohesion, this area might prove a valuable one for investigation.

The findings regarding leadership and cohesion open the possibility of using unit-level assessments before deployment to identify units at risk.¹ When such units are identified, additional training or other interventions to promote unit resilience could be provided. For example, one can imagine that a unit with significant cohesion problems might receive extra training focused on improving both operational readiness and unit cohesion. Models for such training exist both within and outside the military with data supporting their efficacy on measures of team strengthening and increased cohesion.^{1,20} It is not known whether these approaches would also reduce PTSD.

DEPLOYMENT

Individuals deployed to combat zones are often exposed to multiple potentially traumatizing events.^{1,5} Efforts to reduce the emotional impact of these events may be implemented before or following specific events.

Screening and Assessment

Questions pertaining to screening and assessment during the deployment are direct extensions to those before deployment. Individual and unit-level factors could be assessed to identify those at most risk for PTSD. As with screening before deployment, issues of predictive power, measurement, and development of appropriate algorithms for combining data on multiple risk factors need to be addressed. Further, examination of risk factors assessed during deployment must delineate whether the risk is manifest during deployment, upon return home, or both. It is likely that the most effective predictors of chronic PTSD will not be identical to those that identify individuals who experience intense psychological distress during deployment.

One potentially fruitful area of research that has not received much attention to date is the possibility that there are risk markers that are manifest while the individual is deployed but not before deployment (e.g., dehydration, malnutrition, sleep deprivation). Similarly, changes in risk factors during the deployment (relative to predeployment) may provide better prediction of individuals who will manifest chronic PTSD than do factors assessed at a single point in time. To date, no research has examined changes in individual or unit characteristics during the deployment to determine if such changes could be used to identify individuals at risk for PTSD.

One clear need is an easily administered and accurate measure of risk that can be administered close to the time of the traumatic exposure so that treatment could start as soon as possible. The PTSD literature provides some candidates for such early identification. Injuries sustained during the trauma,⁵ peritraumatic dissociation,¹⁴ diagnosis of Acute Stress Disorder (ASD),²¹ intense early symptoms,²² physiological and endocrine reactivity,^{11,23} and exposure to multiple traumas^{1,5} have been associated with chronic PTSD. We should also determine if certain types of traumatic events that occur during combat deployments (e.g., killing, civilian casualties, death of a unit member) are more likely to result in PTSD than are other events.

Intervention During Deployment

PTSD-reducing interventions delivered during the deployment can be separated into two broad categories: (1) prevention strategies delivered regardless of the presence of post-trauma symptoms and (2) clinical interventions delivered only to those identified as having symptoms. In the first group are population health strategies including the COSC and comprehensive soldier fitness programs discussed above as well as trauma-focused approaches such as critical incident stress debriefing or management (CISD/CISM). Clinical interventions include early treatment with protocols developed for chronic PTSD as well as newer interventions specifically designed to address the needs of acute trauma survivors. Notably, almost no systematic research exists on the effects of interventions for PTSD delivered during deployment.

Prevention Programs

The Army's comprehensive soldier fitness program and the Marine Corps' COSC program include components delivered before, during, and after deployment. The extent to which these programs, specifically the elements delivered during deployment, reduce PTSD has not been examined. The potential value of incorporating interventions designed to promote unit-level factors that have been associated with PTSD symptoms (e.g., leadership, cohesion) during deployment has not been examined. Should these programs prove effective, questions pertaining to effective components, mode of delivery, and mechanisms of action should be addressed.

The military has extensive experience with public health campaigns. Although the services have made considerable effort to raise awareness about PTSD and other postcombat difficulties and the availability of treatment resources, an evaluation of full-scale public health campaign around the problems of PTSD in a deployed setting has not been undertaken. As with other attempts to address the issue of PTSD around the demands of repeated combat deployments, one must balance the potential benefits against the potential consequences. Concerns can be raised, for example, that service members fully conscious of the potential emotional consequences of combat may be less effective in prosecuting the war.

Debriefing units following traumatic events, using programs such as CISD/CISM or other strategies, continues despite the apparent lack of efficacy of single-session debriefing.²⁴ Importantly, research that identified potential problems did not examine individuals deployed into combat. Although there is reason to be cautious when examining these approaches, research should assess the risks and benefits of debriefing following combat events, particularly if the approach is being used.

Clinical Post-Trauma Interventions

Throughout the current wars, the military has deployed behavioral health providers into theater to care for deployed service members. Treatments for chronic PTSD including prolonged exposure (PE),²⁵ cognitive processing therapy (CPT),²⁶ and eye movement desensitization and reprocessing (EMDR)²⁷ have been used in theater. Other interventions that have shown some success in reducing PTSD symptoms such as relaxation training, problem-solving therapy, and cognitive therapy also are being delivered in theater. The military also uses medications effective in treating chronic PTSD symptoms to treat individuals while deployed.

Although there are no systematic examinations of these interventions, case studies²⁸ and anecdotal reports of success suggest that early in-theater treatment, particularly with psychotherapy, will prove a fruitful area of research. Of potential interest for treatment developers and researchers is the fact that many of the established approaches to treating acute PTSD or ASD symptoms are being modified to fit the demands of the deployed setting. Research on the impact (positive or negative)

of these modifications is needed. As mentioned above, research on the use of these treatments must evaluate individual psychological health outcomes relative to the individual's readiness to complete his or her military mission.

Recently, interventions have been suggested, and in some cases tested, that aim to disrupt the mechanisms through which the mind processes traumatic events in order to prevent them from consolidating and becoming traumatic memories. These efforts include several pharmacological agents such as cortisol¹¹ and cognitive activities with significant visuo-spatial demands.²⁹ Research on ways to block PTSD development after a trauma is limited to a few small studies or analog studies with results that suggest we are far from identifying a means for blocking the formation of traumatic memories. Still, the potential benefit of interventions that prevent chronic PTSD argues for more research.

Modes of care delivery are complicated in combat zones and represent an area in need of research. Efforts by the military to deliver care in these settings can also inform researchers and treatment developers. The fact that individuals are being treated successfully in the combat zone for combat-related PTSD symptoms questions the generally accepted tenet that one must ensure that patients are physically safe before treating PTSD.³⁰ Also, the long-term impact of treating PTSD in the combat environment is not understood and provides opportunities for research. Similarly, modifications of existing protocols to fit the needs of the deployed setting, such as treatment delivered daily rather than weekly or treatment sessions lasting longer than the standard "50-minute hour," also suggest potential points of inquiry around the general topic of whether there are better ways to package and deliver psychotherapy than the traditional 1-hour weekly session in the office. Also, the military is providing care via telehealth systems allowing treatment when the patient and provider are not at the same location. How well this form of treatment delivery reduces PTSD and how it translates into civilian practice is not yet clear.

Modified Deployment Strategies and Tactics

Issues related to military operations should be examined for their impact on the development of chronic PTSD. For example, the MHAT studies¹ found longer combat tours associated with more PTSD symptoms in theater. Similarly, too little time between deployments is thought to negatively impact adjustment. Other aspects of how units are deployed and used in combat may also impact on the development and persistence of PTSD. Several countries have built in a decompression stop as their service members return home from the combat zone. This allows a brief (typically a few days) respite from the war before service members reintegrate with families and friends. Formal reintegration training where service members and their families are taught skills to encourage a successful reunion should also be examined. Whether these or other aspects of the deployment and redeployment process have a significant impact on the persistence of PTSD symptoms awaits further research.

POSTDEPLOYMENT

During the postdeployment phase, service members must adjust to life away from combat and (possibly) their comrades as well as reintegrate with family, friends, and the civilian community. These processes are made more difficult by the presence of PTSD symptoms. In general, the issues in need of research and development following deployment are similar to those at other points in the deployment cycle. Specifically, the field needs more accurate and effective tools to identify PTSD as well as more effective and efficient treatments for postcombat PTSD.

Screening and Identification

The military regularly screens service members returning from combat for psychological health problems. However, existing screening processes have problems and systematic research is needed to improve them. Available screening tools, though reasonably reliable and valid, rely on service member or veteran reports on face-valid items making it relatively simple to appear healthier or more ill than one actually is. Clearly, there is a need for more objective tools to identify individuals at risk for or diagnosable with PTSD. There is also a need for research to better understand the role that characteristics of the military environment (e.g., command structure, bonding with buddies, repeated deployment), sociopsychological constructs common in military members (e.g., self-reliance, loyalty, stigma), and characteristics of the test and testing environment (e.g., presence of buddies, rumors of delayed homecoming, wording of the tests) influences screening and diagnostic results. In addition to improving psychometric measures, it would be useful to develop biologically based (e.g., physiological, neurological, neurochemical or hormonal) screening and diagnostic tests that could be used in conjunction with psychometric instruments to assess PTSD. Regardless of what approach is taken, research must establish the reliability and validity of any screening tests across multiple combat deployments.

We lack a full understanding of how PTSD symptoms in this population change over time. Research using civilian trauma survivors suggests that the most common response is an initial increase of PTSD symptoms followed by a gradual recovery over time.²⁰ However, anecdotal reports of service members returning from combat describe a delay in PTSD symptom onset. It is not clear whether there is a difference in the development of PTSD following combat and civilian traumas or if something else accounts for this difference in presentations. Regardless, a better understanding of the course of PTSD symptoms among service members, particularly those who may deploy again, is needed.

Postdeployment Interventions

The VA/DoD treatment guidelines for PTSD list several treatments effective for this disorder.³¹ The effectiveness of these treatments with active duty service members has not

been examined, though such studies are underway.³² Studies with veterans have found significant reductions in PTSD but also substantial residual symptoms.^{33,34} Clearly, there is considerable room for research in the area of PTSD treatment for this population. Treatment development and testing is a long process with varied research opportunities (e.g., treatment outcome, mechanism of change, treatment modification). Because of space constraints, we will not list all the treatment research that could be conducted, but we will discuss a few potentially important research directions.

Modification of Existing Treatments

Although existing treatments are generally effective, a good number of individuals do not complete treatment³⁵ or retain some of their symptoms.^{23,36,37} The PTSD treatment literature is replete with attempts to improve existing treatments by adding or subtracting elements or changing the manner in which the treatment is delivered. In general, these attempts have failed to show significant enhancement over the established protocols. We would suggest that researchers looking to improve the treatment of combat-related PTSD attend carefully to the potentially unique aspects of this population when exploring improvements to treatment and treatment delivery. Indeed, some efforts along these lines are already underway to include the use of virtual reality exposure exercises,^{38,39} telemedicine delivery of care,⁴⁰ and delivery of PTSD treatment in primary care settings.⁴¹

New and Different Interventions

Established PTSD treatments were developed in the 1990s and incorporate similar techniques (i.e., exposure to traumatic memories or cues, cognitive therapy, anxiety management). Advances in neuroscience, our understanding of memory, and neurobiological mechanisms related to memory offer possible avenues for a shift in treatment of PTSD. New treatments may combine biological, pharmacological, or neurological interventions into existing treatments or may represent completely new approaches not yet conceived.

An alternate approach to new treatments for PTSD would utilize the military environment. Unit and leader characteristics appear to contribute to resilience (see above), but we are not aware of any study to determine if aspects of military training or leadership could be useful in reducing PTSD symptoms. It is possible that aspects of military training, actions taken by a unit commander, or interventions conducted on the unit might reduce PTSD symptoms among the individuals in that unit. Given the role of unit-level training in the military, we suspect that if such interventions could be developed, they might prove quite effective in this population.

New and Improved Treatment Delivery Strategies

Questions can be asked about who, where, and how PTSD treatment should be delivered. For example, must treatment be delivered by a behavioral health professional in an office in a weekly 1-hour session? Additional research is needed to

understand the potential benefits and costs associated with the use of technological advances (e.g., telemedicine, virtual reality, and smart phones) to deliver existing and new treatments. PTSD is commonly seen in conjunction with a long list of other issues including depression, anxiety, substance use, chronic pain, anger, relationship problems, and other problems. Programs to treat PTSD in the context of these other issues should be an area of future research.

CONCLUSION

PTSD is a problem for a significant number of service members returning from the wars in Iraq and Afghanistan² and impacts their families, communities, and the larger society. Issues related to screening, prevention, identification, and treatment of PTSD among service members and veterans offer many opportunities for innovative and meaningful research. Finding answers to the questions discussed above and many others that are not detailed in the present article will require coordinated and dedicated research efforts.

We have not tried to provide an exhaustive list of research topics. Rather, we have outlined key topics that must be researched to address the problem of PTSD. We also want to offer some cautionary notes for readers motivated to rush out to conduct innumerable research studies.

- (1) The military is a unique organization (or set of organizations) with its own structure, culture, traditions, and processes. It is not clear how well results of research on civilian samples will generalize to military samples. This does not mean we should assume that civilian findings will not generalize to the military. In fact, understanding similarities and differences in PTSD manifest in military and civilian populations is an important area for research.
- (2) The military has a unique mission, to fight our country's wars, that requires certain actions that are not necessarily conducive to maintaining psychological health. Research on PTSD in the military and recommendations based on such research must take this into account. For example, one strategy to reduce PTSD would be to limit wartime activities to those unlikely to engage the enemy. Obviously, this is inconsistent with the military mission. Recommendations must take into account the primary mission of the military.
- (3) Questions about assessment, prevention, and treatment of PTSD in the context of an all-volunteer military actively engaged in multiple, prolonged wars are more complicated than they initially appear. Results of many studies suggested above will impact at multiple levels ranging from the individual service member through families, communities, the military, and our entire society. Even something as seemingly straightforward as identifying individuals with PTSD raises questions about unit morale, mission readiness, need to provide treatment (and its associated costs), disability compen-

sation, and many others. Progress will require coordinated efforts of multidisciplinary teams of scientists, clinicians, military leaders, and policy experts.

In sum, there are many questions to be asked and studies to be conducted. We have identified some that may have the most impact. We have also tried to encourage the reader to think beyond the traditional psychological approaches to examine the unique characteristics of the military environment and culture that might contribute to our understanding of combat trauma and its impact on the men and women who serve in our military.

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Epidemiology and Prevention of Substance Use Disorders in the Military

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ABSTRACT U.S. military service members have been in active combat for more than 10 years. Research reveals that combat exposure increases the risk of substance use disorders, post-traumatic stress disorder, major depression, and tobacco use. The Services and the field of addiction medicine are working hard to find a common definition for prescription drug misuse, which is a growing concern in both the general U.S. population and the force. Meanwhile, leaders at all levels of Department of Defense are diligently working to address barriers to care, particularly stigma related to substance abuse care, by seeking a balance between improving service member privacy in order to encourage self-referral for medical care and a commander's need to know the status of the unit and its combat readiness. The treatment and management of substance abuse disorders are a complex force health issue that requires the use of evidence-based medical interventions and policies that are consistent with them.

INTRODUCTION

As of October 2010, 2,200,594 U.S. service members have deployed in support of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF).¹ There is a uniqueness to OEF and OIF combat actions that include vastly improved survival rates for the wounded, the identification and categorization of traumatic brain injury (TBI), and nonsymmetrical terrorist tactics, just to name a few. The incidence and prevalence of substance use among military members is often used as a fundamental barometer of force health and these conditions co-occur with a broad number of psychological health and physical conditions. This article examines the prevalence and incidence of substance abuse in the military and sets the stage for articles that follow in this special edition of Military Medicine looking at treatments and co-occurring disorders.

PREVALENCE AND INCIDENCE

Civilian and Military Comparison

Though military service members are drawn from the civilian population, a comparison between service members and their civilian counterparts is difficult. Personnel serving in the military are screened before entering the service for many medical and psychological vulnerabilities, which some suggest would make them more resilient than the general population, but service members experience very different risky occupational exposures, the most obvious being combat. Despite this, there is some utility to using the general U.S. population as a comparison group by which to frame this article.

Approximately every 3 years, the Substance Abuse and Mental Health Services Administration (SAMHSA) conducts

a survey of the substance dependence, abuse, and treatment in the United States, which is called the National Survey on Drug Use and Health (NSDUH). In recent years, there has been an ever-growing concern in both the United States and Department of Defense (DoD) about prescription drug misuse including commonly tracked illicit drugs such as marijuana, cocaine, hallucinogens, inhalants, and prescription drugs used for nonmedical purposes. The overall civilian rate of illicit drug use remained fairly consistent from the 2002 to the 2008 NSDUH (8.3% compared to 8% of population, respectively).² In the 2008 survey, prescription drug abuse is defined as “the use of prescription pain relievers, tranquilizers, stimulants, or sedatives without a prescription of the respondent's own or simply for the experience or feeling the drug causes.”³ The definition covers a wide range of behaviors including the misuse of medication to numb emotions, to stay awake for work, or to use a friend or family member's medication. There was a significant increase in the non-medical use of prescription drugs by young adults aged 18 to 25 from 2002 to 2008 (5.5% to 6.3%, respectively).¹ These nonmedical users of prescription medications reported that the most common source for acquiring these medications was from a friend or relative.¹

In order to further understand the suggested increase of prescription drug misuse, respondents in the 2008 NSDUH survey were asked to report only nonmedical use of medication in four categories: pain relievers, tranquilizers, stimulants, and sedatives.¹ In the survey, nonmedical was defined as use without a prescription of an individual's own medication or use for the experience. When prescription medication use for active duty was assessed utilizing the 2008 Health Related Behaviors Survey (HRBS), the active duty members were queried using the NSDUH definition of nonmedical use of prescription medications as well as if individuals were taking their medications in greater amounts than it was prescribed. The broader definition used by the HRBS may increase the likelihood of a positive response to the prescription drug abuse question, which should be considered when

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comparing illicit and prescription drug misuse data between civilian and service members. Of the 20.1 million Americans that responded to the NSDUH and admitted to using illicit drugs in 2008, 6.2 million (2.5%) people reported misusing psychotherapeutic medication, and of those, 4.7 million (1.8%) people used pain relievers nonmedically compared to 10% of service members.^{1,4} In addition to criterion differences, service members differ from their civilian counterparts by typically having access to a better, more reliable health care, and have physical fitness requirements and deployments that often lead to injuries that may result in being prescribed pain relievers and other medications. However, when comparing illicit drug use between the civilian population and service members, civilians have a significantly higher prevalence rate (8.9%) compared to service members (2.3%).^{5,6} The lower prevalence rate for service members can be attributed largely to the DoD implementation of random drug testing.⁶

When examining alcohol use, Bray et al⁷ found rates of military service members aged 18 to 25 showed significantly higher rates of heavy alcohol usage (26%) than did their civilian (16%) counterparts. The trend continued when comparing military members aged 26 to 35 (18%) with their fellow civilians (11%). However, the trend was not statistically significant between military members (10%) and civilians (8%) in the 36- to 45-year age range. As Bray et al⁷ noted, military members aged 46 to 64 exhibited lower rates of heavy alcohol usage when compared to civilians (4% vs. 9%).⁷

Substance Use and Misuse in Military Service Members

Historical vs. Current

Research involving Vietnam War veterans focused on the frequently comorbid diagnoses of post-traumatic stress disorder (PTSD) and substance use disorders (SUDs). The Vietnam Experience Study conducted by the Centers for Disease Control revealed that when compared to non-Vietnam veterans, Vietnam veterans were significantly more likely to develop psychological problems, including problems such as alcohol abuse or dependence (13.7% vs. 9.2%), anxiety (4.9% vs. 3.2%), and depression (4.5% vs. 2.3%).⁸ Studies of Operations Desert Shield and Desert Storm veterans reveal that prevalence rates for psychological health disorders are higher for those service members who have deployed as compared to those who have not.⁹⁻¹² A 2006 study by Fielder et al¹³ reported that there were significant differences in the prevalence rates of anxiety disorders, depression, and drug dependence in those that deployed compared to those that did not, though there was no statistically significant difference in alcohol dependence or abuse diagnoses between the two. However, Fielder et al did report that significant risk factors for SUDs for Operations Desert Storm veterans were being male, enlisted, divorced or single (or living with someone), and deploying in support of Operation Desert Storm.

As the fighting in OEF and OIF (now called Operation New Dawn) reaches nearly a decade, researchers have been examining the impact of deployment and combat action on substance use rates. As noted by Jacobson et al,¹⁴ studies that compare deployers and nondeployers reveal deployers with combat exposure or trauma had higher rates of alcohol misuse than those who were not exposed to combat or trauma.

Alcohol Use

In 2001, the millennium cohort study was initiated to evaluate the long-term health of military service members and to assess the possible impacts of deployment and other military unique experiences on service members' health.¹⁴ The results indicated that deployers with combat exposure were more likely than deployers without combat exposure to have drinking problems before deployment (e.g., baseline) and postdeployment were also more likely to develop a new onset of drinking problems.¹⁴ Baseline symptoms of depression or other psychological health disorders were found to increase the likelihood of new onset of alcohol-related problems, especially in those exposed to combat or trauma. The results of the cohort study also indicated that more women than men reported new onset of heavy weekly drinking while men reported more binge drinking and alcohol-related problems overall.

The results from the millennium cohort study also indicated that Reserve and Guard personnel had a higher prevalence rate of new-onset drinking problems postdeployment than active duty personnel (14.1% to 11.5%, respectively).¹⁴ The researchers suggested that inadequate preparation for deployment and training, a lack of support upon return, increased stress from military to civilian transitions, and lack of military unit cohesiveness contribute to the varying prevalence rate.

The 2008 HRBS results indicated that the overall prevalence of heavy alcohol use for all service members was 20%, which represented an increase from the 2005 HRBS results.¹⁵ Those with the highest prevalence rates of heavy alcohol use were found among cigarettes smokers (26%), personnel aged 21 to 25 years (22%), those who use illicit drugs (21%), those who screen positive for PTSD (21%), and those who hold the rank of warrant officer (20%).⁴ The review of the 2008 HRBS data found that the strongest predictors were being male, a cigarette smoker, and being 21 to 25 years of age.⁴ The results also indicated that being 18 to 20 years old was not an indicator of heavy drinking and being 18 to 25 years old was an indicator of binge drinking (53.8%). Another finding that was consistent with the trends in heavy alcohol use revealed that males had a higher prevalence of binge drinking (45.5%) than females (23.9%).¹⁶

Illicit Drugs

Overall, the results of the 2008 HRBS showed a decrease in illicit drug use and an increase in both heavy alcohol use and reported prescription drug misuse, as noted previously.⁴

Bray et al⁴ suggested that the improved question wording in the 2005 and 2008 versions of the HRBS may partially account for the identified increase in prevalence rates of prescription drug misuse, which are largely attributable to reported increases in misuse of prescription pain medications. Some suggest that the increased rates of prescription drug misuse in 2005 and 2008 may be linked to increased deployments, which may also be linked to increased diagnoses of pain disorders, PTSD, and other psychological health disorders, but further study is needed.⁶ The increased rates from 2002 to 2008 are shown in Figure 1.

Cigarette Smoking

In a 1991 study by Bray et al,¹⁷ they found that despite the fact that service members were significantly less likely to use illicit drugs than their civilian counterparts, they were significantly more likely to smoke cigarettes as well as to engage in heavy smoking. Overall, the prevalence rate for cigarette usage for service members was 44% compared to 39.4% rate of usage by civilians. Bray et al also noted that the statistically significant increase in cigarette smoking in the military services from the 1998 survey to the 2002 survey was the first increase since 1980. In 2005, the prevalence rate of cigarette smoking was 4% higher than the rate in 1980. In the review of the 2008 HRBS, Bray et al⁴ found that the smoking rate for members of the Marine Corps stayed level or increased slightly from 2005 to 2008 with those of the other three services trending downward. Prevalence rates for the Air Force were the lowest of all services over the 28-year period covered by the HRB surveys. The results from the analyses of the 2008 HRBS showed that the prevalence rate of cigarette usage by all service members was 30.6% with the highest adjusted rates by those who were also heavy drinkers (43%) and in the pay grades of E1–E3 (35%).⁴

Nelson et al¹⁸ found that 30.8% of smokers did so to relax or calm down, 29.5% used smoking to cope with stress, and 23.5% used smoking to ease boredom. Cigarette smoking, unlike drinking alcohol, is permitted in deployed locations

and may be an introduction to a stress relief behavior that continues upon redeployment.

Bray and Hourani¹⁹ have suggested that the continued prevalence rates for heavy alcohol use and cigarette smoking are reinforced by on-installation advertisement, the sale of alcohol and tobacco products at lower prices than at civilian retail stores, and the contradiction in messaging between health and moderation and a work-hard-play-hard organization.

Co-Occurring Disorders

Given the increased military operations and frequency of deployments, there is little wonder that medical professionals at military health care and VA health care facilities are seeing an increasing number of service members requesting care for substance use and psychological health disorders.^{20,21}

Post-Traumatic Stress Disorder

Research has shown that any type of exposure to combat increases the risk of SUDs, PTSD, major depression, increased use of health care, cigarette use, and functional impairment in the workplace.^{4,20,22} Research has also shown that high levels of combat exposure was predictive of cigarette use, heavy drinking, PTSD, and suicidal ideation, but not major depression.⁴ Hoge et al²³ studied the impact of combat exposure on rates of alcohol use with co-occurring psychological health disorders and found that the prevalence rates for alcohol use, major depression, or PTSD were significantly higher for service members after their deployment.

All deployed service members, including those who reported low combat exposure, are at increased risk to develop psychological health problems, including PTSD. The results of the 2008 HRBS support this assertion. Bray et al⁴ found that for all serviced members, those reporting PTSD symptoms grew 4% to 11% from 2005 rates (7%) with the Marine Corps showing the greatest increase with 15% acknowledging PTSD symptoms. This information is shown in Figure 2.

In a 2009 study of OEF and OIF veterans who entered the Veterans Affairs health care system from 2002 to 2008, the prevalence of PTSD symptoms and SUDs were higher among

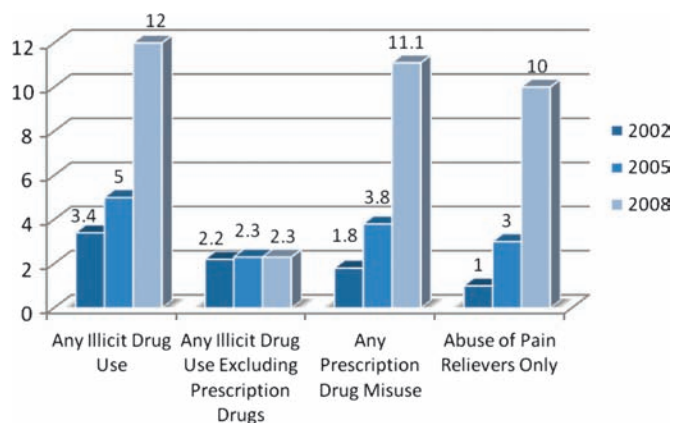


FIGURE 1. Illicit drug misuse by service members: 2002–2008.

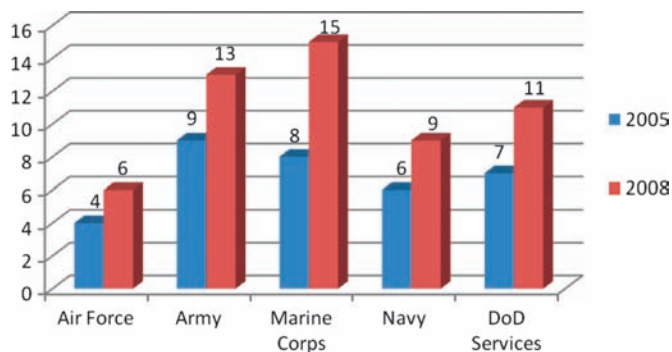


FIGURE 2. Need for further evaluation for PTSD—comparison by service.

veterans 18 to 25 years old compared to their older counterparts age 40 and above with greater combat exposure being associated with higher risk for PTSD.²⁴ The rate of PTSD symptoms for OEF and OIF veterans grew from 13% to 21.8% between the same period. The exact reason for this increase is unclear, but deployment and/or combat exposure is a common factor. It is also possible that DoD efforts designed to encourage service members to seek assistance for their psychological health problems may be helping or PTSD is identified and diagnosed more often because of improved medical provider education and awareness.

Depression

One of the most common comorbid conditions with SUDs is depression. In the 2005 and 2008 HRB surveys, both Army and Marine Corps service members had the highest rate on a depression symptom screener (24% and 26%, respectively), which indicated a need for further depression evaluation and perhaps treatment for depression with a mental health provider.⁴ Bray et al^{4,7} also found that those service members most likely to screen positive for depression also screened positive for PTSD (71%); reported suicidal thoughts (28%); were partnered, but unaccompanied (23%) or single (21%); and were illicit drug users (21%) or cigarette smokers (21%). By far, the most significant predictor of whether a service member would screen positive for depression was if the member screened positive for PTSD.⁴ In a 2009 study of service members with OEF and OIF exposure, Seal et al found, as with previous studies, that female veterans were at higher risk for a diagnosis of depression than male veterans were, but male veterans had over twice the risk for drug use disorders.

Traumatic Brain Injury

With the significant increase in the number of service members in OEF and OIF surviving combat-related injuries, there has been a renewed focus on understanding the effects of TBIs and their impact on other psychological health disorders, including SUDs. From 2001 through the fourth quarter of 2010, over 191,318 service members had been diagnosed with mild, moderate, severe, or penetrating severity TBI.²⁵ A 2009 study looking at TBI and PTSD found that civilians often must cope with mild TBI and PTSD from a single event, and service members often must deal with mild to severe TBI and PTSD from possibly several exposures from multiple deployments.²⁵ As researchers increase their knowledge about how TBI and PTSD interrelate, the information available suggest that further research is necessary to better understand the link between TBI and SUDs.

DISEASE IMPACT

In epidemiological studies in the civilian population, researchers have found that psychological health disorders have a strong correlation with decreased work productivity, increased absenteeism, higher rates of unemployment, and

higher rates of health care utilization.^{26–28} This is consistent with the occupational costs found in the military system including lost days from work, hospitalizations, and restricted duty (e.g., profiles, changes in security clearances, and deployment limitations) for the service members with SUDs and other psychological health disorders.²⁹ The time spent assisting and/or managing the member impacts the mission readiness of that member's unit. As noted previously, research with military populations has demonstrated that OEF and OIF service members and veterans are frequently using substances at higher rates postdeployment. The high prevalence rates of SUDs and other psychological health disorders suggest functional impairment in social and occupational adjustment for service in OEF and OIF.^{9,20,22,30} Bray et al⁴ found that productivity loss was greatest among those that self-reported as being heavy drinkers and that they also suffered the most serious career consequences.

Other ways that SUDs and comorbid psychological health disorders can significantly impact the military mission are through changes in a service member's physical readiness profile, change in security clearance, and deployment limitations. In military units, changes in the availability of service members create additional demands on others. For example, the loss of a service member drives the changing of schedules, attending meetings related to the service member's substance abuse treatment, ensuring that the member makes medical appointments, etc. The impact of SUD and their comorbid disorders is a force health and readiness concern that is hard to overstate.

SUDs can have a devastating impact on families. Hoge et al³¹ examined the link between combat duty and social and family dysfunction, finding that those who served in combat in Iraq were significantly more likely to report decreased marital satisfaction, increased intention to divorce, and increased spousal abuse than those who did not serve in combat roles, especially at the 1-year postdeployment period. The results revealed that spouses suffered from similar rates of depression as active duty members, but are more likely to access psychological health care, though they typically received primary care.

Another key indicator of the occupational burden of military service is the attrition rate from service, which can be both voluntary and involuntary. There has been research that suggests that military service members are at greater risk for discharge in the last decade than any time in the last 25 to 30 years.^{32,33} Hoge et al³⁴ examined psychological health problems reported on postdeployment assessments and found an association between increased utilization of behavioral health and medical services, exposure to combat while deployed and attrition from the military. Hoge et al found that 18.4% of active duty service members, 21% of National Guard, and 20.8% of Reservists returning from OEF and OIF were diagnosed with a psychological health disorder and that over 50% of those members were referred to behavioral health specialty care. However, only 10% of those referred for behavioral health care actually attended their follow-up

appointment. There is an increased rate of psychological health problems at 3 to 4 months after redeployment, which may be a sign that there continues to be a stigma for service members seeking assistance through behavioral health clinics.^{23,31}

ETIOLOGY AND RISK FACTORS

In spite of previous cautions related to comparisons between military and civilian populations, there are similarities, particularly when discussing the etiology and risk factors of SUDs. Although genetic, developmental, and early social risk factors are similar to the civilian population, there are likely behavioral, cognitive, exposure, societal, and environmental risk factors that are unique to military service.

Family norms may play a significant role in affecting substance usage.³⁵ Family risk factors include dysfunctional family dynamics, such as abuse or the modeling of aberrant behaviors.³⁶ SUD rates among individuals raised in alcoholic families are significantly higher than those who did not have a family history of alcohol abuse.³⁶ Similarly, the rates of depression, anxiety disorders, and PTSD can be found in families with a history of psychological health issues, SUDs, and abusive or traumatic behavior. It is essential in a discussion of risk factors to understand that they are not causal, but they can “stack the deck” to make it more likely that someone will misuse substances or be diagnosed with a SUD.²⁴

Ames and Cunradi³⁷ examined the impacts of military culture and access to alcohol as variables affecting alcohol misuse and abuse in the military. The workplace culture in the military can be a risk factor for heavy alcohol use or binge drinking. For instance, if there is a bar located within the unit and everyone is allowed to leave work early on the last Friday of the month and if they go to the bar, this might be considered a risk factor for excessive drinking in that unit. Just as with the civilian population, easy access and availability to alcohol is a known risk factor for military personnel.³⁷ On military installations, alcohol is not only available at the base or postexchange, it is also offered at reduced prices. As Ames and Cunradi noted, service members are also greeted by access to cheap alcohol in establishments just outside of nearly every military facility around the world.

The unique entry criterion for each military service, such as age, gender, or other attributes, may influence prevalence rates of mental health diagnoses. Additionally, each service’s mission, activities, and exposure to events and actions differs and may have a varying effect on members, providing a set of risk factors unique to each service. The potential for a self-selection bias is also present. Individuals have a part in choosing which service best suits their preferences and needs at the time of recruitment. This bias can flow both ways; the service may desire specific types of individuals based on academic or physical performance, or may display more lenient acceptance of, or grant more waivers for, individuals with legal or behavioral issues because of vacancy and recruitment rates that can be affected by deployment operations

tempo.^{38,39} This selection bias, along with mission of the service, can influence the vulnerability for psychological health concerns across a population.

Service culture is part of developing esprit de corps and essential to successful military operations. However, the complexity of culture and norming of behavior may also contribute to higher or lower substance use issues. The cultural environment, peer response, and condoned behavior are of significant influence on the service member’s cognition and behavior related to substance use and abuse.^{16,37}

Recent operations have included a significant effort and contribution by Guard and Reserve service members. Jacobson et al¹⁴ noted that risk factors for both Guard and Reserve personnel for increased drinking included inadequate training and preparation for deployment and redeployment, the additional transition from the military unit to a regular civilian job, and reduced access to medical services, which includes treatment for SUDs after leaving the active duty force. There has been a renewed effort to ensure that Guard and Reserve members receive their service-connected medical care before leaving their active duty tour, to include addressing their SUDs and other psychological health needs.

Research suggests the presence of genetic and environmental components in the development of SUDs.^{40,41} Service members with environmental exposure to combat or other significant stressors may be at increased chance of developing a comorbid disorder such as PTSD or depression.^{40,41} In the general population, genetic factors are linked to dependence on legal substances such as nicotine and alcohol, and illicit substances such as cannabis and cocaine, although environmental experiences unique to a predisposed individual also greatly influence whether or not that individual uses.⁴² This information may be fundamental in the development and focus of prevention strategies.

Significant advancements have been made in the area of psychological resilience. Resilience includes a resistance to negative psychological effects as well as the ability to more quickly recover when overwhelmed. For example, positive emotion has been found to be vital to both the individual’s perception of the traumatic situation and to the efficacy of coping mechanisms used over time.⁴³ Specifically, positive emotional framing contributes to effective coping and survivability. The acceptance of psychological resilience and the identification of skills related to it are helping to combat the deleterious effects of combat exposure, which may decrease the likelihood of service members developing SUDs and other psychological problems.

Without an understanding of the relationship between SUDs, PTSD and other comorbid disorders, and the biopsychosocial factors that contribute to them, it is difficult to formulate an effective prevention strategy.

PREVENTION INITIATIVES

In response to a request by Congress in Section 596 of fiscal year 2010 National Defense Authorization Act, each branch

of the service provided responses regarding the prevention, diagnosis, and treatment of substance abuse. Among the findings was the fact that the services often prefer centralized population-based prevention programs, which can be adapted to specific service cultures.⁴⁴ Although DoD has focused more prevention efforts toward at-risk populations, the report also highlighted the need for continued population-based prevention efforts, as well as treatment services for family members.⁴⁴

The Air Force has focused on providing an intervention to those that are identified as at risk, but not diagnosable, in hopes of mitigating the development of future SUD problems. One of the Air Force's prevention efforts includes the implementation of the alcohol brief counseling (ABC) program in 2008. The ABC program is an individualized, targeted preventive intervention for service members seen in the Alcohol and Drug Abuse Prevention and Treatment (ADAPT) Program. In addition, the Air Force offers a number of prevention programs that target the 18- to 24-year-old age group who are at highest risk for developing SUDs. The prevention programs include the Social Norms Project, Culture of Responsible Choices, and Enforcing the Underage Drinking Laws Program.

The Army is attempting to diminish resistance to SUD care that may arise from command involvement and reduce stigma by promoting early self-identification of soldiers with alcohol problems. As part of their prevention efforts, the Army has initiated the confidential alcohol treatment and education pilot (CATEP) program to allow self-referrals to the Army Substance Abuse Program (ASAP) without command notification. According to the interviews from the single study done involving CATEP, as well as from feedback to instructors, the CATEP program is well-received by attendees because of the confidentiality, though additional program evaluation needs to be done.⁴⁵

In the last decade, much attention has been paid to the construct of resilience. As noted previously, psychological resilience is associated with the ability to bounce back when difficult or negative emotional events or experiences occur.⁴⁶ Although the concepts behind resiliency have been around for years, and the concepts have been taught to members of the special operations communities and in other select arenas, the utility of resiliency training for a much wider audience has only recently been realized. One example where resiliency principles are being utilized to help combat substance abuse problems is in the Michigan Army National Guard's (ARNG) "Buddy to Buddy" program, which consists of peer support and resilience teams.⁴⁷ With a mission of providing training and resources in order to enhance soldier-to-soldier support and resilience, one of the main goals is to help reduce stigma associated with accessing care and resources, which may prevent ARNG soldiers from seeking help before it becomes a serious problem or an alcohol-related incident occurs.

In order to reduce the number of substance-related incidents at commands, the Navy's goal has been to create a training program to develop a pool of prevention specialists for every naval installation. The prevention specialist course

is a 2-week course that provides intensive education and training on how to design and implement evidenced-based prevention programs.⁴⁴ The final project for the course is to create a prevention program for the installation where the trainee is assigned. Each specialist can then take the project back to their home installation and implement the project.⁴⁴ Since the program's inception, the Navy has provided training slots for personnel from the Air Force and the Army, who will also become trained prevention specialists.

The Marine Corps has a prevention program called Building Alcohol Skills Intervention Curriculum (B.A.S.I.C.) Training that was designed to help unit and squad leaders increase the skills of young Marines who drink.⁴⁸ To garner support for the B.A.S.I.C. Training program, junior Marines, squad/unit leaders, and senior leaders are briefed about the alcohol-related beliefs and behaviors each of these groups of Marines may contribute to problem drinking and perhaps eventually to SUDs.

Each branch of the service has focused on prevention in hopes of mitigating the number of service members, veterans, and family members who will be affected by SUDs.

CONCLUSIONS: WAY AHEAD

As the 10-year milestone of OEF is marked, there is a growing interest in understanding the long-term impacts of the war. The civilian population has a significantly lower rate of heavy drinking and binge drinking than service members 18 to 25 years old.⁷ Though prescription drug misuse actually declined in the civilian population in 2008, there are indicators of an increase in prescription drug use by service members.^{3,4} Due in large part to this increased usage, the DoD announced in February 2012 that each service will expand prescription drug testing to include all pain medications by the end of fiscal year 2012.⁴⁹ Along with SUDs, medical treatment facilities and Veterans Affairs health care facilities are reporting increasingly higher numbers of service members and veterans seeking care for psychological health disorders than in previous conflicts.

There is still a continuing concern that service members are reticent to seek help because of the stigma associated with receiving psychological health care, especially for SUDs. Numerous studies have cited mental health stigma as a barrier to service members seeking psychological health care.²³ Even when members are identified through the postdeployment screening processes, they are often hesitant to seek care and stigma is believed to be part of the reason. Hoge et al³⁴ reported that concerns about stigma were highest among soldiers and marines who were in need of psychological health services.

The relationship between SUDs and their comorbid conditions is complex, making targeted prevention efforts difficult. For example, if there is a strong relationship between smoking and alcohol abuse, is the relationship such that a large reduction in tobacco use would reduce drinking behavior? Though

simplistic, this is but one example that demonstrates the need for a coordinated effort across force health concerns. The development of SUDs is not linear and neither will be successful strategies that impact them.

The Army has piloted the CATEP program, which has been expanded in hopes of getting individuals to reach out for assistance before it becomes a problem. The Air Force has been attempting to destigmatize service members seeking psychological health services by providing more specific guidance for psychological health providers on communications with command.⁵⁰ The Navy is working to train prevention specialists in order to provide more direct prevention services. In spite of the best intentions and efforts, there remains a continuing and growing need for SUD services and empirically based interventions, many of which will be discussed in the articles that follow.

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Evidence-Based Screening, Diagnosis, and Treatment of Substance Use Disorders Among Veterans and Military Service Personnel

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ABSTRACT Substance use disorders (SUDs) are among the most common and costly conditions in veterans and active duty military personnel, adversely affecting their health and occupational and personal functioning. The pervasive burden of SUD has been a continuing concern for the Department of Veterans Affairs (VA) and Department of Defense (DoD), particularly as large numbers of service members return from Operations Enduring and Iraqi Freedom. The VA and DoD have prioritized implementation of evidence-based practices and treatment services to enhance the recognition and management of SUD in general medical and SUD specialty-care settings. This article summarizes the clinical practice guidelines for identifying, diagnosing, and treating SUD in VA and DoD general medical and SUD specialty-care settings, highlights evidence-based pharmacotherapy and psychosocial interventions for managing SUD, and describes barriers to successful treatment of veterans and service members at risk for SUD in VA and DoD health care systems.

INTRODUCTION

Significant health, military readiness, social and personal consequences of substance use conditions are a continuing concern for the Department of Defense (DoD).¹⁻² In 2009, the Department of Veterans Affairs (VA) and DoD released a revised clinical practice guideline (CPG) for management of substance use disorders (SUDs) to provide evidence-based recommendations to identify patients at risk of SUD, to promote early engagement and retention of patients who can benefit from such practices and to improve outcomes of patients with substance use conditions.³ This article summarizes evidence-based guidelines for screening, diagnosis, and treatment of common SUD in patients seen in VA and DoD general medical, mental health, and SUD specialty-care settings.

SCREENING AND INTERVENTION FOR TOBACCO AND UNHEALTHY ALCOHOL USE

Screening and brief intervention (SBI) is a comprehensive public health care approach that integrates the recognition and management of unhealthy substance use in general health care settings.⁴ The VA and DoD support population-based screening annually for alcohol and tobacco use. Population-based screening for drug use disorders is not recommended

due to the lower prevalence and lack of evidence for effective treatment of drug use disorders in primary care.⁵ Further research is needed on the feasibility and clinical utility of integrating questionnaires to screen for drug use disorders in busy primary care settings. Furthermore, the U.S. Preventative Services Task Force found insufficient evidence about the potential harms and benefits to recommend population-based screening and follow-up for drug use disorders in primary care.⁶ Based on these recommendations, the screening guidelines described below apply primarily to detection of alcohol and tobacco use problems, and providers should consider selective case finding of drug use disorders in high-risk populations (e.g., hepatitis C, HIV positive, suicidal ideation, psychiatric conditions).⁷

Screening and Treatment for Nicotine Dependence

Successful implementation of evidence-based practice guidelines⁸ has resulted in high rates of annual SBI for tobacco use in the VA.⁹ Consistent with the U.S. Public Health Services Update of CPG on the Clinical Treatment of Tobacco Use and Dependence,⁸ VA and DoD providers are encouraged to ask all patients if they use tobacco products, advise all tobacco users to quit and assess the willingness of all tobacco users to make an attempt to quit at the time of the screening. National rates of asking and advising abstinence from tobacco products in the VA increased rapidly to 95% and have remained stable.⁹ However, rates of cessation therapy were much lower for many years as less than 10% of patients with positive screens for tobacco use received smoking cessation medications.¹⁰ Since 2002, the VA has implemented a series of policies to increase the use of nicotine replacement therapy (NRT) and bupropion among

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patients interested in trying to quit smoking. From fiscal years 2004 to 2008, prescriptions for NRT and bupropion among patients who were also prescribed NRT increased 49% and 62%, respectively,¹¹ suggesting VA policies have improved prescribing of smoking cessation medications in the VA health care system.

Providers are encouraged to offer smoking cessation medications to all patients interested in quitting. There are seven FDA-approved medications that may be offered, including two non-NRT medications, bupropion SR, and varenicline, and five NRT medications, nicotine gum, nicotine inhaler, nicotine lozenge, nicotine nasal spray, and nicotine patch. Although there are no well-accepted algorithms to guide optimal selection among the first-line medications, combination pharmacotherapies have been shown to be superior to monotherapies in promoting abstinence.^{12,13} Providers are encouraged to consider effective combinations of NRT, which include use of long-acting nicotine formulation (patch) in combination with a short-acting formulation (gum, inhaler, lozenge, or nasal spray). Combination NRT provides constant levels of nicotine offered by the patch while the short-acting nicotine replacement delivers nicotine at a faster rate and is used as needed to manage cravings and withdrawal symptoms that may occur during potential relapse situations. As the combination of the nicotine patch and bupropion SR has also been shown to be more effective than monotherapies,^{8,12} providers should also consider this combination of medications. Nicotine inhaler and nasal spray are nonformulary medications in the VA. In addition, due to safety concerns, varenicline is a second-line medication for smoking cessation in the VA that requires close monitoring for adverse events and only should be used if patients have failed NRT, bupropion SR, or combination therapies in the past year or have a medical contraindication for use of these medications.¹⁴

Definition of Unhealthy Alcohol Use and Goals of Screening

The National Commission on Prevention Priorities ranked screening for unhealthy alcohol use and counseling as the third prevention priority for U.S. adults.¹⁵ Unhealthy alcohol use reflects the spectrum of risk ranging from those who drink above recommended limits (e.g., risky or hazardous drinking) to severe alcohol dependence.¹⁶ Screening for unhealthy alcohol use should determine the number of drinks consumed in a typical week and the maximum number of drinks consumed on an occasion in the past year (i.e., heavy or binge drinking). Table I provides definitions of recommended drinking limits for men and women.¹⁷

The primary goals of screening for unhealthy alcohol use are to identify patients who drink above recommended limits or drink despite contraindications to alcohol use and to determine whether patients are candidates for a brief alcohol intervention (BI) or referral to SUD specialty

TABLE I. National Institute on Alcohol Abuse and Alcoholism Recommended Drinking Limits

Men <65 Years of Age	Women and Persons >65 Years of Age
No more than 14 drinks a week	No more than 7 drinks a week
No more than 4 drinks on any occasion	No more than 3 drinks on any occasion

Standard-sized drinks are 12-ounce beer, 5-ounce wine, or 1.5-ounce hard liquor.

care.^{18,19} Contraindications to any alcohol use include liver disease or hepatitis C, medical conditions potentially exacerbated or complicated by drinking (e.g., pancreatitis or congestive heart failure), medications that have adverse interactions with alcohol and pregnancy or trying to conceive. Because patients who screen positive for these contraindications are unlikely to be in treatment for their alcohol use, providers should provide a BI or referral to treatment if indicated.

Recommended Screening Tests and Brief Interventions for Unhealthy Alcohol Use

The use of brief validated screening instruments is critical to ensure both valid and effective screening.²⁰ The SUD CPG recommends the Alcohol Use Disorders Identification Test Consumption Questions (AUDIT-C)²¹ and the Single-Item Alcohol Screening Questionnaire (SASQ)²² as valid screens for past-year unhealthy alcohol use. Providers should consider a screen positive for unhealthy alcohol use if a patient's AUDIT-C score (range from 0–12) is ≥ 4 points for men or ≥ 3 points for women or a patient reports drinking four or more (women) or five or more (men) drinks in a day in the past 12 months on the SASQ. Active duty service personnel involved in an incident in which substance use is suspected to be a contributing factor are required to be referred to SUD specialty care for a comprehensive evaluation. The current recommendation for annual screening is consistent with preventive screening for other disorders in VA and DoD primary care settings and the past-year assessment window of the AUDIT-C.

A BI for unhealthy alcohol use is patient-centered, empathetic brief counseling, lasting from several minutes to an entire visit and may be offered by a provider without expertise in addiction treatment.²³ Components of BIs include a provider expressing concern that the patient is drinking at unhealthy levels, giving feedback linking alcohol use and medical, social, or mental health consequences and providing personalized feedback related to a patient's specific medical concerns (e.g., hypertension, depression or anxiety, insomnia, diabetes). Providers should also support the patient in choosing a drinking goal if he or she is ready to make a change and offer a referral to SUD specialty-care, if appropriate.²⁴ A BI can be tailored to both the specific needs of a given population or health

care setting and can be used as a stand-alone treatment as well as for engaging those in need of more intensive treatment. Many patients may initially decline voluntary referral, but provider encouragement and support over time may improve the patient's willingness to attend the referral appointment, though mandatory reporting requirements may exist for active duty patients. Based on expert consensus, the SUD CPG recommends that referral to SUD specialty care should be offered in cases when patients may benefit from a more comprehensive evaluation of their substance use or from more intensive motivational interviewing, have been unsuccessful in trying to reduce their substance use on their own or do not respond to a BI, have been diagnosed with a SUD or have returned to use after previously receiving SUD treatment.

Patients at high risk for an alcohol use disorder and who are unwilling to accept a referral to SUD specialty care can be engaged in monitoring of alcohol-related problems in general medical settings using repeated BIs that have a medical focus. The goal of these medical visits is to engage patients in clinical interactions that motivate a decrease in drinking without initially requiring abstinence. Repeated BIs focused on monitoring and feedback on alcohol biomarkers^{25–27} or medical symptoms associated with alcohol use,²⁸ and adherence to medications to decrease drinking have been shown to reduce alcohol use.²⁹ Common traditional alcohol biomarkers for monitoring moderate to chronic heavy drinking include carbohydrate-deficient transferrin (CDT), gamma glutamyl transferase (GGT), and mean corpuscular volume (MCV).³⁰ Feedback on abnormal biological indicators of liver function, blood glucose in diabetic patients and blood pressure in hypertensive patients have also been shown to be effective in reducing alcohol use.²⁷ Medical management³¹ or similarly brief interventions with efficacious FDA-approved medications for alcohol dependence, such as naltrexone²⁹ or off-label use of topiramate,^{32–33} and baclofen³⁴ also has been found to improve drinking outcomes in patients with alcohol dependence.

ASSESSMENT AND DIAGNOSTIC EVALUATION

Successful treatment of SUD begins with a comprehensive biopsychosocial assessment and diagnosis. While the essential purpose of the assessment is to obtain information needed to accurately identify and treat SUD, it also marks the beginning of the therapeutic process.^{3,35,36} Clinical interactions should be supportive and demonstrate the same patient-centered approach recommended for BI.^{3,37} Due to limited resources, most comprehensive and diagnostic evaluations occur in specialty care, but these procedures can be delivered in general medical and mental health settings if providers with appropriate training are available in such settings.^{38–40} However, active duty personnel involved in an incident in which a contributing factor is suspected to be substance use are required to be referred to specialty care for evaluation.

Comprehensive Biopsychosocial Assessment

Treatment needs are determined using comprehensive and multidimensional assessment procedures, typically in the form of structured clinical interviews and standardized assessments. Advanced training is required to conduct comprehensive evaluations and specific requirements vary by military department.^{38–40} A comprehensive biopsychosocial assessment includes a history of the substance use disorder, including precipitating factors and current symptoms and risks (see SUD CPG for domains of patient history), with permission, collateral interviews with individuals who can provide insight into the patient's substance use, laboratory tests for infectious diseases and consequences of substance use, mental status examination, identification of assets, vulnerabilities and supports and patients' perspective on current problems, treatment goals and preferences.³ A clinical interview and several independent instruments can be used to collect this information or a single, comprehensive instrument that assesses several functional domains can be used (e.g., Addiction Severity Index).⁴¹ A complete evaluation is important to properly diagnose patients with SUD and develop an effective treatment plan, but for patients presumed to have less severe symptoms, the assessment should at least include screening of the above elements using a multidimensional screening instrument. In addition to formulating a diagnosis of SUD and co-occurring conditions, results are used to determine if patients require behavioral or physiological stabilization and a referral to the appropriate treatment setting.

Diagnosis

The Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition (DSM-IV-TR)⁴² is the current and primary diagnostic system used in the United States, however these diagnostic criteria are undergoing revision.⁴³ Currently, SUD includes substance dependence and substance abuse with DSM-IV-TR criteria as shown in Tables II and III. The essential feature of both disorders is a maladaptive pattern of substance use that leads to clinically significant impairment or distress.

Treatment Plan

The comprehensive assessment should include a diagnostic formulation, summary of past treatment response and integrated summary of clinically relevant information. Providers should consider the patients' willingness to engage in treatment as well as the patients' treatment goals and preferences and evaluate how their strengths, limitations and presenting problems will affect the treatment process and outcomes. To improve adherence to initial treatment priorities and outcomes, the treatment plan should involve input from the patient⁴⁴ and unit command^{38–40} for active duty personnel. Collectively, this information supports the initial treatment priorities and informs the appropriate

TABLE II. DSM-IV-TR Criteria for Substance Dependence⁴²

<p>“A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by 3 (or more) of the following 7 criteria, occurring at any time in the same 12-month period:</p> <ol style="list-style-type: none"> (1) Tolerance, as defined by either of the following: A need for markedly increased amounts of the substance to achieve intoxication or desired effect Markedly diminished effect with continued use of the same amount of the substance. (2) Withdrawal, as defined by either of the following: The characteristic withdrawal syndrome for the substance (refer to DSM-IV-TR for further details) The same (or a closely) substance is taken to relieve or avoid withdrawal symptoms. (3) The substance is often taken in larger amounts or over a longer period than was intended. (4) There is a persistent desire of unsuccessful efforts to cut down or control substance use. (5) A great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking) or recover from its effects. (6) Important social, occupational or recreational activities are given up or reduced because of substance use. (7) The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression or continued drinking despite recognition that an ulcer was made worse by alcohol consumption).”
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intensity of treatment. Provided it is consistent with military policies, it may be possible to manage some patients with less severe and chronic SUD outside of specialty-care. With regard to patient level of care placement, the American Society of Addiction Medicine criteria are the most widely accepted placement system criteria.⁴⁵ The criteria consider problem severity in six dimensions in making recommendations for specific levels of care with patients with greater problem severity requiring more intensive treatments. Because appropriate levels of treatment may be lim-

TABLE III. DSM-IV-TR Criteria for Substance Abuse⁴²

<p>“A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by 1 (or more) of the following, occurring at any time in the same 12-month period:</p> <p>Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home. Recurrent substance use in situations in which it is physically hazardous. Recurrent substance-related legal problems. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.</p> <p>The symptoms have never met the criteria for substance dependence for this class of substance.”</p>
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ited in deployed environments, some military personnel may need to be evacuated to higher levels of care.

Treatment Setting

While the intensity of treatment should match the severity of the substance use problems, interventions should be provided in the least restrictive setting required to support their effectiveness and patient safety. If appropriate, less severe and chronic SUD may be treated in general health care settings. Although it is impractical for most general health care settings to offer psychotherapy interventions, pharmacotherapy, and medical management for alcohol use disorders can be provided effectively by medical providers in these settings.^{3,29} If patients’ substance use severity and co-occurring psychiatric and psychosocial problems require more intensive psychosocial interventions, SUD specialty care is typically more appropriate. In order to ensure patients have access to needed mental health services, the VA established essential components of substance use disorder services that must be implemented and available at VA facilities.⁴⁶ Table IV shows a summary of services required for the treatment of SUDs at VA facilities. The implementation of these services at all VA facilities will be monitored quarterly to ensure they are available to patients who need them.

TREATMENT

Perhaps no other early treatment goal is as important as facilitating patients’ engagement and retention in treatment as these factors consistently predict a successful outcome.⁴⁷⁻⁵⁰ Clinical interactions that demonstrate a nonjudgmental, empathic and patient-centered approach are more likely to enhance

TABLE IV. Summary of Services That Must be Made Available When Clinically Indicated to All VA Patients With SUD

<ol style="list-style-type: none"> (1) Medically supervised withdrawal management (2) Co-ordinated and intensive substance use treatment required to establish early remission from SUD, which includes either <ol style="list-style-type: none"> (a) Intensive Outpatient services >3 hours/day >3 days per week, or (b) Mental health residential rehabilitation treatment program that specializes in SUD services (3) At least 2 empirically supported psychosocial interventions, including motivational enhancement therapy, cognitive behavioral therapy for relapse prevention, 12-step facilitation counseling, contingency management and SUD-focused behavioral couples counseling or family therapy. (4) Evidence-based pharmacotherapy for alcohol dependence and pharmacotherapy for opioid dependence with approved, appropriately regulated opioid agonists delivered in either an approved opioid treatment program or office-based Buprenorphine treatment. (5) Long-term management for substance use conditions and coexisting psychiatric and medical conditions. (6) Evidence-based pharmacotherapy and psychosocial interventions for co-occurring mental health conditions

Per Veterans Health Affairs Handbook for Mental Health Services.

the provider-patient alliance and promote opportunities to address other treatment goals.³⁷ Resolution or remission of substance use problems is important to prioritize early in treatment as early duration of abstinence is associated with long-term outcomes.^{47,50-52} Other goals include enhancing psychosocial functioning and preventing relapse to substance use and return of substance use problems. These goals can be achieved using several intervention strategies, including evidence-based interventions focused on the addictive behaviors, supplemental interventions for other psychosocial problems and focused clinical encounters.

Recommended Evidence-based Interventions

Evidence-based pharmacotherapy and psychosocial interventions are typically initiated based on patient preference and the availability of local expertise and resources to provide services. If indicated, pharmacotherapy should be offered for patients with alcohol use disorders and opioid dependence,

and coordinated with psychosocial interventions provided in specialty care. Naltrexone, acamprosate and disulfiram have received FDA approval as adjunctive treatments for alcohol dependence. Several systematic reviews support the efficacy of naltrexone and acamprosate,⁵³ and a recent systematic review supports the efficacy of disulfiram.⁵⁴ Despite FDA approval and strong support in the literature, pharmacotherapy for alcohol use disorders is underutilized in the VA, with approximately 3% of patients with an alcohol use disorder in 2007 receiving at least 1 prescription for acamprosate, naltrexone, or disulfiram.⁵⁵ To improve use of these medications, efforts are underway to identify and examine patient, provider and facility-level barriers and supports for pharmacotherapy for alcohol use disorders.

Opioid agonist treatment (OAT) is the recommended first-line treatment for opioid dependence and includes administering an opioid agonist medication, such as methadone or sublingual buprenorphine/naloxone. Such medications have been shown to prevent withdrawal, reduce cravings and

TABLE V. Summary of Effectiveness of Psychosocial Interventions During Early Recovery (First 90 Days) on Condition Specific Outcomes of SUD (Use or Consequences) or General Psychosocial Functioning

Interventions (alphabetical)	First Line Alternatives At Least as Effective as Other Bona Fide Active Interventions or Treatment as Usual				Added Effectiveness as Adjunctive Interventions in Combination With Pharmacotherapy and/or Other First Line Psychosocial Interventions				Comments
	Alcohol	Opioids	Stimulants/Mixed	Cannabis	Alcohol	Opioids	Stimulants/Mixed	Cannabis	
Behavioral Couples Therapy	+++	N/A	+++	N/A	+/-	+	?	N/A	Effective for Male or Female Patients with SUD and Partners; Improves Marital Satisfaction
Cognitive Behavioral Coping Skills Training	+++	N/A	+++	++	+	+++	N/A	++	
Contingency Management/Motivational Incentives	N/A	N/A	N/A	N/A	+	+++	+++	N/A	
Community Reinforcement Approach	+++	N/A	+	N/A	N/A	N/A	+	N/A	Complex Intervention
Motivational Enhancement Therapy	+++	N/A	N/A	?	+++	?	+/-	+	May Improve Treatment Engagement as Adjunct to Treatment As Usual for Stimulants; Some Evidence for Those With Low Readiness or High Anger
Twelve-Step Facilitation	+++	N/A	N/A	N/A	++	N/A	+	N/A	Alcoholics Anonymous Participation is Correlated With Outcome—Appears to Mediate Twelve-Step Facilitation Effects

+++ Based on meta analysis of comparison with bona fide alternative interventions.
 + or ++ Based on one (+) or more (++) individual trials in comparison with bona fide alternatives.
 N/A Evidence not available.
 +/- Evidence inconsistent across outcomes.
 ? Benefit questionable.

the effects of illicit opioids, and have been associated with improvements in treatment retention, abstinence from opioids, and psychosocial functioning.⁵⁶ OAT has also been associated with decreases in drug-related criminal behavior and HIV risk behaviors.⁵⁷ OAT can be provided in specialty-care clinics licensed to prescribe methadone, or office-based settings, although buprenorphine is the only opioid agonist medication approved for office-based settings. Typically, patients requiring greater structure and intensity of comprehensive services are better served in specialty-care settings. As noted in the SUD CPG, OAT is generally not a treatment option for active duty personnel.

Because of limited resources, most specialty-care settings are unable to offer multiple psychosocial treatment options. While many psychosocial interventions are empirically supported for treatment of SUD,⁵⁸ there is no clear evidence that any one intervention is superior or particularly effective for a specific patient's characteristics.⁵⁹ Providers should consider the following interventions that have been developed into published treatment manuals and evaluated in randomized trials: Behavioral Couples Therapy, Cognitive Behavioral Coping Skills Training, Community Reinforcement and Family Training, Motivational Enhancement Therapy, a Twelve-Step Facilitation and Contingency Management/Motivational Incentives therapy.³ Table V summarizes the strength of the evidence supporting the above mentioned interventions and the first line and adjunctive treatment roles they serve for condition specific outcomes of SUD.

Recovery Care and Support

A comprehensive assessment may identify other biopsychosocial problems that could affect improvement in substance use and functional status outcomes. Such problems may interfere with access or engagement with treatment interventions or increase the risk of relapse. These may include relationship difficulties with family and social relationships, engagement in a supportive recovery environment, underemployment and unresolved or pending legal or disciplinary problems. Even if problems were the result of substance use behaviors, they may persist even after early recovery is established. Rather than increasing the intensity of interventions focused on SUD, providers should consider interventions that address specific problems.⁴⁷ For instance, Behavioral Couples Therapy may also focus on reducing alcohol use in the identified patient and improving the overall marital satisfaction of both the patient and the spouse or partner.⁶⁰ Issues with supportive recovery environment could be addressed with a referral and patient participation in community self-help groups such as Alcoholics Anonymous.⁶¹⁻⁶⁴

Management of Co-Occurring Medical and Psychiatric Disorders

Co-occurring medical and psychiatric disorders are common among veterans with problematic substance use.^{65,66} Unipolar

affective disorders (61%) and post-traumatic stress disorder (PTSD) (41%) are the most common psychiatric diagnoses among VA patients with psychiatric disorders, 1 in 5 of whom have a co-occurring SUD diagnosis. Of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) veterans treated in the VA, 82% with alcohol use disorders and 86% with drug use disorders have at least 1 co-occurring psychiatric disorder.⁶⁶ The most common psychiatric disorder among OEF and OIF with an alcohol use or drug use disorders is PTSD (63%). Severe medical and psychiatric conditions that impact improvement in substance use outcomes should be evaluated and treated concurrently with the treatment of substance use problems. Engagement in SUD treatment and overall coordination of care may be improved if multiple services are provided in the most accessible setting.⁶⁷ However, referrals for medical and psychiatric services should be provided for conditions that cannot be managed appropriately in the setting of substance use treatment. Regardless, ongoing coordination among providers of these services is essential to the overall quality of care.⁷

Because of the high prevalence of co-occurring PTSD and SUD and a recommendation from the National Quality Forum to coordinate the care of both SUD and mental health conditions, the VA increased efforts to better integrate the treatment of SUD and co-occurring psychiatric disorders. As part of these integration efforts, the VA authorized funding for SUD specialists in specialty PTSD care at each of the VA facilities⁶⁸ and the VHA Handbook on Uniform Mental Health Services prioritized the implementation of evidence-based pharmacotherapy and psychosocial interventions for patients with SUD and other mental health conditions.

Assess and Monitor Response to Treatment

Periodic assessment of treatment response, using standardized self-report and laboratory measures, is essential to evaluating patients' progress in treatment and providing information necessary to further adapt treatment interventions.^{69,70} Typically, the timing of periodic assessments reflects the stage and intensity of services with reassessment occurring daily in acute inpatient settings, weekly in residential settings and weekly in the initial weeks of a new treatment episode, followed by monthly evaluations in outpatient settings. Results of assessments provide a measure of a patient's response to treatment and should be used to inform changes to care. Improvements on measures signal that a patient is progressing as expected, whereas worsening or lack of change on measures suggests that the provider evaluate the adequacy of the treatment plan, consider alternative interventions (e.g., pharmacotherapy), and consult with the patient and other members of the treatment team to identify factors that may be interfering with treatment progress.

Common indicators of treatment response include ongoing substance use, cravings, psychological distress, exposure

to risky environments, stressful situations, and unsupportive family and friends, side effects of medication, participation in self-help meetings and engagement in addiction specialty care. Traditional biomarkers of heavy alcohol consumption (e.g., CDT, GGT, MCV) and the new biomarker, ethyl glucuronide (EtG), may be useful for providing objective measures of ongoing alcohol use.³⁰ Several valid self-report instruments are available to measure substance use and other important outcome domains. A brief list of measures with well documented psychometric properties and in the public domain can be found in a recent publication on treating addiction⁷¹ or easily accessed using the following url (http://www.guilford.com/cgi-bin/cartscript.cgi?page=etc/miller11.html&dir=pp/addictions&cart_id=897890.1358). The Brief Addiction Monitor (BAM), a 17-item, multidimensional questionnaire designed to assess several of the above indicators at baseline and periodic follow-up is another measure available in the public domain (<http://www.mentalhealth.va.gov/providers/sud/index.asp>).³

Development of Aftercare/Recovery Plan

As patients improve, the treatment team should collaborate with patients to plan how to achieve the remaining goals, consider reducing the intensity of SUD specialty care, or develop an aftercare plan. Transitions to less intensive levels of care should involve coordinated follow-up with medical or behavioral health providers involved in patients' care to monitor progress, including the risk of relapse and management of co-occurring medical and psychiatric conditions. Because the risk of relapse is high during early recovery, an aftercare plan should include a written strategy to facilitate periodic contact with treatment services in the form of individual, group, or telephone contacts to monitor the risk of relapse and the need for relapse prevention skills. The plan may also encourage active involvement with community support for recovery and biological monitoring of substance use and medical consequences. Active duty personnel are required to have a written, individualized aftercare plan that describes their rehabilitative responsibilities, including a quarterly evaluation of the patient's progress conducted by a committee comprised of a substance abuse counselor, the patient and the patient's commanding officer.^{38,39}

Barriers to assessment and treatment in the military population

Studies have identified several barriers to the initiation and completion of substance use treatment in military and VA settings. There are limits to the confidentiality of military service personnel in SUD specialty-care as DoD policies require that a commanding officer be notified when a service member voluntarily receives services for alcohol use disorder and be included as a member of the treatment team once

treatment is started.^{1,39,40} Additional limits of confidentiality may exist for special active duty populations such as aircrew members. A zero tolerance policy on the misuse of drugs, including prescription medications, is likely to represent another significant barrier to those seeking substance use treatment services.^{72,73} Service members have reported that obtaining time off from military duties to attend treatment is difficult,⁷⁴⁻⁷⁶ and deployed service members have consistently reported limited access to appropriate care.⁷⁵ Lastly, service members report concerns about the negative effect the use of behavioral health specialty care may have on their reputation and career.⁷⁴⁻⁷⁶ A recent amendment to the Code of Federal Regulations⁷⁷ that allows for sharing of previously protected medical records between the VA and DoD is likely to augment this barrier to care, particularly for National Guard and Reserve service personnel who receive their care from the VA health care system. Prior to this change in policy, VA patient records involving the diagnosis, prognosis, or treatment of SUD were protected from disclosure to the DoD.

Although several barriers to care in the military population overlap with those of veterans receiving care in the VA such as stigma and logistical challenges to receiving care, there are also barriers unique to veterans treated in the VA. Much like active duty members, stigma, discomfort with help-seeking and negative beliefs about mental health care are consistently reported as important barriers to seeking mental health care.⁷⁸ OEF and OIF veterans treated in the VA have also reported concerns about not fitting in with older veterans from previous eras who remain the majority of those served.

CONCLUSION

Population-based SBI are fundamental to the management of SUDs in health care settings. Patients requiring more intensive treatment services should be referred to SUD specialty care for a comprehensive assessment of their treatment needs and the development of treatment goals. Several evidence-based pharmacotherapy and psychosocial interventions are available for the treatment of common SUD, but the importance of empathic, nonjudgmental, and patient-centered clinical interactions should not be overlooked. Future research and changes in policy have the potential of reducing barriers to SUD specialty-care in military settings.

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Next Steps in Addressing the Prevention, Screening, and Treatment of Substance Use Disorder in Active Duty and Veteran Operation Enduring Freedom and Operation Iraqi Freedom Populations

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ABSTRACT The two articles presented previously in this volume provide state-of-the-art reviews of the etiology, epidemiology, screening and treatment of substance use disorder (SUD). This article identifies next steps in research and development for understanding and treating SUD in Operation Enduring Freedom/Operation Iraqi Freedom service members and veterans. Four promising areas are reviewed: advances in psychopharmacological treatment of SUD, innovations in behavioral treatments, the use of technological advances for the screening and treatment of SUD, and integration of treatment services. Future directions are explored and suggestions for research, development and implementation of each of these trends are discussed.

INTRODUCTION

This article reviews four areas of research or policy considerations pertaining to treatment of substance use disorder (SUD) in military members and veterans: advances in psychopharmacological treatments, development and implementation of behavioral interventions, the use of technological advances for screening and treatment, and integration of SUD care with other treatment services.

Psychopharmacological treatments for SUD can be most readily provided across the whole spectrum of health care delivery with minimal additional training since physicians are already comfortable with prescribing medications. Many efficacious behavioral interventions for SUD have not been widely translated into routine clinical practice, so understanding implementation needs is paramount to getting more patients who need it effectively treated. Technological advances have the novel capacity to move SUD intervention out of the health care setting per se and into the daily lives of patients available in real time so that patients can access them readily, inexpensively, and where and when they really need them. Integration of SUD treatment with other basic health services will also be essential to get these efficacious interventions to all who need them.

ADVANCES IN PSYCHOPHARMACOLOGICAL TREATMENTS FOR SUD

We first address tobacco, alcohol, and opioid use disorders, SUDs for which pharmacotherapies currently exist, then provide additional comments regarding cannabis, stimulant, and sedative-hypnotic use disorders for which there are no approved pharmacotherapies.

Currently, about 25% of individuals who receive tobacco use treatment achieve long-term abstinence,¹ indicating better pharmacotherapies are needed. Agents that show promise in preclinical and/or early human studies include the opioid antagonist, naltrexone,² the nicotinic partial agonist, cytisine,³ the alpha adrenergic antagonist, prazosin,⁴ and nicotine vaccine.⁵ These agents should be further evaluated in humans generally and in military and veteran populations specifically.

The most efficacious approved pharmacotherapy for smoking cessation, varenicline,¹ exemplifies scientific and policy challenges in providing services to military and veteran populations. Varenicline is a partial agonist at the alpha4-beta2 nicotinic receptor; as such, it produces some of the reinforcing effects of nicotine while simultaneously blocking nicotine's access to the receptor. Varenicline has a Food and Drug Administration (FDA) required boxed warning for psychiatric side effects and cardiovascular events; however, evidence implicating varenicline as the cause of psychiatric side effects derives only from anecdotal reports. More rigorous epidemiologic or controlled trial data indicate that, except for sleep disturbance, varenicline does not have an elevated psychiatric risk profile above other tobacco-cessation medications or placebo,⁶⁻⁸ suggesting other factors inherent in tobacco use and/or quitting are responsible for the anecdotal observations. Since military and veteran tobacco users are likely to have high rates of co-occurring psychiatric disorders, rigorous data about the efficacy and safety of varenicline in these populations are needed. Because the evidence for these side effects is weak, policy should encourage cautious and judicious use of varenicline when indicated. Currently in the Department of Veterans Affairs (VA), there are additional systems barriers to its use. Based on anecdotal reports, varenicline is contraindicated in airline pilots and has cautions about motor vehicle use and other demanding psychomotor activities. Future research is needed to clarify safety limitations.

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Combined nicotine replacement with both long acting and prn (as needed) medications (e.g., patch plus gum or lozenge) is an additional area in which treatment could be improved. Such combined interventions have superior efficacy to either agent alone without any added safety concerns,¹ yet providers have little awareness of this approach and should be encouraged to prescribe the combination.

With respect to alcohol use disorders, the approved medications clearly benefit some patients though they have less than optimal efficacy overall. Disulfiram and naltrexone have been extensively studied in veteran populations with evidence of modest efficacy and adequate safety.^{9,10} Disulfiram inhibits the enzyme aldehyde dehydrogenase, a key enzyme in the metabolic pathway for alcohol, thereby causing a buildup of acetaldehyde which results in the unpleasant alcohol-disulfiram reaction if an individual consumes alcohol while on disulfiram. Naltrexone is a mu-opioid receptor antagonist. It is believed that alcohol mobilizes endogenous opioids in the brain to produce a reinforcing effect. Naltrexone is believed to block this effect by its antagonism of the mu-receptor. The largest study done with naltrexone in veterans with alcohol dependence,¹¹ a 1-year randomized, double-blind, placebo-controlled trial, showed a highly significant reduction in days of alcohol use for all participants without a significant difference between active medication and placebo conditions. However, subsequent analysis of a subsample of participants who provided blood for a genetic substudy did show a statistically significant reduction in alcohol use for the naltrexone-treated participants even with less experimental power.¹² Thus, further research should determine which veterans are most likely to have a good response to naltrexone. Medication adherence is one of the predictors of response in non-veteran populations.¹³ An extended release intramuscular injection preparation of naltrexone which obviates concerns over adherence obtained FDA approval for treatment of alcohol dependence in 2006.¹⁴

Acamprosate is proposed to work by stabilizing inhibitory and excitatory networks in the brain, which may be dysregulated by prolonged alcohol use. Since efficacy of acamprosate seems marginal in the wider population, further evaluation in military and veteran cohorts is probably not warranted. Topiramate, an anticonvulsant which also stabilizes inhibitory and excitatory systems, while not FDA approved, has shown fairly robust evidence of efficacy and safety in a multisite randomized clinical trial¹⁵ and warrants further study in military and veteran populations. A number of agents, including gabapentin,¹⁶ another anticonvulsant and prazosin,^{17,18} an alpha1 adrenergic antagonist which blocks some of the effects of norepinephrine in the brain, also show promise for alcohol use disorders in preclinical and early clinical studies. Among these medications, prazosin stands out because of its potential to treat alcohol use disorders and post-traumatic stress disorder (PTSD) simultaneously.

Underutilization of existing pharmacotherapies for alcohol use disorders is a key problem.^{19,20} More widespread

prescribing of these medications must be encouraged. For example, at present, there are substantial barriers to the prescribing of extended release intramuscular naltrexone in the VA. Further research on the efficacy of this medication compared to oral medications, including oral naltrexone, could inform policy makers about when and for whom the more expensive extended release preparation is indicated.

A similar pattern can be noted with respect to approved pharmacotherapies for opioid use disorders, which include methadone, buprenorphine, and naltrexone. Methadone is a full agonist opioid medication that binds to the mu-opioid receptor and stimulates it replacing the opioids which were misused. Buprenorphine is a partial mu-opioid agonist that also binds to the receptor but does not activate it to the same degree as does a full agonist yet still replaces the misused opioids. In comparison to pharmacotherapy for alcohol use, pharmacotherapies for opioid use disorders are highly effective. Yet, in the case of the VA, most veterans with opioid use disorders still do not receive any of these efficacious treatments.²¹ The use of buprenorphine and naltrexone could and should be expanded via education, training, and provision of mentoring support to practitioners. Methadone can only be provided through federally licensed and accredited opioid treatment programs. The VA has approximately 35 of these programs among 175 facilities. Given the amount of infrastructure required to establish a program, it does not seem practical to initiate programs in regions with small numbers of veterans. To some extent, access can be created by contracting with community programs.

At present, the active duty military does not permit treatment of opioid use disorders with medications. This policy warrants re-examination, particularly for military members who develop opioid use disorders as a consequence of treatment with opioids for painful conditions incurred in the line of service. In many cases, methadone treatment would not be practical. However, buprenorphine treatment would be possible, and available evidence shows that humans stabilized on a dosage of this partial opioid agonist can safely perform complex psychomotor functions.²² Naltrexone by either oral or extended release injectable forms should be acceptable as well.

Available evidence suggests little use of cannabis, cocaine, methamphetamine, or nonprescribed sedative hypnotics among active duty military personnel. These substances are frequently used and result in SUD among veterans.

At present, there are no obvious candidate compounds for cannabis addiction. Promising potential agents for treatment of cocaine addiction include cocaine vaccine,²³ disulfiram,²⁴ and vigabatrin,²⁵ which blocks the reuptake of gamma-amino butyric acid, the major inhibitory neurotransmitter. The latter medication also showed a signal for methamphetamine addiction as does naltrexone²⁶ and "replacement" therapy with other stimulants such as methylphenidate,²⁷ although such an approach remains quite controversial. Anticonvulsants have a strong evidence base for management of sedative-hypnotic

withdrawal,²⁸ but there are no good candidates for long-term pharmacotherapy of sedative-hypnotic addiction. As with methamphetamine, the idea of “replacement” therapy for benzodiazepine addiction, while certainly also controversial, has also gained some traction because of the futility many practitioners have experienced in trying to get patients to stop benzodiazepines.²⁹

BEHAVIORAL INTERVENTIONS

Behavioral interventions for treating SUD in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) populations are of critical importance, and Hawkins et al (this volume) provide an excellent list of current, evidence-based psychosocial interventions. We anticipate the development of new treatment options, with particular emphasis on treatment of SUD with comorbid disorders. Yet, the central focus of research, we believe, will be a better understanding of how best to implement current evidence-based treatments (EBTs).

General and Specific Treatment Factors and Therapist Competence

There are a number of treatments that have established effectiveness for treatment of SUD. Criteria to establish a treatment as “evidence-based” vary according to the criteria employed and are typically drawn from randomized clinical trials. Other supportive evidence can be taken from positive findings across populations and research groups as well as manuals and procedures that define and guide treatment.³⁰ The VA and Department of Defense (DoD) issued SUD treatment guidelines³¹ list six such treatments with good to excellent empirical support: Behavioral Couples Counseling, Cognitive Behavioral Coping Skills Training, Community Reinforcement Approach, Contingency Management/Motivational Incentives, Motivational Enhancement Therapy (MET), and Twelve-Step Facilitation (p 22). Yet there is virtually no evidence that these specific approaches outperform each other when directly compared,^{32,33} nor are there established guidelines for selecting one treatment for a particular client.³⁰ These points are not lost on those developing VA/DoD guidelines, which highlight the difficulty of accurately matching patients to treatment and suggest considering general therapeutic factors (e.g., therapist skill, therapeutic alliance, etc.) when establishing treatment services (see below).

Thus, one promising direction for future development of psychosocial treatments is an understanding of the relative benefits and potential interaction of treatment specific and general treatment factors. In fact, management of these critical aspects of therapist competence is a focus of dissemination in evidence-based care. There is emerging evidence that adherence to treatment protocols is not simply or linearly related to treatment outcomes. Barber et al demonstrated that when therapeutic alliance was strong early in treatment, therapist adherence to the treatment protocol was irrelevant to patient outcome.³⁴ However, when alliance was less strong, a moderate level of counselor adherence (vs. high or low)

was associated with best outcomes.^{34,35} Such complex interactions may be one reason that associations between counselor adherence and competence with treatment outcomes have not been consistently observed.³⁶

Effective therapist performance in EBT of SUD likely varies with respect to differences in counselors, clients, and treatments. VA/DoD treatment guidelines emphasize the importance of clinical judgment for many features of treatment not specified in protocols and emphasize processes such as treatment engagement and use of community resources independent of treatment protocol.³¹ A recent survey of practicing VA counselors suggests that practitioners combine various components of different EBTs in their ongoing work.³⁷ An analysis of a multisite trial of MET for drug use disorders found more variability in therapist adherence to and competence in the MET protocol within therapist case loads than between therapists.³⁸ Higher client motivation and greater client substance use were associated with less counselor adherence. Clearly, an understanding of the nature of therapist competence within evidence-based practice is only beginning to be developed, and there is great need to develop more specific models of how best to provide evidence-based care in a manner that adapts to patient differences and needs.

Improving Implementation

Even with well-established EBTs and well-established models for optimum use, moving from the research clinic to the daily treatment of veterans and active duty personnel will continue to be a challenge. Research findings about treatment do not naturally migrate from university laboratory to clinics. Implementation science will no doubt make significant contributions to the ongoing improvement of SUD care in future years.^{39,40} Damschroder and Hagedorn have recently provided an overarching, Consolidated Framework for Implementation Research (CFIR).⁴¹ The CFIR integrates an array of constructs previously articulated and describes factors with respect to interventions, outer setting (e.g., funding, billing, policies that influence agency function), inner setting (e.g., agency culture and organizational functioning), characteristics of individual practitioners, and processes of implementation (e.g., planning, executing). Few empirical tests of SUD implementation have been conducted, and Damschroder and Hagedorn call for future formative evaluation within implementation trials and the development of predictive models of sustainability.⁴¹ They further note the critical lack of information with respect to core vs. adaptable components of interventions, a problem also observed by Lash et al,⁴² within continuing care programs in SUD, which are often modified based on setting and resources (e.g., use of group or telephone modalities) rather than empirically based models. Manuel et al noted that implementation programs that include an organizational focus are more likely to be effective than those that only target individual practitioners and also suggest that more success may come from implementation of specific practices or processes in comparison to complete EBTs.³⁰

One model addressing implementation at an organizational level is measurement-based care (MBC). MBC is a responsive and flexible approach to the organization and sequencing of treatments specifically developed to address the variation and complexity inherent in SUD patients and, thereby, improve treatment outcomes.⁴³ This model calls for the provision of consistent feedback to providers about patient response over the course of treatment through repeated measurement allowing clinicians to detect nonresponse or deterioration and then adapt or modify treatment to achieve more favorable outcomes.⁴⁴ These adjustments include changing the frequency, duration, intensity, clinical focus, setting, or provider; or augmenting treatment with medications, groups, or individual sessions.

Recognizing this potential, the VA is implementing MBC in treating SUD using the Brief Addiction Monitor (BAM), a 17-item, self-report measure assessing patients' frequency of substance use along with risk and protective outcome factors. Currently, more than 80 VA sites are administering the BAM, and the VA intends to extend the use of the BAM to all VA SUD treatment programs by 2012. Ongoing research should ascertain the value of the BAM implementation.

In addition to supporting MBC, the VA is beginning to train clinical staff working in SUD in EBT protocols, such as MET, Cognitive Behavioral Therapy, and Behavioral Marital Therapy, following models developed for dissemination of evidence-based care for PTSD.⁴⁵ This model goes far beyond a traditional workshop and includes protocol manuals, group experiential training, ongoing coaching and supervision from experts, and review and certification of tapes of clinical sessions. Ongoing evaluation of the training program will guide subsequent efforts.

TECHNOLOGY IN TREATMENT OF SUD

Technological advances could also improve SUD screening and treatment. Problem recognition and delayed-treatment seeking pose major challenges in the early stages of SUD.⁴⁶ Web-based, personalized drinking assessment and feedback (PDAF) is a cost-effective and convenient screening and brief intervention that has been shown to be efficacious for increasing problem recognition and reducing alcohol use.^{47,48} Based on a personal and private assessment, web-based PDAF provides feedback about alcohol use, information about peer norms for use, psycho-education about alcohol and drug use, and strategies to abstain and/or reduce harm from use. This technology has recently been implemented in military and VA settings demonstrating good potential for reducing alcohol use.^{49,50} Another technological approach utilizes online patient profiles to improve problem recognition of SUD by the clinician. One such program, "My Healthe Vet," involves completion of alcohol and drug screening questionnaires by the patient before an appointment alerting the clinician to the need for intervention and possible referral to specialty SUD care.⁵¹ Although the implementation of these technologies is feasible in veteran populations, their feasibility in military settings needs evaluation.

Once SUD is identified, there are multiple barriers to accessing SUD treatment for military members.⁵² To reduce fear of repercussions and stigma, web-based PDAF could provide information on policies and procedures about SUD treatment specific to one's military branch, information normalizing treatment seeking, and a menu of treatment options. Telemedicine, involving diagnosis and intervention using real-time telecommunications technologies, could increase access to SUD treatment. A growing body of research demonstrates that this practice is comparable to traditional in-person treatments in outcomes, therapeutic alliance, and patient satisfaction in the VA and private sector and can be used in individual and group treatment formats.⁵² However, more research is needed on the use of this technology for the treatment of SUD. Other forms of "e-therapy," such as online chat rooms, have been effectively instituted in the VA and private sector.^{53,54} Another promising next step is use of virtual environments in which individuals can interact online with supportive others.⁵⁵ Individuals can anonymously and conveniently attend community support groups, explore treatment options, and socially network with others who may help them engage in more intensive treatment services. Regardless of modality, these technologies allow for instant and flexible access to help and could serve as a first step in seeking treatment. However, future studies should evaluate OEF/OIF service members' and veterans' attitudes about and likelihood of using these technologies, and if they actually increase access to treatment.

Once in SUD treatment, technology could be used to enhance self-monitoring, skill acquisition/implementation, goal setting, and engagement in aftercare. VA is already piloting a web-based program called "My Recovery Plan" that can be accessed via "My Healthe Vet".⁵¹ This program allows for tracking recovery goals, organizing and scheduling health care needs/recovery tasks, contact with clinicians via confidential email, and access to interactive self-help content to complement in-person counseling. Clinicians also have access to a program that provides a user-friendly means of monitoring a patient's treatment progress. The development of SUD specific smart phone applications could help monitor use, track cravings and urges, and identify in real time activities and situations that put one at risk for relapse.⁵⁶ Global positioning and biofeedback features could alert the patient to elevations in these risk factors, provide reminders to prompt the use of coping strategies, and present motivational stimuli to increase success in abstaining. These programs could help monitor the relationship between substance use and other comorbid disorders common to personnel who served in OEF/OIF. Finally, the use of virtual reality is being explored to reduce reactivity to drug and alcohol cues and augment coping skills practice.^{55,56} Similar to advances for increasing access, these technological approaches need to be investigated to establish their appeal, feasibility, and effectiveness in OEF/OIF and other populations.

Technological advances can also improve SUD clinician training in new and evidence-based practices. Although traditional continuing education workshops show limited

effectiveness, research has provided some support for training enhancements (e.g., coaching, feedback, and ongoing supervision) to SUD treatment providers.³⁰ Of these, virtual human technology has the potential to augment these training enhancements. This technology allows providers to rehearse interactions with simulated patients programmed to meet specific training needs on computer software.⁵² It also features live recording of these simulated encounters so critical incidents can be identified and evaluated to provide more performance-enhancing feedback during supervision.

Technological applications come with many benefits described above. However, technologies also have downsides including: threats to security and confidentiality, laws related to location of provider and accreditation, resistance from providers to use them, limited resources of patients rendering them inaccessible, and motivating patients to use them.^{52,57,58} Finally, technology cannot totally replace in-person care, and these services may be best delivered in the context of having some support from a trained therapist. Future research focusing on the development of technologies for SUD treatment should also assess and address these potential challenges.

INTEGRATION OF SUD TREATMENT WITHIN AND ACROSS HEALTH CARE SYSTEMS

To expand the reach of SUD care, SUD services need to be integrated within more general health care systems, in particular primary care, rather than existing as a specialty service reached only by referral.⁵⁹ Indeed, 90% of patients with SUD do not seek specialty care,⁶⁰ yet two-thirds of primary care visits are related to psychosocial issues, including SUD.⁶¹ There is preliminary evidence that integrated care leads to positive clinical outcomes for those with alcohol problems.⁶²

How best to achieve integrated SUD and primary care remains challenging. Integration can take many forms—often not based on treatment design, but rather on unique features of clinic and staff resources and organization and financing as well as client populations. Integration has been described under three general forms: co-ordinated between independent organizations, each with its own treatment system—this usually making use of strong referral processes between separate treatment groups; colocated, where behavioral and medical services share physical location and share some resources but retain separate organizational identities; or fully integrated, where all providers serve the same organization or treatment system, typically where patient treatment plans include both medical and behavioral components.⁵⁹

An evidence base to support integration efforts is in its infancy. To date, no specific method or measure of integration was associated with best outcomes in clinical trials.⁶³ Most reviews rely on qualitative descriptions of the more successful efforts. Barriers to implementation of integrated SUD and primary care include the need for information technology to facilitate work of interdisciplinary teams, policies to manage privacy regulations for sensitive information with

respect to SUD, and having or developing workforce capacity and established roles for such integrated procedures.⁶⁴

Both VA and the DoD are adopting Patient Centered Medical Home models⁶⁵ (see below), which seek to adopt health information technology and decision support systems to create more interdisciplinary, cost effective primary care with improved continuity of care. In 2009, the VA initiated an extensive effort to transition primary care into patient aligned care teams (PACT), following models of Patient Centered Medical Home.⁶⁵ Within this implementation was a reorganization of roles and staffing at each VA facility to support the provision of behavioral health care within primary care. Interdisciplinary staffs are organized into small teams to provide care for a panel of veterans. The functioning of the teams, including integration of behavioral health with routine alcohol and tobacco screening and early intervention, is supported by a series of national trainings and ongoing consultation from the VA National Center for Health Promotion and Disease Prevention as well as a series of regional collaborative learning programs. Additionally, each VA facility added specific staff with expertise in health psychology to train and support patient aligned care teams in the screening and management of behavioral health and SUD issues.

An integrated mental health strategy was developed from a joint DoD/VA mental health summit in 2009 on issues common to both departments to improve the access, effectiveness, and efficiency of mental health services. The integrated mental health strategy developed 28 strategic actions which fall under 4 strategic goals: early recognition of mental health conditions; delivery of effective EBTs; implementation and expansion of preventive services; and education, outreach, and partnerships with other providers, organizations, and agencies. Processes were identified to support quality of care and continuity across departments. Each aim is developed collaboratively with both DoD and VA administrations and each carries specific objectives, timeframes, and performance assessments. For example, as described above, integrating mental health services into primary care is one aim shared by DoD and VA. Specific performance measures of integration include the number and proportion of clinics that have mental health services and numbers and proportions maintaining training in integrated care. Consistent with technology advances described above, advances in web-based access will be evaluated for integration and continuity across departments. Shared processes will include screens for alcohol and tobacco use. The VA program of outreach to veterans involved in the criminal justice system, a common occurrence for those with SUD, will be evaluated for extension to active military personnel. Public health messaging is also part of the joint effort. Both DoD and VA seek to decrease stigma, improve public awareness of availability and effectiveness of mental health treatments, and encourage service members and veterans to seek care as soon as problems are identified. Future reviews will no doubt provide early evaluations of this initiative.

In addition to the effort to integrate SUD treatment into routine health care, a need exists within this effort to integrate the pharmacological and behavioral interventions for SUD mentioned in this article. As these forms of intervention often get delivered somewhat separately, having an integrated service delivery package could maximize treatment potential. Several studies have demonstrated that combining specific pharmacologic and behavioral interventions works better than using only a single form of treatment. For example, the COMBINE Study showed that combining naltrexone with a medical management intervention meant to mimic a treatment that could be readily promulgated in primary care significantly increased per cent days abstinent for alcohol dependent patients compared to the medical management intervention combined with placebo.⁶⁶ Similarly, in treatment of opioid dependence, combining naltrexone with contingency management significantly reduced the probability of illicit opioid use compared to either treatment alone.⁶⁷ Bupropion, a medication efficacious for smoking cessation and depression, but with virtually no efficacy by itself for cocaine dependence when combined with contingency management, significantly reduced cocaine use compared to either treatment alone.⁶⁸ Based upon these findings, future work should develop additional innovative approaches to combining pharmacologic and behavioral interventions for SUD that would be practical for application in primary care settings.

CONCLUSION

In anticipating future developments for the identification and treatment of SUD, it is fairly straightforward to assume that assessment methods will continue to be refined and that treatments will continue to be developed and evaluated in comparison to existing standards of care and other control conditions. In this review, we note several areas that hold current and future promise. There are a number of medications being developed to improve pharmacotherapy for tobacco, alcohol, and opioid use disorders and considered for substances in which there are currently few or no good treatment options. Additionally, changes in policies and practices in DoD and VA may need to be considered to implement use of these medications. Several evidence-based behavioral interventions have been shown to be effective treatments for SUD's; however, which to choose for a given patient and how to deliver them effectively remains an issue. Further research into how therapist competence and general and specific treatment factors relate to treatment selection and implementation is needed. Additionally, the application of CFIR and MBC models hold promise for effective use of empirically-based treatments and to individualize treatments to better fit the needs of OEF/OIF personnel seeking help for SUD. Technological advances may be effective for augmenting SUD treatment by improving problem recognition, access, social connection, and coping skills among a population that is mostly comprised of younger men and women who are familiar and comfortable with the use of

mobile technologies as part of daily living. However, these technologies should be developed to augment SUD treatment in the context of collaboration with trained SUD providers. Finally, the movement toward integrating SUD treatment into primary care is vital to improving the first line of offense in the screening, prevention, and treatment of SUD. Collaboration between DoD and VA is crucial to ensuring continuity of care for OEF/OIF personnel engaging in treatment for SUD. Collaboration between active duty and VA health care systems can only augment the quality of research and treatment.

ACKNOWLEDGMENT

This work was supported by the Center of Excellence in Substance Abuse Treatment and Education at VA Puget Sound Health Care System and by the Research and Development Service, Department of Veterans Affairs.

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Prevalence of DSM-IV Major Depression Among U.S. Military Personnel: Meta-Analysis and Simulation

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ABSTRACT A meta-analysis of 25 epidemiological studies estimated the prevalence of recent Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) major depression (MD) among U.S. military personnel. Best estimates of recent prevalence (standard error) were 12.0% (1.2) among currently deployed, 13.1% (1.8) among previously deployed, and 5.7% (1.2) among never deployed. Consistent correlates of prevalence were being female, enlisted, young (ages 17–25), unmarried, and having less than a college education. Simulation of data from a national general population survey was used to estimate expected lifetime prevalence of MD among respondents with the sociodemographic profile and none of the enlistment exclusions of Army personnel. In this simulated sample, 16.2% (3.1) of respondents had lifetime MD and 69.7% (8.5) of first onsets occurred before expected age of enlistment. Numerous methodological problems limit the results of the meta-analysis and simulation. The article closes with a discussion of recommendations for correcting these problems in future surveillance and operational stress studies.

INTRODUCTION

Major depression (MD) is generally recognized to be among the most burdensome of all disorders in the U.S. population¹ because of its high prevalence² and strong adverse effects on role functioning.³ As exposure to highly stressful life experiences is one of the most consistently documented risk factors for MD,⁴ it is not surprising that exposure to combat has been shown to be a powerful predictor of MD.⁵ Indeed, available research suggests that MD might be as common as,⁶ or perhaps even more common than,⁷ post-traumatic stress disorder (PTSD) among combat veterans. Yet, much more research has been carried out on the prevalence and correlates of PTSD than MD among military personnel.⁸

In an effort to synthesize available data on the prevalence of MD and its relationship to deployment experience, we carried out a quantitative literature review and meta-analysis of the recent literature on the epidemiology of MD among U.S. military personnel. We were mindful in planning this analysis that a recent review found a high range of MD prevalence estimates in studies of military personnel.⁶ The authors of that review cautioned that assessments of MD in the reviewed surveys were typically based on unvalidated screening scales rather than clinical interviews and that many studies used convenience samples rather than probability samples. We consequently limited our review to epidemiological studies that,

with a few notable exceptions, used probability sampling methods and validated measures of MD.

Despite considerable information in the reviewed studies on current prevalence of MD, little data exist on lifetime prevalence or age-of-onset of MD among military personnel. Such data could be valuable in determining if military personnel with current MD had first onsets before versus only after enlistment. This information could have important implications in areas such as large-scale public health interventions and Physical Evaluation Boards. Even though direct data on lifetime prevalence are absent, simulation methods can be used to make indirect estimates. Messer et al⁹ did this to estimate lifetime prevalence of selected mental disorders in the Army from the Epidemiologic Catchment Area (ECA) study,¹⁰ a large community epidemiological survey of mental disorders. We extend the work of Messer et al here by using similar methods to estimate lifetime prevalence and age-of-onset of MD. The data used to carry out this simulation are from the National Comorbidity Survey Replication (NCS-R),¹¹ a national survey of the prevalence and correlates of DSM-IV mental disorders in the civilian U.S. household population.

METHODS

The Meta-Analysis

The Literature Search Strategy

We searched PubMed (NCBI), Embase (Elsevier), and PsycINFO (EBSCO) for relevant studies published between January 1, 1990 and April 21, 2011 using relevant controlled vocabulary terms for (i) depression, (ii) military personnel, and (iii) prevalence. (A detailed description of the full search strategy is available on request.) The search yielded 1,216 non-duplicated articles for review. We also contacted leading

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researchers in the epidemiology of mental disorders in the military for additional studies and searched for relevant reports. We focused on studies with a sample size of at least 1,000 individuals that provided estimates of recent prevalence of DSM-IV MD based on a validated screening measure (with demonstrated concordance to a diagnostic interview) or a diagnostic interview in a probability sample of individuals currently (at the time of the survey) serving in the U.S. Armed Forces. Studies that focused on clinical populations were excluded.

Two independent raters reviewed the abstracts and, based on the inclusion criteria, identified 32 articles and 13 reports for detailed review. Nineteen of these studies were subsequently excluded because they did not meet the inclusion criteria or used the same data as another publication that was included. (A detailed description is available on request). There were 26 remaining articles and reports (Table I). One¹² used a subsample of a larger dataset.¹³ Because detailed information on MD by demographic characteristics was only available in the former,¹² that study was included in the analysis examining sociodemographic correlates of MD but not in the regression analyses. We included several studies in which MD was assessed with a version of the Patient Health Questionnaire (PHQ)-9 that included an additional requirement of self-reported functional impairment even though we were unable to find a validation study for this version of the PHQ-9. This was done because, as described below, we were able to develop a calibration for this version of the scale that approximated the more standard version. With regard to random sampling, none of the studies considered here was based on an unrestricted probability sample of the entire Army. The baseline Millennium Cohort Study¹⁴ and the periodic Department of Defense Surveys of Health-Related Behaviors among Military Personnel¹⁵⁻¹⁹ were based on representative samples of military personnel who were not deployed at the time of sample selection, whereas the other studies we refer to as probability surveys were based on samples of military personnel in more restrictive sampling frames, but in each case either selected a probability sample of military personnel from the frame or attempted to survey all personnel in the selected units or time periods. Several reports did not use probability sampling methods,²⁰⁻²³ but were included because they contained prevalence estimates for individuals currently deployed at the time of data collection that otherwise would have been strongly underrepresented in our analyses. A small number of the studies included respondents in the National Guard or Reserves who might have been recently deactivated at the time of data collection.

Each of the retained studies was entered into a data file for quantitative analysis. The variables included the prevalence estimate, the measure on which the prevalence estimate was based (see below), the sample size, information about whether the assessment was anonymous or not, and the deployment status of respondents at the time of data collection (currently deployed, previously deployed, or never deployed). A study was coded as anonymous only if this

was explicitly stated. Studies coded not anonymous included confidential surveys in which identifying information was available but not disclosed to anyone not connected to the research and surveys that were mandatory for all service members returning from deployment, which were maintained in the permanent medical record. In cases where a single study included respondents with more than one deployment status and a MD prevalence estimate was presented separately by deployment status, the subsamples with different deployment statuses were treated as separate samples and entered as distinct observational records in the data file.^{24,25,28,30} In cases where the study included respondents with more than one deployment status but MD prevalence was not reported by deployment status, we treated the study as a single observational record and entered information in the data file for the proportions of respondents that were currently deployed, previously deployed, and never deployed. In cases where these proportions were not reported in the study, they were estimated based on the best available information. (A detailed description of the estimation methods is available on request.) The majority of assessments across studies were from respondents who had previously deployed (83.8%). Smaller proportions had never deployed (14.4%) or were currently deployed (1.8%) at the time of data collection. Studies that assessed MD longitudinally³¹ or cross-sectionally at two time points (3 and 12 months post-deployment)¹³ were treated as separate observational records. The subsamples in one especially large study²⁶ were also treated as separate observational records. This resulted in a total of 37 observational records in the final data file representing a total of 712,698 assessments.

Measures of MD in the Reviewed Studies

The measures of MD in the reviewed studies include the PHQ-2,⁴⁰ PHQ-8,⁴¹ PHQ-9 with a severity coding scheme,⁴² PHQ-9 with a DSM-IV coding scheme (PHQ-9/DSM-IV),³⁴ PHQ-9/DSM-IV with an impairment requirement,²⁷ the three-item version A Burnam depression screen,⁴³ the eight-item Burnam depression screen,⁴⁴ and the Center for Epidemiologic Studies Depression Scale (CES-D).⁴⁵ Recall periods were 1 week, 2 weeks, or 1 month before interview (Table I). These recall periods were treated as equivalent in assessing recent prevalence for the analysis. All the measures are screening scales; that is, although they assess some of the key symptoms of DSM-IV MD, they are designed to generate quick estimates of possible diagnosis rather than definitive diagnoses. We were unable to identify any studies using diagnostic interviews that met our inclusion criteria.

Quantitative Analysis of the Reviewed Studies

Quantitative analysis was carried out to examine effects of methodological factors (the measure on which the prevalence estimate was based, sample size, anonymous versus not anonymous) and deployment status on MD prevalence estimates. Random-effects multilevel regression analysis was

TABLE I. Description of Studies Included in the Analyses

Study ID	Branch ^a					Deployment Status ^b			Anonymous ^c	Measure ^d	RP ^e	RR ^f (%)	Prevalence of MD (%)	Years ^g	(n) ^h	Citation
	A	N	AF	M	CG	PD	CD	ND								
1a	X					X		X	Yes	5	3	54 ⁱ	6.0	2003	4,529	Cabrera 2007 ²⁴
1b	X					X			Yes	5	3	54 ⁱ	7.8	2004	2,392	Cabrera 2007 ²⁴
2a	X					X		X	Yes	4	3	77	11.4	2003	2,418	Hoge 2004 ²⁵
2b	X			X		X			Yes	4	3	53	14.5	2003	3,500	Hoge 2004 ²⁵
3a ^j	X			X		X			No	1	2	+ ^k	3.5	2003–04	16,318	Hoge 2006 ²⁶
3b ^j	X			X		X			No	1	2	+ ^k	6.1	2003–04	222,620	Hoge 2006 ²⁶
3c ^j	X			X		X			No	1	2	+ ^k	2.7	2003–04	64,967	Hoge 2006 ²⁶
4	X					X			Yes	5	3	59	5.3	2006	2,464	Hoge 2008 ²⁷
5a	X					X		X	Yes	4	2	89	2.0	2007–08	1,910	Kline 2010 ²⁸
5b	X					X			Yes	4	2	89	5.1	2007–08	625	Kline 2010 ²⁸
6	X					X			No	6	1	48	37.4	2005	4,089	Lapierre 2007 ²⁹
7a	X					X		X	No	3	2	+ ^k	4.5	2004–08	6,943	Luxton 2010 ³⁰
7b	X					X			No	3	2	+ ^k	10.1	2006–09	6,943	Luxton 2010 ³⁰
8a ^l	X					X			No	1	2	+ ^k	4.7	2004–06	56,350	Milliken 2007 ³¹
8b ^l	X					X			No	1	3	+ ^k	10.3	2005–06	56,350	Milliken 2007 ³¹
8c ^l	X					X			No	1	2	+ ^k	3.8	2004–06	31,885	Milliken 2007 ³¹
8d ^l	X					X			No	1	3	+ ^k	13.0	2005–06	31,885	Milliken 2007 ³¹
9	X					X			No	4	2	+ ^k	4.2	2005–07	1,301	Reger 2009 ³³
10	X	X	X	X	X	X		X	No	4	2	36	3.2	2001–03	76,476	Riddle 2007 ¹⁴
11a ^m	X					X			Yes	5	3	58	5.0	2005–07	2,454	Riviere 2011 ¹²
11b ^m	X					X			Yes	5	3	71	7.3	2005–07	1,415	Riviere 2011 ¹²
12a ⁿ	X					X			Yes	4	3	62	16.0	2004–07	4,723	Thomas 2010 ¹³
12b ⁿ	X					X			Yes	4	3	62	15.7	2004–07	3,749	Thomas 2010 ¹³
12c ⁿ	X					X			Yes	4	3	62	11.5	2004–07	2,607	Thomas 2010 ¹³
12d ⁿ	X					X			Yes	4	3	62	15.9	2004–07	1,501	Thomas 2010 ¹³
13	X							X	Yes	3	2	91	15.9	2004	1,090	Warner 2007 ³⁵
14	X	X	X	X		X		X	Yes	7	1	70	17.6	1995	16,193	Bray 1995 ¹⁵
15	X	X	X	X		X		X	Yes	7	1	59	16.1	1998	17,264	Bray 1999 ¹⁶
16	X	X	X	X		X		X	Yes	8	1	56	18.8	2002–03	12,756	Bray 2003 ¹⁷
17	X	X	X	X		X		X	Yes	7	1	52	22.3	2005	16,146	Bray 2006 ¹⁸
18	X	X	X	X	X	X		X	Yes	7	1	72	21.1	2008	28,546	Bray 2009 ¹⁹
19	X							X	Yes	5	3	++ ^o	5.0	2004	2,064	MHAT-II 2005 ²⁰
20	X							X	Yes	5	3	++ ^o	8.0	2005	1,124	MHAT-III 2006 ²¹
21	X			X				X	Yes	5	3	++ ^o	7.7	2006	1,767	MHAT-IV 2006 ²²
22	X							X	Yes	5	3	++ ^o	7.2	2007	3,114	MHAT-V 2008 ²³
23	X							X	Yes	5	3	++ ^o	4.8	2009	1,360	MHAT-VI 2009a ³⁶
24	X							X	Yes	5	3	++ ^o	4.9	2008–09	2,442	MHAT-VI 2009b ³⁷
25	X			X				X	Yes	5	3	++ ^o	4.8	2010	1,246	MHAT-VII 2011 ³⁸
26 ^p	X	X	X	X		X			No	2	2	44	10.8	2007–08	1,041	Schell 2008 ³⁹

With the exception of studies 19 to 22, the studies used probability sampling methods to select samples.

^aA, Army; N, Navy; AF, Air Force; M, Marines; CG, Coast Guard.

^bPD, Previously deployed; CD, Currently deployed; ND, Never deployed. 83.8% of assessments across studies were from respondents who had previously deployed, 14.4% never deployed, and 1.8% currently deployed.

^cSee the text for the definition of anonymity.

^dPHQ-2 = 1, PHQ-8 = 2, PHQ-9 = 3, PHQ-9/DSM-IV = 4, PHQ-9/DSM-IV + Functional impairment (FI) = 5, CES-D = 6, 3-item version A Burnam depression screen = 7, 8-item Burnam depression screen = 8. (Information on the cut-points used for these scales is available on request.)

^eRP, Recall period: 1 week = 1, 2 weeks = 2, 1 month = 3.

^fRR, Response rate. Although RR is reported based on the information provided in the publications, it should be noted that there is wide variation in the ways response rates are reported in the literature. Even though standards for reporting response rates exist (http://www.aapor.org/Response_Rates_An_Overview1.htm), few of the studies included in our analysis reported information about their response rate calculation methods in enough detail to tell which of these definitions they used.

^gYears: Year(s) when data were collected.

^hIf available, the sample size is reported as the number of respondents actually screened for depression (which in some cases is different from the total number of respondents included in analyses in the studies).

ⁱThis is an estimate based on personal communication with Dr. Hoge (September 20, 2011).

^j3a is a subsample of respondents surveyed after return from Operation Enduring Freedom, 3b from Operation Iraqi Freedom, and 3c from other locations.

^kStudies 3 and 7 to 9 are based on the mandatory Postdeployment Health (Re)Assessment or equivalents and response rates were not reported.

^l8a and 8b are longitudinal assessments of a sample of active duty soldiers (approximately 6 months between assessments); 8c and 8d are equivalent for a sample of National Guard and Reserve soldiers.

(continues)

used to analyze the data.⁴⁶ This is the preferred method for quantitative meta-analysis because it allows information about both sample size and study characteristics to be included in the analysis. The random effects model includes terms both for sampling error (sample-size dependent) and model error (representing effects of study-specific variation independent of sample size, such as unobserved variations in measurement methods, population, and context). In this way, the model gives more weight to larger than smaller studies but does not allow any single very large study to swamp the effect of smaller studies because weighting takes into consideration the extent to which each observation deviates from the overall pattern in the full sample and down-weights observations that have large deviations. The analysis was carried out initially with the observed study prevalence estimate as the outcome and subsequently repeated with recalibrated measures of prevalence described below. The coefficients in these models were then used to estimate the prevalence of DSM-IV MD separately for deployed, previously deployed, and never deployed military personnel by generating a predicted prevalence estimate from the model coefficients separately for respondents in each of the three deployment statuses based on assumptions about calibrations used to equalize estimates across types of measures described below. As we found that anonymity of reports is significantly related to elevated prevalence estimates, the predicted prevalence estimates were made based on the assumption that MD was assessed in an anonymous survey. Standard errors of the prevalence estimates were generated using the jackknife resampling method.⁴⁷

The Simulation

The Sample

As noted in the introduction, the simulation study was based on the NCS-R,¹¹ a 2001–2003 national face-to-face survey of the prevalence and correlates of DSM-IV mental disorders in the adult (ages 18+) civilian U.S. household population. The response rate was 70.9%. The interview was conducted in two parts. Part 1, completed by all 9,282 respondents, assessed a core set of DSM-IV mental disorders, whereas Part 2, administered to all Part 1 respondents who screened positive for at least one Part 1 disorder ($n = 4,235$) plus a probability subsample of other Part 1 respondents ($n = 1,457$), assessed additional disorders and correlates. The Part 2 sample was weighted to adjust for differential probabilities of selection and the undersampling of respondents with no Part 1 disorder. A final poststratification weight was used to match the Part 2 sample to the 2000 census on a variety of sociodemographic and geo-

graphic variables. These sampling and weighting procedures are discussed in more detail elsewhere.⁴⁸

Sample Matching

We subsampled Part 2 NCS-R respondents to create a weighted subsample that matched the population of active duty Army personnel as closely as possible. We focused on Army personnel rather than military personnel more generally because the simulation was carried out as part of planning for the Army Study To Assess Risk and Resilience in Servicemembers (Army STARRS; <http://www.armystarrs.org>).

Subsampling began by limiting NCS-R respondents to those in the age range 18 to 65 with at least a high school education (or general education diploma [GED]) who were employed and had health insurance. We then excluded respondents who would be ineligible for Army service based on (1) conviction of a felony or serving at least 1 year in prison; (2) handicaps, including deafness, blindness, paralysis, or a missing limb; (3) chronic physical disorders, including cardiovascular disorders (heart attack, stroke, hypertension, heart disease), respiratory disorders (COPD, asthma), diabetes, ulcer, HIV-AIDS, epilepsy or seizure disorder, Crohn's disease, cancer (except skin cancer), severe migraines, and extreme obesity; and (4) severe mental disorders, including schizophrenia, other nonaffective psychoses, bipolar (BP)-I disorder, and serious suicide attempts that occurred before the imputed age of enlistment. These exclusions are overinclusive in that they remove people who might have entered the Army with waivers or developed chronic conditions after enlistment.

Once the NCS-R sample was restricted in these ways, we selected a series of eight weighting variables available in the NCS-R and the Defense Department Defense Manpower Data Center (DMDC) master personnel dataset for Army personnel who were on active duty in December 2007 (<http://www.virec.research.va.gov/Non-VADataSources/DMDC.htm>). The eight weighting variables were age, sex, race-ethnicity (non-Hispanic black, non-Hispanic white, Hispanic, and all others), education (high school graduates including those with a GED, some post-high school education without a bachelor's degree, and bachelor's degree or more education), marital status (married, never married, and previously married), U.S. citizenship (yes or no), nativity (i.e., born in the United States yes or no), and religion (Protestantism, Catholicism, Judaism, Eastern [Buddhism, Hinduism, Islam], other, and atheist or no religion). These variables were selected for weighting because they are known to be significantly related to mental disorders and to have a significantly different distribution among Army personnel than the general U.S. population, although coarseness of some weighting categories makes the matching inexact.

Table I (continued)

^mThe data used in Riviere et al.¹² (collected at 3 months [11a] and 12 months [11b] postdeployment) are a subsample of the data used in Thomas et al.,¹³ but the former is used to calculate ORs because it reports additional information about prevalence by demographic characteristics.

ⁿCross-sectional samples of Active Component and National Guard soldiers were assessed at 3 months (12a and 12c, respectively) and 12 months (12b and 12d, respectively).

^oNo response rates are available for studies 19 to 25 (Dr. Bliese, personal communication, August 29, 2011).

^pRespondents who were discharged or retired were excluded.

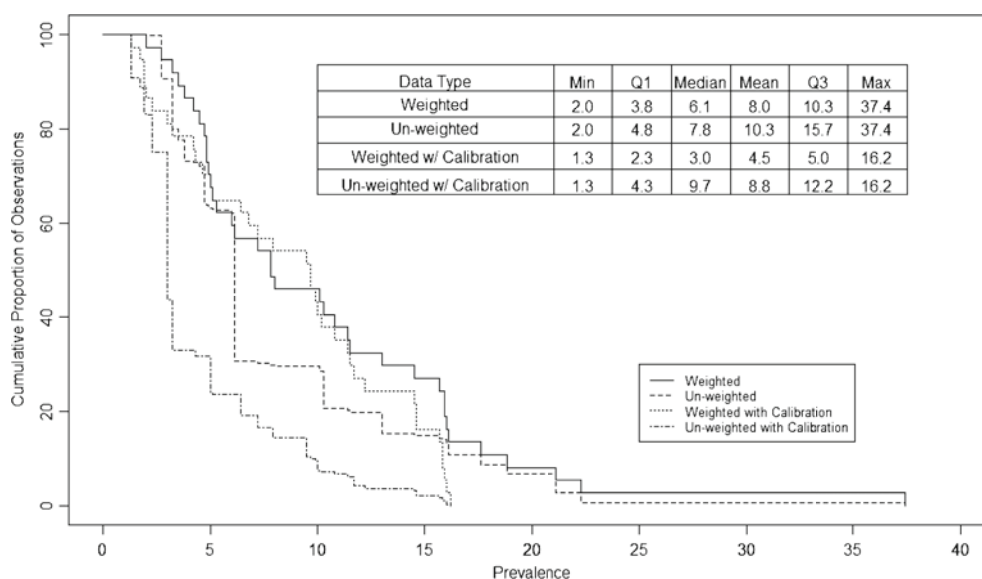


FIGURE 1. Inverse cumulative distribution function of MD prevalence based on studies included in the analyses (based on 37 observational records containing a total of 712,698 assessments).

The NCS-R weights were generated by using an exponential weighting function to make the distributions of the eight weighting variables in the adjusted NCS-R sample agree with the distributions in the DMDC dataset. (A detailed description of weighting procedures is available on request.)

Regression-based imputation was used to assign an estimated age of enlistment to each NCS-R respondent by estimating a multiple regression equation using cross-tabulations of weighting variables from the DMDC in which the eight variables were used to predict age of enlistment. The regression coefficients from that equation were then applied to the NCS-R dataset to impute individual-level estimates of age of enlistment to match the DMDC distribution conditional on the matching variables.

Measurement of DSM-IV MD in the NCS-R

MD was assessed in the NCS-R with Version 3.0 of the World Health Organization Composite International Diagnostic Interview (CIDI),³² a fully structured lay-administered interview that generates diagnoses for commonly occurring DSM-IV mental disorders. Good concordance was found between CIDI diagnoses and blinded clinical assessments in a NCS-R clinical reappraisal study.⁴⁹ The CIDI yields information on lifetime history, age at first onset, and presence of MD in the past year. Diagnoses were assigned based on reports of symptoms, duration, and intensity as specified in the DSM-IV.

RESULTS

The Meta-Analysis

MD Prevalence Estimates in the Reviewed Studies

MD prevalence estimates vary widely across the 37 observational records, from a low of 2.0% to a high of 37.4% (Fig. 1).

Figure 1 shows the proportion of studies with prevalence estimates above the levels on the horizontal axis. There are four different lines in the figure based on the cross-classification of two dichotomous distinctions: (i) either using a weight to adjust the 37 different studies for variation in sample size or treating the studies as equal in importance regardless of sample size and (ii) either using a calibration method described below to adjust prevalence estimates or considering prevalence estimates in the metrics reported in Table I. For current purposes, the reader should focus only on the two lines without calibration.

The upper left corner of the figure shows that 100% of studies, by definition, have a prevalence estimate of 0.0% or more. The line for the unweighted (for variation in sample size across studies) and uncalibrated distribution across studies shows that median prevalence (i.e., the prevalence of the study with the 19th highest prevalence out of the 37 studies) is 7.8%, the mean 10.3%, and the interquartile range (IQR: 25th–75th percentiles) is 4.8 to 15.7%. Weighting for variation in sample size across observations substantially reduces estimates both of central tendency (median from 7.8 to 6.1%; mean from 10.3 to 8.0%) and spread (IQR from 4.8 to 15.7% to 3.8 to 10.3%).

One possible reason for the wide variation in these prevalence estimates is that the different screening scales might differ in sensitivity and specificity. Published validity studies are consistent with this possibility, suggesting that the PHQ-9 with severity scoring has the highest sensitivity and that the eight-item Burnam scale has the highest specificity (Table II). These validation studies typically administered a gold standard clinical reappraisal interview to a probability subsample of people shortly after they were administered the screening scale. The clinical interviewers typically were blinded to the screening scale scores. These validity studies were conducted

TABLE II. Sensitivity and Specificity of Screening Measures Compared to Diagnostic Interviews

Measures ^a	Sensitivity (%)	Specificity (%)	(n)	Criterion ^a	Reference
PHQ-2	83	90	580 ^b	Overview of SCID-DSM-III-R and Diagnostic Questions from PRIME-MD, Major Depressive Disorder, Past Month	Kroenke et al (2003) ⁴⁰
PHQ-9	88	88	580 ^b	Overview of SCID-DSM-III-R and Diagnostic Questions from PRIME-MD, Major Depressive Disorder, Past Month	Kroenke et al (2001) ⁴²
PHQ-9/DSM-IV	77	94	3,001 ^b	Formal Interview Based on DSM-IV; SCID-DSM-IV; Overview of SCID-DSM-III-R and Diagnostic Questions from PRIME-MD, Major Depressive Disorder ^d	Wittkamp et al (2007) ⁵⁰
Burnam-3A	81	95	3,116 ^c	DIS-DSM-III, Major Depressive Episode or Dysthymia, Past Year	Rost et al (1993) ⁴³
Burnam-8	77	97	3,116 ^c	DIS-DSM-III, Major Depressive Episode or Dysthymia, Past Year	Rost et al (1993) ⁴³
20 Item CES-D	80	71	425 ^b	SCID-DSM-III-R, Major Depressive Disorder, Past Month	Fechner-Bates et al (1994) ⁵¹

^aPRIME-MD, Primary Care Evaluation of Mental Disorders; SCID, Structured Clinical Interview for DSM-IV/DSM-III-R; DIS, Diagnostic Interview Schedule. The PHQ-8 and PHQ-9 with severity coding scheme have very similar operating characteristics⁵² and are highly correlated⁵³ and are thus treated as equivalent. To our knowledge, there are no studies that examined the sensitivity and specificity of the PHQ-9/DSM-IV plus self-reported functional impairment at the cut point used in this study.

^bData were collected in primary care clinics.

^cData were collected in a community sample.

^dPooled results from 4 studies that compared the PHQ-9/DSM-IV with various structured interviews using a random effects model. Only 1 study provided the time frame of the criterion, which was past month.

in civilian populations, though, mainly in primary care samples, making it unclear whether the estimates of sensitivity and specificity in these studies generalize to nonpatient samples of military personnel.

It is possible to adjust prevalence estimates in a screening scale to approximate estimates of “true” prevalence if information is available on the sensitivity and specificity of the screening scale. For example, if we know that sensitivity is 50% (i.e., half of the true cases are detected by the screening scale) and specificity is 100% (i.e., all the true noncases are classified as noncases by the screening scale), then the estimated prevalence is only 50% as high as the true prevalence, meaning that the best estimate of true prevalence is two times the prevalence estimate in the screening scale. A standard formula exists for converting prevalence estimates in screening scales to estimates of true prevalence based on information about sensitivity and specificity.⁵⁴ We used that formula to adjust the prevalence estimates based on the screening scales in each of the studies reported in Table II. The estimates of sensitivity and specificity used in doing this were the published estimates of sensitivity and specificity for these screening scales. However, these transformations yielded implausible estimates of true MD prevalence. This was most clear in quite a few studies where estimated prevalence was strongly negative (i.e., not merely within sampling error of 0.0%, but substantially less than 0.0%).

A negative prevalence, of course, is impossible. So, what does it mean to find that adjusted prevalence estimates are negative? (Detailed results of this estimation exercise are

available on request but are not presented here because so many of the estimates are implausible.) It means, quite simply, that the sensitivity and specificity estimates in the published validity studies of the screening scales do not apply to the samples considered here. That is, the true sensitivity and specificity of the screening scales in the studies where they were used must have been different than the sensitivity and specificity estimated in the methodological studies of the screening scales. There are a variety of reasons why this might be the case, but the most plausible one is that the samples used in the original validity studies of the screening scales might have been different than those in the substantive studies reported in Table II (e.g., more severe cases of MD, which would lead to differences in rates of detection). We have no way to produce more accurate estimates of sensitivity and specificity for the studies in Table II, as these studies did not include the blinded clinical reappraisal interviews with probability subsamples of respondents that would be required to calculate independent estimates of sensitivity and specificity for these specific studies. Based on these facts, we abandoned the attempt to correct prevalence estimates in these studies for differential sensitivity and specificity.

Yet, the substantial variation in prevalence estimates across these studies raises the possibility that between-measure variation in concordance with clinical diagnoses could be important. In the absence of being able to correct for this variation by using sensitivity–specificity adjustments, we turned to a different method: calibration of the prevalence estimates across studies to a common metric by making use

of the fact that a number of epidemiological studies—some of them in military samples and others in civilian samples—have reported MD prevalence estimates based on two or more of the measures used in the 37 observational records considered here. Access to these within-study pairs of prevalence estimates allowed us to create prevalence ratios to transform prevalence estimates based on one measure to estimates based on another measure. The common metric we transformed to was the DSM-IV coding scheme for the PHQ-9. The latter scheme, used in five of the 25 studies considered here, requires at least five of the nine PHQ-9 questions about criterion A symptoms of MD to be reported as having occurred more than half the days over the recall period and for at least one of these questions to involve either depressed mood or anhedonia. One study reported prevalence estimates based on this PHQ-9/DSM-IV coding scheme as well as on the PHQ-9 severity coding scheme and the PHQ-2.⁵⁵ Three separate articles from a second study reported prevalence estimates based on this same set of three coding schemes.^{34,40,42} Two other studies reported prevalence estimates based on both the PHQ-9/DSM-IV and the version of the PHQ-9 coding scheme that requires impairment.^{13,25} We used the weighted average ratios of prevalence estimates based on these alternative coding schemes to transform prevalence estimates based on other measures to PHQ-9/DSM-IV prevalence estimates. In cases where no study existed that presented prevalence estimates based on both the PHQ-9/DSM-IV coding scheme and one of the other measures, we made indirect calibrations using a third measure. For example, although

there were no studies that included prevalence estimates based on both the CES-D and the PHQ-9/DSM-IV coding scheme, one study presented both CES-D and PHQ-2 prevalence estimates,⁵⁶ whereas two others presented both PHQ-2 and PHQ-9/DSM-IV prevalence estimates,^{34,40,55} allowing us to multiply these two separate ratios together to generate a synthetic CES-D versus PHQ-9/DSM-IV calibration ratio to adjust prevalence estimates in the one study that used the CES-D to estimate depression prevalence.

As shown in Figure 1, this calibration exercise substantially reduces the average prevalence estimates from median and mean of 6.1 and 8.0% in the weighted raw data to 3.0 and 4.5% in the weighted calibrated data as well as in the IQR (from 6.5% [between 3.8 and 10.3%] in the raw data to 2.7% [between 2.3 and 5.0%] in the calibrated data).

Multiple Regression Analysis

The test for the variance of random intercepts is significant in the random effects model of the raw outcomes ($\chi^2_1 = 13.0$, $p < 0.001$), indicating significant heterogeneity among observations. This supports the decision to use the random effects model. Methodological and substantive variables are both significant predictors of variation in MD prevalence estimates across the 37 raw observational records (Table III). With regard to methodological factors, prevalence estimates differ significantly by type of screening scale ($\chi^2_7 = 37.1$, $p < 0.001$) and are significantly higher in anonymous than identified surveys (odds ratio [OR] = 3.1, $t = 4.2$, $p = 0.002$). With regard to substantive factors, prevalence estimates

TABLE III. Association Between Anonymity of Survey, Deployment Status and Type of Measure and Prevalence of MD Using Random Effects Models with Logit Links

	Model A. DV: Prevalence as Reported in Articles ^a		Model B. DV: Prevalence Adjusted Based on Calibration of Measures ^a		Model C. Model B Without Dummies for Measures	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Intercept	0.0*	(0.0–0.0)	0.0*	(0.0–0.0)	0.0*	(0.0–0.0)
Anonymous						
Yes	3.1*	(1.7–5.6)	2.9*	(1.6–5.3)	3.0*	(1.9–4.8)
No	1.0	—	1.0	—	1.0	—
Measure						
3-Item Burnam	5.9*	(3.0–11.5)	1.0	(0.5–1.9)		
8-Item Burnam	6.3*	(2.5–16.2)	0.9	(0.6–3.8)		
CES-D	24.9*	(8.2–75.4)	3.2*	(1.1–9.6)		
PHQ-2	2.9*	(1.1–7.5)	0.6	(0.2–1.6)		
PHQ-8	5.0*	(1.6–15.6)	0.9	(0.3–2.8)		
PHQ-9	5.8*	(2.5–13.3)	0.9	(0.4–2.1)		
PHQ-9/DSM-IV	1.9	(1.0–3.8)	0.8	(0.4–1.6)		
PHQ-9/DSM-IV+FI	1.0	—	1.0	—	1.0	—
Deployment Status						
Currently	2.7*	(1.4–5.2)	2.2*	(1.2–4.1)	2.3*	(1.4–3.6)
Previously	3.2*	(2.6–3.9)	2.5*	(2.0–3.1)	2.5*	(2.0–3.1)
Never	1.0	—	1.0	—	1.0	—

DV, Dependent variable; FI, Functional impairment.

^aThe 8 coefficients associated with type of measure differ significantly from each other in Model A ($\chi^2_7 = 37.1$, $p < 0.001$) but not Model B ($\chi^2_7 = 2.2$, $p = 0.95$), suggesting that the calibration, which was based on data independent of the studies analyzed here, succeeded in correcting for between-scale differences in concordance with clinical diagnoses.

* $p < 0.05$.

are significantly higher among the currently deployed (OR = 2.7, $t = 3.4$, $p = 0.006$) and previously deployed (OR = 3.2, $t = 12.7$, $p < 0.001$) than the never deployed. It is important to recognize that results are based on a multivariate analysis, which means that ORs for each predictor are net of those for other predictors.

The results are different when the same model is used to predict variation in recalibrated MD prevalence estimates. The most dramatic difference is that estimated prevalence is no longer predicted significantly by type of screening scale ($\chi^2_7 = 2.2$, $p = 0.95$), indicating that the recalibration exercise was successful. However, survey anonymity remains significantly associated with elevated prevalence (OR = 2.9, $t = 4.0$, $p = 0.002$). Furthermore, the currently deployed and previously deployed continue to have significantly higher prevalence estimates than the never deployed, although these ORs are somewhat lower than when the model is estimated on the raw data (OR = 2.2, $t = 2.7$, $p = 0.020$ for currently deployed; OR = 2.5, $t = 9.8$, $p < 0.001$ for previously deployed). These significant ORs change only modestly in a model that deletes predictors for type of screening scale.

MD Prevalence Estimates Based on the Best-Fitting Regression Model

Based on the assumption that the higher MD prevalence estimates in anonymous surveys are more accurate than the lower estimates in nonanonymous surveys, the parameters of the best-fitting random-effects model for the calibrated data were used to generate best estimates of MD prevalence for anonymous surveys. As noted above in the section on analysis methods, the jackknife resampling method was used to generate estimates of standard error (SE). Best estimates of current MD prevalence (SE) are 12.0% (1.2) for the currently deployed, 13.1% (1.8) for the previously deployed, and 5.7% (1.2) for the never deployed.

Other Correlates of MD

A number of surveys report MD prevalence by sociodemographic variables and/or by branch of service. We calculated ORs for these estimates within studies and then summarized these results by computing weighted (by sample size) averages of ORs across studies. Women are found consistently to have higher rates of MD than men with a mean (range) OR of 1.6 (1.1–1.9) across studies (Table IV). Prevalence also is higher among respondents with no more than high school education (3.0 [2.0–3.6]) or some college education (1.8 [1.6–2.1]) relative to college graduates. Prevalence generally is unrelated to race–ethnicity. Prevalence is consistently higher among enlisted (2.8 [1.9–3.6]) personnel than warrant officers (1.1 [0.9–1.2]) or commissioned officers (the contrast category, with an implicit OR of 1.0). In addition, MD generally is estimated to be more common among younger (up to ages 24 or 25) than older (older than 24 or 25) respondents (2.0 [1.0–2.2]) and among the unmarried (either never married or previously married) than the married (1.8 [1.0–2.0]). The studies that compared MD across services

report consistently higher prevalence in the Army (2.0 [1.6–2.1]), Navy (1.7 [1.3–1.8]), and Marines (2.0 [1.4–2.3]) than the Air Force.

The Simulation

Current Depression Prevalence Estimates in the Simulation Data

A question can be raised how the prevalence estimates reported above for current MD compare to the general U.S. population. The comparable prevalence estimate (SE) in the simulated NCS-R data is 1.3% (0.6). To be clear, this is the rate we would expect in a representative sample of people in the U.S. population who have the same sociodemographic profile (e.g., age, sex, race–ethnicity, and education) and history of pre-enlistment health problems as the members of the U.S. Army. The 1.3% MD prevalence estimate is substantially lower than the estimates reported above in the meta-analysis. Even though the NCS-R simulation uses a different measure of MD than any of the meta-analysis surveys, the NCS-R measure has been validated in the general population and shown to yield a prevalence estimate very similar to the estimate based on blinded clinical reappraisal interviews using DSM-IV criteria.² We would consequently expect that the meta-analysis estimates, based on calibration to the PHQ-9/DSM-IV, would be comparable to the simulated NCS-R/DSM-IV estimates.

Lifetime Depression Prevalence Estimates in the Simulation Data

As noted in the introduction, much less is known about lifetime prevalence than current prevalence of MD among military personnel. The simulated NCS-R data show that 16.2% of the sample has a lifetime history of MD, that 69.7% of these lifetime cases (i.e., 11.3% of the total sample) had first onsets before enlistment (i.e., before the age when we would have expected them to enlist based on their sociodemographic profile), and that the remaining 30.3% of lifetime cases (i.e., 5.5% of the total sample) had first onsets only after enlistment (Table V). The majority of those with current MD had first onsets before enlistment (77.9%). The latter is higher than the 69.7% of lifetime cases with pre-enlistment MD, suggesting that MD persistence is higher among early-onset than later-onset cases. This higher persistence is indirectly indicated by the fact that the ratio of current to lifetime prevalence is higher among respondents with pre-enlistment (8.8%) than postenlistment (5.4%) MD.

Given the much higher prevalence of current MD among Army personnel than expected from the simulations, it is unclear from these data what percent of actual Army personnel with current MD had first onsets before enlistment. The high current prevalence estimates from the meta-analysis could reflect either a dramatic increase in current prevalence among lifetime cases once they enter the Army, a dramatic increase in postenlistment first onset, or a combination. If it is true that 11.3% of actual Army personnel had a history of MD before enlistment, and if postenlistment onsets were

TABLE IV. Sociodemographic Correlates of MD: Weighted Average and Range Across Studies of Within-Study ORs

	Weighted Average	Minimum	Maximum	Number of Studies	(n)
Gender ^a				8	
Female	1.6	1.1	1.9		42,982
Male	1.0				135,194
Race–Ethnicity ^b				7	
African American, non-Hispanic	1.1	0.7	1.4		26,617
Hispanic	1.1	0.9	1.3		23,572
Other	1.2	1.0	1.3		7,433
White, non-Hispanic	1.0				116,289
Education				6	
High School or Less	3.0	2.0	3.6		63,616
Some College	1.8	1.6	2.1		60,529
College Graduate or Higher	1.0				43,236
Age ^c				8	
24/25 or Younger	2.0	1.0	2.2		53,022
25/26 or Older	1.0				125,135
Marital Status ^d				7	
Not Married	1.8	1.0	2.0		65,596
Married	1.0				105,028
Rank				6	
Enlisted	2.8	1.9	3.6		129,648
Warrant Officer	1.1	0.9	1.2		4,319
Commissioned Officer	1.0				33,414
Service ^e				6	
Army	2.0	1.6	2.1		58,279
Navy	1.7	1.3	1.8		36,942
Marine Corps	2.0	1.4	2.3		22,985
Air Force	1.0				45,319

Between 6 and 8 studies were used to examine each of the 7 correlates. Six studies were the same for all 7 correlates.^{14–19} The other studies used varied across correlates, as described in the following notes. Within each study ORs were calculated and then a weighted average OR was calculated across studies.

^aFor gender, we used the postdeployment sample of Luxton et al.³⁰ and the combined 3- and 12-month assessment of Riviere et al.¹²

^bThe race–ethnicity categories reported here are the ones used in the largest set of studies.^{15–19} One other study used the categories “Caucasian,” “African American,” “Hispanic,” and “Asian” (we coded the latter as “other”),²⁴ whereas another used the categories “White non-Hispanic,” “Black non-Hispanic,” and “other.”¹⁴ In this case, we coded the category “other” as “Hispanic” because the majority of this group is assumed to be Hispanic.

^cThe largest set of studies used here^{15–19} provided information on age ≤ 25 and ≥ 26 , whereas the other studies^{12,14,24} provided information on age ≤ 24 and ≥ 25 .

^dAlso based on Riviere et al.¹² “Not married” includes “never married,” “divorced/widowed,” and “single” (and “separated” in the largest set of studies,^{15–19} this is unclear for the other studies). In one study,¹⁵ “married” includes living in a marriage-like relationship, whereas in others^{16–19} only legally married personnel were included as “married” (this is unclear for the rest of the studies).

^eIn Riddle et al.,¹⁴ Navy and Coast Guard are combined.

TABLE V. Simulated Lifetime, 12-Month and Past 30 Days Prevalence Estimates of DSM-IV/CIDI Major Depressive Episode and Dysthymic Disorder in the Subsample of NCS-R Respondents Weighted to Approximate the Population of Active duty Army Personnel ($n = 1785$)

	Prevalence		Prevalence of Disorder That Began Before Enlistment		Prevalence of Disorder That Began Only After Enlistment		Proportion of Prevalence Because of Disorder That Began Before Enlistment	
	%	(SE)	%	(SE)	%	(SE)	%	(SE)
I. Lifetime Prevalence	16.2	(3.1)	11.3	(2.7)	5.5	(1.7)	69.7	(8.5)
II. 12-Month Prevalence	6.3	(2.1)	5.0	(2.1)	1.4	(0.3)	79.8	(7.9)
III. Past 30 Days Prevalence	1.3	(0.6)	1.0	(0.5)	0.3	(0.1)	77.9	(11.3)

Respondents are all ages 18 to 65 years, have at least a high school education, and are employed with health insurance to match the broad sociodemographic profile of Army personnel. All NCS-R respondents who were ever convicted of a felony or served at least 1 year in prison were excluded from the sample. All NCS-R respondents with handicaps or physical or mental disorders that would normally lead to rejection from Army enlistment or discharge were excluded from the sample. The handicaps included deafness, blindness, paralysis (of one or both arms, legs or sides of the body), and a missing limb (hand, foot, arm or leg). The physical disorders included cardiovascular disorders (heart attack, stroke, hypertension, heart disease), respiratory disorders (COPD, asthma), diabetes, ulcer, HIV or AIDS, epilepsy or seizure disorder, Crohn’s disease, cancer (except skin cancer), severe migraines, and extreme obesity. The mental disorders included schizophrenia and other nonaffective psychoses, BP-I disorder, and serious suicide attempts that occurred before the imputed age of enlistment.

double the estimate in the simulation data (i.e., 11.0% rather than 5.5%), then the ratio of current to lifetime prevalence would have to be at least 25% among the never deployed (5.7/22.3) and 50% among the currently (12.0/22.3) and previously (13.1/22.3) deployed to generate the estimates of current prevalence found in the meta-analysis data.

DISCUSSION

The meta-analysis reported here was limited by the fact that a wide range of MD screening scales were used in the different studies and by the fact that prevalence estimates vary significantly by type of screening scale. We attempted to address this problem by transforming the screening scale prevalence estimates to a common metric based on the results of published validity studies. This attempt failed, though, as some "corrected" prevalence estimates were less than zero. This means that the sensitivity and specificity estimates reported in the published validity studies, all of which were carried out in civilian samples and mostly among primary care patients, do not apply to the military samples considered here. The calibration approach we used to address this problem was limited by the fact that it required the assumption that prevalence ratios across different screening scales in a single survey could legitimately be generalized across surveys. Future epidemiological studies of depression in the military should address this problem more directly by using the same screening measure. This would be consistent with recent recommendations for use of common data elements in surveillance and operational stress research.⁵⁷

It is noteworthy that none of the screening scales included an exclusion for bipolar disorder (BPD). This means that they screened for major depressive episodes (MDE), not for major depressive disorder (MDD), and that some unknown proportion of these cases represents depressive phases of a BPD. As bipolar-I (BP-I) leads to military discharge and is so dramatic during the manic phase that it is likely to have a high rate of detection, we would not expect many cases of MD in the military to be associated with BP-I. But, BP-II and subthreshold BPD are together much more common than BP-I³ and often go undetected. Intervention implications are quite different for BPD than MDD, making it important to distinguish between the two. Future epidemiological studies of depression in the military should address this problem by including a BPD screen and the MD screen. This is being done in the Army STARRS study, but we are unaware of any other large-scale military epidemiological survey that has done so.

It would also be useful to include a small clinical reappraisal component in each future major epidemiological survey of military mental health even if a consistent MD screening scale was used. Repeated validity studies are needed because variation in the accuracy of any screening scale across studies can be influenced by survey conditions (e.g., anonymity, rationale, the context created by preceding survey questions, and the physical conditions of respondents at the time of survey implementation) that vary across studies.⁵⁸

Another methodological feature that could usefully be added to future military epidemiological studies would be a nonrespondent adjustment process. This could include a nonrespondent subsampling outreach phase in which limited information is obtained from a probability subsample of survey nonrespondents. Or it could use administrative databases (e.g., information from military electronic medical records about history of diagnoses of mental illness) to weight the survey data for underrepresentation of personnel with profiles associated with high risk of MD or other mental disorders. Methods of these sorts have been used successfully to address sample bias in other epidemiological surveys.⁵⁹ Weighting seems like an especially attractive approach in military surveys in light of the existence of an extensive series of administrative databases for all military personnel.

A related limitation of our meta-analysis is that the samples, although largely based on probability selection methods within the units studied, often used nonprobability methods to select units and, within units, to select critical times in the unit life cycle. This led to over-representation of combat units as well as to over-representation of the months just before deployment and just after redeployment. Although it would theoretically be possibly to correct for these sampling biases with weights, the logistical complexities of doing so made this impossible in practice. As a result, caution is needed in drawing inferences from our summary results because of the likely skewed distributions in our samples of military occupation specialties (MOSs), units, and timing of deployment histories. Not all of the samples considered in our meta-analysis shared this last limitation, as some surveys were representative of all military personnel in one or more branches of service. However, in order to use the data from these studies to adjust the results across all studies, we would have needed to work with individual-level data rather than the aggregate data available to us. This highlights another limitation of our meta-analysis; that it was based on summary published results rather than on secondary analysis of individual-level data. More fine-grained analysis could have been carried out in individual-level secondary analysis, including but not limited to, using weights to adjust sample composition for the over-representation of some MOSs, types of units, and deployment histories. Pooled secondary analysis of existing survey data has been of great value in advancing our understanding of the epidemiology of depression in the general population.⁶⁰ The same could be true for research on depression (and other mental disorders) in the military if de-identified individual-level data were made available.

Our simulation had only a limited set of variables, some of them relatively coarse, to match the NCS-R national household sample with the characteristics of Army personnel. Failure to control for the many unmeasured selection factors that might influence both enlistment in the Army and depression could have distorted the results. In addition, the simulation was designed to provide data on what the prevalence and age-of-onset distribution of depression would have been

expected to be among Army personnel if they had not joined the Army. Although that kind of information is potentially useful in assessing the impact of Army experiences, in the context of the much higher current prevalence estimates in the meta-analysis than the simulation, it tells us nothing about the lifetime prevalence of postenlistment onset depression or about the persistence of either pre-enlistment or postenlistment depression.

Our estimates of current MD prevalence in the military are much higher than the 30-day prevalence estimate obtained for sociodemographically comparable civilians in the simulation study. It needs to be noted that the MD prevalence estimates from the meta-analysis were generated based on the parameters for anonymous surveys, whereas the simulation results are based on confidential (but not anonymous) interviews from a general population survey. Previous research indicates that respondents are more likely to provide accurate information on sensitive questions in anonymous versus confidential questionnaires,⁶¹ but this would explain only a small part of the difference in MD prevalence estimates. The finding that the prevalence estimate was higher for the previously than currently deployed could be an artifact in that the previously deployed personnel considered here over-represented those who had recently returned from deployment. Current prevalence among military personnel was estimated to be higher for women than men, young than old, the unmarried than the married, and those with lower than higher rank and education. These correlates are broadly consistent with those found in general population surveys.^{2,62}

We estimated that 16.2% of respondents in the simulation data had a lifetime history of MD and that the majority (69.7%) of these lifetime cases had first onsets before expected time of enlistment. We have no comparable lifetime prevalence estimate in the meta-analysis data although we would expect that lifetime prevalence among military personnel would be higher because of a presumed larger number of postenlistment onsets than at comparable ages in the general population. In the absence of a direct estimate of persistence, though, we have no way to know how much higher the prevalence of postenlistment onsets are in the military than the general population or the proportion of current cases that had first onsets before enlistment. However, the high estimated pre-enlistment lifetime prevalence in the simulation data, when coupled with the finding that early onset is positively associated with persistence, leads us to speculate that a substantial minority or perhaps even a majority of military personnel with current depression had first onsets before enlistment. To the extent that this is true, secondary preventive interventions with recruits having a pre-enlistment history of depression (or other mental disorders that predict subsequent depression) might be effective in reducing incidence of subsequent depressive episodes among military personnel. More direct data would be needed, though, on lifetime history, age-of-onset, current prevalence, and severity of current depression in representative military samples

before any such interventions could reasonably be planned. The Army STARRS study is collecting such data for the Army, but we are unaware of any attempt to collect comparable data for other branches of the military.

ACKNOWLEDGMENTS

The authors thank MAJ Owen Hill, Craig McKinnon, and Monika Wahli of the Injury Epidemiology Research Section, Military Performance Division, U.S. Army Research Institute of Environmental Medicine, Natick, MA, for providing guidance as well as weighting information from the Total Army Injury and Health Outcomes Database (TAIHOD). This study was supported by the Department of the Army and funded under cooperative agreement number U01MH087981 with the U.S. Department of Health and Human Services, National Institutes of Health, National Institute of Mental Health (NIH/NIMH, 1U01MH087981-01).

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Screening, Diagnosis, and Treatment of Depression

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ABSTRACT The U.S. military and its civilian partners have identified that psychological health problems such as depression and traumatic brain injury represent a significant threat to the health and readiness of the military force. Depression is a growing problem in the military with rates increasing from 2007 to 2010 across all services. Depression can be correlated with negative outcomes such as risk of suicide, risk of harm to others, incarceration, family problems including divorce, and occupational and social problems such as unemployment and homelessness. The military seeks to mitigate and prevent these negative outcomes through screening, diagnosis, and treatment of disorders such as depression. To support that effort, we have reviewed a sample of the literature base to support best practices for the screening, assessment, and treatment of depression within the Military Health System.

INTRODUCTION

Military service members are at risk for experiencing numerous potentially co-occurring psychological and physical health problems following deployment(s); moreover, research indicates that there are substantial barriers to seeking care.¹ Psychological health conditions such as Major Depressive Disorder (MDD) may coexist with other psychological health problems, physical health problems, or other interpersonal stressors.² These clinical and physical health factors have also been associated with other poor outcomes including incarceration, divorce, and suicide.³⁻⁵

The Military Health System (MHS) and its federal and civilian partners have established numerous efforts to address the psychological health needs of service members and their families ranging from predeployment resilience training to postdeployment clinical care. Military research and clinical efforts have been impressive; and today, the scientific community understands more about the health and wellness of service members than when the conflicts began in 2002.

Despite advances in civilian and military research, depression remains a concern for the MHS. This article will focus on the screening, diagnosis, and treatment of depression. Although efforts have been made to focus on military and veteran literature, a preponderance of published literature on depression focuses on civilian samples. It is well known in the civilian literature that mood disorders are commonly experienced. The Diagnostic and Statistical Manual of Mental Disorders-IV-TR (DSM-IV-TR) estimates lifetime prevalence rates of MDD as high as 25% for females and an estimated lifetime prevalence rate of 12% for males in U.S. samples.⁶ Depression has been linked to many negative outcomes including suicide, divorce and family discord, violence, and substance use suggesting that developing comprehensive

approaches to screen, diagnose, and treat are warranted. Post-traumatic stress disorder (PTSD) and traumatic brain injury (TBI) have received much attention in the research literature and media, and yet depression among military personnel remains a significant health challenge. For example, a recent study of Soldiers and Marines returning from deployment identified a 15% rate for MDD.⁷⁻¹⁰

This paper is not intended to be an exhaustive review of the extant literature. Instead, we sampled the literature base to discuss screening, diagnosis/evaluation, and treatment specific to depression. The Department of Defense (DoD) has recognized that psychological health problems such as depression represent not just a threat to the performance and well-being of its warriors, but also to the fighting forces ability to meet its mission demands. It is hoped that this review shall serve to inform researchers, providers and senior and line leadership on the evidence base relative to screening, diagnosis and treatment of depression.

SCREENING

Screening is an important strategy to detect the presence of clinical phenomena and psychological distress.¹¹ Although not diagnostic, screening is useful to identify individuals who may be or are at risk for experiencing a clinical disorder (e.g., depression and PTSD).^{12,13} The military is engaged in a number of screening endeavors. Most notable are the Post Deployment Health Assessment (PDHA) and the follow-up screen (within 180 days of return from deployment), the Post Deployment Health Reassessment (PDHRA). The PDHA and PDHRA are broad self-report screens, which address numerous clinical phenomena such as mood and anxiety disorders and TBI. Data from these screens are used to support efforts at providing clinical care. Presently, data are not available on the validity, reliability, sensitivity, or specificity of the PDHA and PDHRA. Data from these sources have been retrospectively examined to identify clinical health patterns and barriers to care

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for returned military personnel.¹ Further, the military has completed a series of in-theater broad screening missions known as the Mental Health Advisory Team (MHAT) in the Army and the Behavioral Health Needs Assessment Survey (BHNAS) in the Navy. These screening procedures provide single point-in-time data to address the health of the force.¹⁴ In light of this, we will examine screening in the context of risk assessment and symptom reporting.

Risk Assessment

Risk assessment is critical to identifying individuals who are at risk for harm to self or others.¹⁵ The American Psychological Association code of ethics specifically addresses risk of harm to self or others.¹⁶ The primary goal of any treatment is to ensure the safety of the patient. The literature indicates that depressed persons are at higher risk for harm to self or others compared with nondepressed cohorts.¹⁷⁻²⁰

The literature on risk of suicide indicates that screening and/or specifically asking about suicide does not increase the risk of suicide.²¹ Suicide risk screening materials generally include information about the level of intent for self-harm, if a plan has been developed, and if the individual has the means (e.g., weapon or pills) to complete his/her plan.²² Research generally indicates that the use of cognitive behavioral therapy (CBT) or dialectical behavior therapy (DBT) are preferred for patients with suicide risk; however, these treatments require significant training to deliver. Further, clinicians often require a crisis intervention model. For this reason, a model called Collaborative Assessment and Management of Suicide (CAMS) has been developed to address the causes of suicide risk in patients. This model applies traditional risk factors (identified above) as well as qualitative and quantitative assessments to identify the nature and magnitude of the suicide risk problem. The clinician employs their chosen approach to manage the risk, as they and their patient are now informed by the CAMS model. Built into these screening procedures should be a safety mechanism to ensure that individuals who endorse violence to self or others are seen by a qualified professional to determine the appropriate course of action up to and including hospitalization.^{23,24}

Symptoms

MDD is a clinical mood disorder characterized by at least one major depressive episode without a history of other mood episodes such as mixed, manic, or hypomanic. Table I referenced at the conclusion of this article represents the clinical criteria for a major depressive episode.⁶ As noted, there is significant overlap among the mental health disorders with regard to symptoms across populations. For example, sleep impairment and psychomotor agitation or hypervigilance are prominent features in both depression and PTSD.^{6,25} For this reason, effective screening procedures detect the self-identified presence of symptoms and

TABLE I. Major Depressive Episode Criteria

Depressed mood most of the day nearly every day
Markedly diminished interest in all or nearly all activities
Significant weight loss or weight gain (change of more than 5% in a month)
Insomnia or hypersomnia nearly every day
Psychomotor agitation or retardation nearly every day
Fatigue or loss of energy nearly every day
Feelings of worthlessness or excessive inappropriate guilt
Diminished ability to think or concentrate
Recurrent thoughts of death and suicidal ideation

distress, but do not diagnose. Instead, effective screening procedures yield relevant data that inform more comprehensive evaluations where symptom architecture relative to diagnosis can be identified.

DIAGNOSIS

Patient presentations can be complex. For this reason, many clinicians develop clinical case formulations. Clinical case formulations are case maps, which categorize and organize clinical variables such as depressive symptoms, aggressive behaviors, and maintaining or reinforcing factors. One model of clinical case formulation is the clinical pathogenic map (CPM). The CPM organizes clinical variables and identifies the multiple relationships between clinical variables such that treatment may be targeted to produce the highest impact. A comprehensive evaluation is required to develop an accurate CPM.²⁶ Establishing an accurate and global clinical formulation is essential to develop treatment plans that meet patients' unique needs. This may increase the probability of treatment success by matching effective treatment models with the clinical problems they are designed to address.²⁷

For the purposes of this article, we divide clinical examinations into three parts. These three parts are mental status examination and presentation, comprehensive history, and structured clinical interview with additional diagnostic measures.

Mental status identifies key clinical constructs such as speech, motor activity, hygiene, and cognitive processes, etc.²⁸ This can be accomplished using standardized tools such as the Mini-Mental State Examination (MMSE). The MMSE asks the patient to address various constructs of cognitive functioning such as orientation (time and place), immediate and delayed verbal recall, and attention. A score below 26 generally indicates cognitive impairment.²⁹ Other features of mental status and presentation can be identified through behavioral observation. Identifying mental status provides a context for understanding patient functioning.

A complete history includes, but is not limited to family structure, early childhood development, education, prior criminal activity, past clinical and physical health problems, social and occupational history, relationship status,

and prior neurological insult or event(s) (e.g., TBI or stroke).³⁰ A comprehensive examination provides context to a case conceptualization and identifies if there is a personal or family history of psychological health problems or preexisting risk factors, which may be relevant to current psychological status.³¹

Clinicians may use semistructured clinical interviews such as the Structured Clinical Interview for DSM-IV (SCID) or the diagnostic interview schedule (DIS). These interviews provide questions, which relate to DSM-IV Axis I (psychological health disorders) and Axis II (personality disorders). The advantage of semistructured interviews is that they are standardized for administration and scoring.³² Additionally, measures such as the SCID are well researched and scientifically accepted.³³ Because they comprehensively address disorders identified in the DSM-IV, structured clinical interviews help rule in or rule out co-occurring disorders and can increase the accuracy of diagnostics.³⁴

The American financier and philanthropist Bernard Baruch said “If all you have is a hammer, everything looks like a nail.” If a clinician believes that a patient is depressed, he/she is likely to find this in unstructured questioning. This strategy may find an existing depression but fail to find other problems. Similarly, it may identify features of depressions which are part of another discrete diagnosis. For example, PTSD and depression have a number of overlapping symptoms (e.g., sleep impairment, psychomotor agitation, and clinical distress). Instituting evidence-based care for PTSD (exposure therapy) is unlikely to produce desired effects. Thus, accurate diagnostics are needed to guide prescribed models of care and reduce the risk of implementing proscribed treatments.³⁵

Thus, a comprehensive evaluation is recommended to limit errors associated with inaccurate or partial diagnosis. A global assessment that captures an array of potential phenomena as opposed to searching for a discrete disorder such as depression (clinical bias) appears likely to facilitate the appropriate treatment modalities.³⁶ A comprehensive evaluation should provide substantial data to develop an idiographic case conceptualization which identifies a constellation of clinical variables that comprise psychological health problems and maintain clinical distress and disease processes. As described above, comprehensive evaluations inform clinical case conceptualization or clinical pathogenic mapping constructions.³⁷

Confounds or Barriers to Diagnosis

Stigma or the perception that being identified as having a psychological health problem, is a significant barrier to seeking care. The literature on stigma associated with psychological health problems suggests that a significant percentage of military members who would benefit from clinical assessment and treatment do not seek or receive such treatments. These barriers tend to be based

in stigma-associated beliefs such as it will be bad for one's career or one will be viewed as weak by their leadership or peers.¹

TREATMENT

The treatment of depression as a single disorder has been well studied in the literature. Notably, research has focused on psychotherapeutic interventions, psychopharmacological interventions, and combination therapies.^{38,39} We will examine treatment types, treatment effectiveness, outcome measures, and confounds or barriers to seeking and/or completing treatment.

Psychotherapies for Depression

The VA/DoD Clinical Practice Guidelines (CPG) for depression highlight recommended procedures for addressing depression in military and veteran populations.⁴⁰

CBT has been identified as an evidence-based treatment for individuals with depression.^{41,42} CBT focuses on thoughts, feelings, and behavior to address distress and impairment associated with a host of clinical phenomena such as depression, anxiety, and substance abuse.^{43–45} CBT applies a behavioral strategy and a cognitive strategy to address psychological distress. The behavioral component in Beck's model of CBT is called behavioral activation. This strategy includes asking the patient to re-engage in a previously enjoyed activity (e.g., exercise, music, and art), which has likely decreased in frequency since the individual began to experience depression, as decreased interest in activities and events are often noted in patients with depression.⁴²

The cognitive strategy posits that distress and mood disorders are associated with inaccurate thinking and belief systems.⁴¹ CBT clinicians ask their patients to identify their thoughts and feelings using a thought record form. These forms are used in therapy to identify erroneous or inaccurate thinking. Clinicians use these data with their patients to identify the inaccurate thinking, denote the type of error such as catastrophic thinking or over generalization, and work toward cognitive restructuring where patients change how they think which purports to impact affect.

A number of other psychotherapy models have been examined in the context of depression. Over the past decade, mindfulness-based approaches have been examined with greater frequency. The mindfulness therapies, such as Acceptance and Commitment Therapy (ACT), differ somewhat in their approach from CBT. Rather than working to decrease distress through changing thinking, ACT uses strategies that focus on living a valued existence. ACT does not attempt to reduce distress; instead, ACT clinicians help individuals identify things that are valuable to them (what they want their lives to be about) and identify how to live in service of those values. This model identifies that distress is a normal part of human existence; however, through values-based living,

individuals may find that life is more meaningful. As a corollary, depression tends to remit. This is achieved not through trying to decrease depression, but rather through increasing value and meaning.⁴⁶

Interpersonal Psychotherapy (IPT), a time-limited evidence-supported treatment for depression, has a basis of support. IPT conceptualizes the problem as illness based (i.e., depression is an illness) as opposed to a personal defect or flaw. The goal of IPT is to support the patients and assist them in managing interpersonal situations through development of interpersonal skills.⁴⁷

Psychopharmacological Treatments for Depression

The use of psychopharmacological agents to treat depression is common. This approach conceptualizes depression as a chemical imbalance in the brain, which requires the introduction of medication. The use of pharmacological agents for depression has progressed over the decades.⁴⁸ This review will focus on the three most common antidepressant medication classes as well as nonprimary approaches such as electroconvulsive shock therapy (ECT).

Monoamine oxidase inhibitors (MAOIs) were the first well-studied class of medication targeted to treat depression. The list of MAOIs includes medications such as isocarboxazid, phenelzine, and tranylcypromine. This older class of medications for depression has been found to be effective in a number of studies.⁴⁹ MAOIs are purported to prevent the breakdown of monoamine in the brain. Monoamine is then associated with other mood-specified neurotransmitters such as serotonin, epinephrine, and norepinephrine. Despite this, MAOIs are associated with a risky side-effect profile, which has resulted in their reduced use. MAOIs are now considered a last-line treatment for depression.⁵⁰

Tricyclic antidepressants (TCAs) such as amitriptyline, imipramine, and paroxetine were initially discovered in the 1950s. TCAs are purported to impact the reuptake of the mood-specified neurotransmitters such as serotonin and norepinephrine. The result is increased concentrations of these neurotransmitters, which have been associated with improved mood and reduced depressive symptomatology. TCAs have large side-effect profiles, which have resulted in their reduced use.⁵¹

Currently, the selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) are considered frontline pharmacological strategies for the medical treatment of depression. SSRIs such as fluoxetine, sertraline, paroxetine, citalopram, and escitalopram act by preventing the reuptake of the mood-specified neurotransmitter serotonin. SNRIs such as duloxetine, venlafaxine, and desvenlafaxine act by preventing the reuptake of the neurotransmitters serotonin and norepinephrine. It is proposed that high concentrations of extracellular serotonin and norepinephrine are associated with improved mood and decreased depressive symptomatology.^{51,52} Generally,

SSRIs and SNRIs have lower side-effect profiles, although some increased risk of suicide has been noted especially among adolescents.⁵³

SSRIs and SNRIs are widely used; however, their effect may be variable and side-effect profiles (e.g., sexual side effects and weight gain) may reduce patient's ability to tolerate continued use. Further, their effectiveness may not be preferable to effective psychotherapies.^{54,55}

Recently, other classes of medications have been examined in the context of their antidepressant properties. Specifically, atypical antipsychotics (e.g., risperidone) as an adjunctive treatment to SSRIs have been examined in individuals with severe and unremitting unipolar depression. In several studies, the atypical antipsychotics were associated with marked improvement in depression symptoms and severity.⁵⁶

Although it is not a pharmacological agent, the use of ECT has been identified as a viable treatment for individuals with severe and unremitting depression, where other medication strategies have not been effective. A 2004 meta-analysis reported that ECT was favorable to other treatment strategies (SSRI, TCA, MAOI, etc.), especially for severe and unremitting depression.⁵⁷ Despite the apparent benefits of ECT, side-effect profiles (e.g., memory impairments, headache, nausea, and muscle aches) have been reported. Generally, these effects are reported as transient; however, long-term impairments have been reported.⁵⁸

A number of studies indicate that combining psychotherapy with antidepressant medications is associated with more favorable outcomes than psychotherapy or medication alone. This line of research suggests medication is beneficial to initially stabilize the patient, whereas evidence-based psychotherapies such as CBT provide a context and skill set to manage affect, reduce distress, and decrease depressive symptom architecture.⁵⁹

Outcome Measures

It is often difficult for a patient to objectively identify psychological health symptomatology. A goal of developing outcome measures is to accurately depict the presence, intensity, and severity of symptoms and the distress associated with a psychological health problem.⁶⁰ A common challenge to developing and using outcome measures is that they rely upon self-report. Self-report measures are subject to error associated with over- and underreporting of symptoms. Over- and underreporting may be impacted by certain factors such as desire to not appear impaired (underreporting) and secondary gain such as disability or heightened perception of impairment (overreporting). It is difficult to account for these factors, especially without collateral sources. Despite this, self-report measures remain a common approach to addressing outcomes.⁶¹

The Beck Depression Inventory Second Edition (BDI-II) is a commonly used measure to address the presence and

severity of depression. This measure, which relies on self-report data, is a 21-item, two-factor scale (affect and somatic scales). Each statement series on the BDI-II is scored on a 4-point (0–3) scale (e.g., 0 = I do not feel sad; 1 = I feel sad; 2 = I am sad all the time and I can't snap out of it; and 3 = I am so sad or unhappy that I can't stand it), with a range of 0–63. The BDI-II provides the following cutoff scores: 0–13 (minimal depression), 14–19 (mild depression), 20–28 (moderate depression), and 29–63 (severe depression). Other common depression screeners include the Hamilton Rating Scale for Depression and the Patient Health Questionnaire-9 (PHQ-9), which are frequently used in military settings.⁶² Additionally, the Outcomes Questionnaire 45 (OQ 45) and Outcomes Questionnaire 10 (OQ 10) are outcomes-based measures designed to alert medical professionals to psychological distress in their patients. These measures are brief (45 and 10 items, respectively) and easy to administer. The items are standardized; further, the OQ 45 contains risk assessment items for suicide, substance abuse, and potential for violence at work.

As noted above, self-report and nonactuarial clinical judgment may be error-laden. A number of attempts at detecting depression via biomarkers (homocysteine) have been developed, though findings are preliminary.⁶³ Although these approaches are intriguing, there is no accepted biomarker panel for depression. The use of self-report measures is likely to be commonly used for the foreseeable future irrespective of their limitations.

Confounds or Barriers to Treatment

Barriers to care have been a concern for the Defense Department. Hoge and colleagues addressed barriers to care in their 2004 seminal article examining large data sets of returned Soldiers. Perceived stigma was identified as a key barrier to receiving/seeking care in this military sample. The following questions regarding barriers to care were significantly endorsed by respondents: “leadership might treat me differently, I would be seen as weak and unit members would have less confidence in me.”¹

Thus, stigma likely represents a limitation to receiving care for psychological health problems such as depression. Presently, the military has a number of antistigma programs to address stigma (e.g., Real Warriors Campaign). These programs are designed to inform leadership, service members, and their families that the best thing they can do for their health and career is to seek help. Through policy such as changing mental health reporting requirements on security clearance forms and programs such as Real Warriors, the military has taken large steps to reduce stigma among those experiencing psychological health problems.

CONCLUSION

Military service members are at risk for experiencing numerous potentially co-occurring psychological health

problems following deployment(s). Depression is of significant concern to DoD and the military services. We have identified that depression represents a significant threat to the health and well-being of military personnel who return from Iraq and Afghanistan. Negative outcomes associated with depression are costly to the individual, family, community, and services. This article reviewed screening, diagnosis, and treatment models. Findings indicate that each component is required for successful outcomes. Moreover, screening, assessment, and diagnosis should be evidence supported. The literature indicates that preferable clinical outcomes are associated with screening and assessment procedures that are standardized followed by treatment modalities that are well studied and documented as effective in identified populations.

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Mild Traumatic Brain Injury Screening, Diagnosis, and Treatment

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ABSTRACT The majority of combat-related traumatic brain injury (TBI) within the U.S. Armed Forces is mild TBI (mTBI). This article focuses specifically on the screening, diagnosis, and treatment aspects of mTBI within the military community. Aggressive screening measures were instituted in 2006 to ensure that the mTBI population is identified and treated. Screenings occur in-theater, outside the contiguous United States, and in-garrison. We discuss specific screening procedures at each screening setting. Current diagnosis of mTBI is based upon self-report or through witnesses to the event. TBI severity is determined by specific Department of Defense criteria. Abundant clinician resources are available for mTBI in the military health care setting. Education resources for both the patient and the clinician are discussed in detail. An evidence-based clinical practice guideline for the care of mTBI was created through collaborative efforts of the DoD and the U.S. Department of Veterans Affairs. Although symptoms following mTBI generally resolve with time, active treatment is centered on symptom management, supervised rest, recovery, and patient education. Medical specialty care, ancillary services, and other therapeutic services may be required.

INTRODUCTION

Traumatic brain injury (TBI) is a widely recognized injury resulting from the current conflicts in Afghanistan and Iraq. TBI occurs when a trauma-induced external force results in temporary or permanent neurologic dysfunction. TBI severity ranges from mild to severe; TBI may be classified as a closed or penetrating injury. The majority of combat-related TBI within the U.S. Armed Forces fall in the mild TBI (mTBI) range, which is commonly known as concussion.¹ The overall Department of Defense (DoD) approach to TBI care follows a continuum of care. This continuum includes the prevention, surveillance, screening/assessment, diagnosis, case management, treatment, rehabilitation, and reintegration of service members who have suffered a TBI.² This article focuses specifically on the screening, diagnosis, and treatment aspects of mTBI within the military community.

SCREENING

Approximately 77% of TBI cases seen within the U.S. military population are classified as mTBI.¹ Aggressive screening measures were instituted in 2006 to ensure that the mTBI population is captured by military TBI surveillance.³ TBI screenings occur in-theater, at Landstuhl Regional Medical Center (LRMC) in Germany, at military treatment facilities (MTFs), at home duty stations after deployment, and within the Veterans Affairs (VA) system. From the year 2000 through November 15, 2011, there have been 233,425 medically diagnosed TBIs worldwide within the DoD, of which 178,961 were classified as mild.⁴ Reliance on service member self-report,^{5,6} and co-occurring conditions^{7,8} can make TBI screening very challenging. If a service member has been exposed to

an external force or mechanism of injury that could potentially cause TBI (i.e., blast exposure, vehicular crash and/or rollover, blunt trauma, fall, sports-related injury, gun-shot wound above the neck, or a combination of these entities), immediate screening is indicated.⁹

In-theater, event-based screening occurs as soon as safely possible following exposure to a traumatic event.¹⁰ This initial evaluation is commonly performed by combat medics/corpsmen on the front line or by forward operating bases. Severe injuries are usually easily recognized, requiring resuscitation and evacuation. Those without obvious injuries are then assessed for TBI. The Military Acute Concussion Evaluation (MACE) is widely used as a screening tool for mTBI (Table 1).¹¹

The cognitive evaluation portion of the MACE uses the Standardized Assessment of Concussion (SAC),³ which is well validated in sports concussion. The MACE has recently been updated in February, 2012 (Table I) with different versions of the SAC to avoid familiarization with repeated administrations. The MACE typically takes less than 10 minutes to administer. In addition to the history and brief neurologic exam (eye, motor, speech, and balance testing), it measures four cognitive domains including orientation, immediate memory, concentration, and delayed recall.¹² Appropriate administration of the MACE requires that the clinician avoid altering the word lists, digit spans, or order of the exam. According to the new version of the MACE, All three components of the MACE should be recorded in the medical record following the mnemonic CNS

- Cognitive results (Total out of 30)
- Neurologic exam results (Green = all normal exam, Red = any abnormal exam results)
- Symptom results (A = No symptoms, B = 1 or more symptoms)

The MACE is intended to be given during the initial assessment and as part of the cognitive evaluation during

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TABLE I. Major Changes in the 2012 Version of the MACE

- Instructions are now embedded with the questions
- The first two pages focus only on whether or not there was an injury event and AOC/LOC/PTA. Questions about symptoms and previous concussions have been moved to the end of the tool
- The second page clarifies when to stop the MACE
- Three more versions of the cognitive tests have been added
- A balance test has been added to the neurological evaluation
- The neurological evaluation provides better guidance
- The summary page provides more room to record cognitive test scores results
- The last page explains the proper interpretation of the cognitive score, evaluating concussion recovery, and ICD-9 coding tips

exertional testing.¹¹ If no loss of consciousness (LOC) or alteration of consciousness (AOC) is noted during the initial portion of the MACE, the MACE can be stopped, and clinicians should consider other causes for the service member's symptoms. The concussion management algorithm states that a cognitive score of <25 or the presence of symptoms requires consultation with a provider. It is important to remember that MACE scores do not diagnose a concussion.¹¹

Acute assessment of concussion is very important on the battlefield as it may lead to better outcomes and increased rates of return to duty (RTD).¹² Medics must determine which level of care is required next for the service member based on the Concussion Management Algorithms for the deployed setting (discussed in the "Treatment" section).¹⁰ The Concussion Management Algorithm for deployed settings (CMA) was recently updated in 2012 (Table II). A copy of the updated CMA can be requested online: <http://www.dvbic.org/material/concussion-management-algorithm-cma-pocket-cards>. Important updates to the CMA are included (Table II). All service members exposed to a blast or other mechanism of injury, including those who screened negative, are mandated to rest for 24 hours before returning to duty. The commander/commanding officer, however, has the right to waive the rest period if the service member is deemed vital to the mission.¹⁰

Mandatory events requiring concussion evaluation include:

- 1) Any service member in a vehicle with a blast event, collision or rollover
- 2) Any service member within 50 meters of a blast
- 3) Anyone who sustains a direct blow to the head
- 4) Command directed-such as, but not limited to, repeated exposures

If there are any red flags noted immediate provider consultation or emergent evacuation is indicated.

Since March 2006, all service members arriving at LRMC and all Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) (changed to Operation New Dawn [OND] October 2010) service members returning from theater receive a TBI screen regardless of the medical condition or injury that required medical evacuation. This ensures that the

TABLE II. Major Changes in the 2012 Version of the Concussion Management in Deployed Settings

- **Combat Medic/Corpsman Algorithm:**
 - Includes recommendations for initial management of concussion in consultation with a provider
 - Provides instruction to consult provider with exertional test results for return to duty determination
 - Clarifies directives and emphasizes assessment, identification of red flags, consultation with a provider, and distribution of educational brochures to patients
- **Initial Provider Algorithm:**
 - Includes concussion history with added guidance for first, second and third concussion in 12 months
 - Clarifies guidance on neuroimaging/CT and consultation
- **Comprehensive Concussion Algorithm:**
 - Advises to consider NCAT and functional assessment
- **Recurrent concussion Algorithm:**
 - Advises to consider NCAT and functional assessment
 - Includes the Balance Error Scoring System (BESS) to guide the balance assessment
- **Other:**
 - The list of information sheets now includes: Acute Stress Reaction Fact Sheet, Acute Concussion Educational Brochure, Neurobehavioral Symptom Inventory, Line Leader Fact Sheet, Coding Guidance, and DCoE NeuroCognitive Assessment Tool (NCAT) recommendations
 - Exertional testing clarified
 - ICD-9 coding tips added

majority of service members get an assessment before returning to their home duty station. LRMC uses a standard patient questionnaire which inquires about any blast exposures, motor vehicle accidents, falls, or direct blows to the head that may have resulted in loss of consciousness (LOC) or AOC.¹³ From May 2006 to October 2008, nearly 18,000 patients completed this initial screening questionnaire at LRMC.¹³ Of these patients, 16% of outpatients and 31% of inpatients screened positively for being at risk for TBI.¹³ If the service member cannot be screened because of medical issues such as intubation and/or heavy sedation, a notation is made in the medical record to re-evaluate for TBI at a later time. The mTBI screen includes the date of injury, service member's recollection of the injury, distance of the blast, position in the vehicle (if applicable), use of protective gear, symptoms at the time of injury, specific injuries to the head/face/neck, and whether there was an on-scene evaluation.¹³ The screener also asks about current symptoms and any previous concussion/head injury history. If it is determined that there was a change in consciousness and it is clinically appropriate (e.g., the service member is not heavily medicated, in pain, or psychiatrically impaired), the MACE is then administered to determine cognitive status.¹¹ Obtaining the history, MACE, initial Glasgow Coma Scale (GCS) score, and reviewing of the computed tomography (CT) scan or magnetic resonance imaging (MRI) scan (if performed),

allows for accurate determination of whether a service member has sustained a concussion. If deemed negative, this is documented and the service member does not need further testing; this service member may potentially RTD if no other medical conditions are present. However, if it is determined that the service member sustained a mTBI, the screening team makes recommendations for disposition. This disposition may be a home duty station or a designated TBI center based upon anticipated treatment needs of the service member.

If the service member's prognosis is presumed critical from other injuries and/or unlikely to report to duty or managed at the LRMC outpatient clinic, he/she is medically evacuated to a major MTF for ongoing care, such as Walter Reed National Military Medical Center (WRNMMC) in Bethesda, Maryland, or San Antonio Military Medical Center (SAMMC) in Texas. Both treat service members from deployments with mTBI and have the added capability of managing severe comorbidities and injuries that may co-occur with mTBI.

At the treatment facility, a screener reassesses all inpatients and outpatients based on their mechanism of injury. For example, if a service member screened positive for a mTBI at LRMC, but was medically evacuated for an unrelated condition, a mTBI consult note including a treatment plan is still completed and recorded in the electronic medical record. Obtaining a good interview is critical, and it is essential that LOC, AOC, post-traumatic amnesia (PTA), imaging findings, and initial and current symptoms are clearly noted. The screening process can be further complicated by ongoing treatment for other injuries such as frequent surgeries for wound cleaning and orthopedic surgeries, necessary sedation, pain, and fatigue. When able, service members fill out symptom questionnaires on concussion-related symptoms and acute stress symptoms.

A service member's current state of health is evaluated soon after returning from the theater (no later than 30 days), using the Post Deployment Health Assessment (PDHA)¹⁴ at the unit during out-processing. The PDHA is an electronic questionnaire mandated by the Assistant Secretary of Defense for Health Affairs that assesses the service member and assists military health providers in identifying and providing present and future medical care.¹⁴ Questions on the PDHA include whether the service member (1) has experienced any mechanism of injury that may have caused a head injury, (2) was diagnosed with a concussion/head injury in theater, (3) is experiencing symptoms, and (4) circumstances following the event (see "Diagnosis" section for specifics).¹⁴ If the service member answers "yes" to any of the questions, a referral is made to a provider for further evaluation. A recent study showed that out of these four questions, questions 1 and 2 above demonstrated a higher correlation to clinician-diagnosed TBI.¹⁵

Another screening tool used within the Defense Department is the Warrior Administered Retrospective Casualty Assessment tool (WARCAT). This was developed at Evans Army Community Hospital, Fort Carson, Colorado, in June 2005. It has subsequently been adopted by some of the other stateside concussion clinics. This tool is used in addition to the

PDHA and PDHRA to capture more detailed information about possible injuries and symptoms. In comparison, the WARCAT is more detailed about type of improvised explosive device blast, direction and approximate distance from blast, specific vehicle type and position, helmet information, and initial treatment on the scene. It also inquires about prior history of concussions, whereas the PDHA and PDHRA inquire only about the recent deployment. The WARCAT is a standardized form that the service member fills out for the provider to review. It can be found at: <http://evans.amedd.army.mil/srp/>.

In April 2007, the VA health care system implemented a mandatory computer-based screening tool to identify OEF/OIF veterans who sustained a mTBI.¹⁶ This screen is completed whenever a veteran presents at the VA for any clinical appointment including but not limited to primary care, mental health, or dental appointments.¹⁶ It is not indicated if the veteran has a separation date before September 11, 2001 or did not serve in OEF/OIF or current conflicts. The screen is not necessary if a prior diagnosis of concussion was made. The screen consists of questions very similar to other screening tools. These questions are:

- Whether the veteran experienced any exposures to blast/explosion, vehicular accident, fragment, bullet wound, or fall
- Which symptoms were immediately noticed neurologically and physically
- Symptoms that may have begun or gotten worse after the event
- Current symptoms

When a veteran answers "yes" to one or more questions in each of the four sections, then the VA considers the veteran to have screened positive for a possible mild TBI and this veteran should be offered a follow-up evaluation with a specialty provider who can determine whether the veteran has a mild TBI.

DIAGNOSIS

TBI severity is determined by specific criteria: initial GCS score (if available), AOC, LOC, PTA, and structural imaging (Table III).⁹ The initial GCS score with mTBI is normally between 13 and 15. Theater conditions are often challenging as the attending combat medic/corpsman may be treating several casualties under grueling conditions while under fire and assessing for life or death injuries. The GCS can also be obscured by other factors such as medications or hypovolemic shock. AOC must be immediately related to the head trauma.⁹ Typical symptoms are looking and feeling dazed and uncertain of what is happening, confusion, difficulty thinking clearly or responding appropriately to mental status questions, and being unable to describe events immediately before or after the event.⁹ An AOC of less than 24 hours is considered a mTBI according to the Defense Department severity rating.¹⁷

PTA is any loss of memory for events immediately before or after the injury.⁹ With a mTBI, this period can extend up to

TABLE III. Severity Ratings for TBI

Criteria	Mild	Moderate	Severe
Structural Imaging	Normal	Normal or Abnormal	Normal or Abnormal
LOC	0–30 minutes	>30 minutes and <24 hours	>24 hours
AOC/Mental State	≤24 hours	>24 hours	>24 hours
PTA	≤24 hours	>24 hours and <7 days	>7 days
GCS ^a	Score: 13–15	Score: 9–12	Score: 3–8

^aGCS is not part of the official DoD definition for TBI but is commonly used in practice.

24 hours.⁹ Abnormal structural imaging attributed to the injury will result in the individual being considered clinically to have greater than mild injury.⁹

Symptoms especially the cluster of headaches, dizziness, nausea, and vomiting are common after an acute concussion^{18,19}. However, it is important to note that these symptoms alone do not constitute a diagnosis of mTBI. Further work is needed to identify clinically useful self-report measures that assess mTBI and post-traumatic stress disorder (PTSD) and associated symptoms among OEF/OIF Veterans.^{5,20}

Abnormal physical findings on exam, whether noted on the brief neurological exam (completed by the attending combat medic/corpsman), or the more comprehensive evaluations (Level II–Level V facilities and the VA) are critical signs of potentially serious health conditions. The neurologic exam should include assessment of eyes (pupillary reflex, extraocular movements), speech (fluency and word finding), motor (grip strength and pronator drift), balance (tandem Rhomberg test), and a cognition (concentration, delayed recall). CPGs exist to guide the primary care management of symptoms after the diagnosis is confirmed and are reviewed in the “Treatment” section below.⁹ Those with neurologic deficits should be considered for management at a location where imaging is available.

A service member who has prolonged symptoms without signs of improvements should be screened for concomitant psychological distress, which is most commonly an acute stress reaction or PTSD. If positive, the service member is referred to behavioral health for further evaluation.⁹

Conventional head CT and MRI scans are normal for the majority of mTBI patients^{21,22}. Furthermore, these tools are not sensitive to detecting diffuse axonal injuries (DAI) in mTBI.²² The MRI technique of diffusion tensor imaging (DTI) can detect microscopic white matter tract lesions in the brain.²³ DTI has provided a tool for detecting DAI and other microstructural changes in white matter^{24,25} associated with mTBI injury severity.²⁶ The DoD is currently interested in using DTI as a biomarker and has assisted in the research on this modality. Other research studies proposed for TBI diagnosis are serum biomarkers,²⁷ other advanced neuroimaging studies (including spectroscopy and positron emission tomography scans),^{28,29} brain acoustic monitoring,³⁰ state-of-the-art developments in research with blast waves,³¹ and cumulative concussions.³²

TREATMENT

There are abundant resources for clinicians caring for mTBI in the military health care setting. Because these resources must

undergo revisions as new information becomes available, it is best for the provider to access the most up-to-date resources online. Resources and references for mTBI treatment in the military are discussed in the following sections.

In general, treatment of mTBI is centered on symptom management, supervised rest, and recovery. Symptoms usually fall into three categories: somatic (e.g., headache, dizziness, weakness, sensitivity to light and sound), cognitive (e.g., difficulties with attention, memory, and language), and psychological/behavioral³³ (e.g., irritability, depression, anxiety, personality changes). All of these symptom areas need to be addressed. Often, there is an overlap of symptoms of concussion and psychological/psychiatric disorders that need to be treated concurrently.^{7,34–37} Physical injuries sustained in addition to the mTBI must also be taken into consideration.^{36,38} Clinicians are being encouraged to treat nonspecific symptoms regardless of etiology.^{39,40} Sleep disorders are also common.⁴¹ In addition to medical specialty care, ancillary services, neuropsychological testing,⁴² and other therapeutic services may be required.⁴¹

In addition to symptom management, patient education regarding expected outcomes can play an important role in mTBI treatment.⁴³ Education should emphasize rest and recovery, gradual supervised resumption of work and social responsibilities, compensatory strategies, and modification of the environment.⁹ Additionally, the service member should be educated about prevention of further injuries.⁹ It is important that the service member understands what their diagnosis is and what the expected course of recovery will be. Approximately 85% to 90% of patients who have sustained a combat mTBI improve with no lasting clinical difficulties.^{9,41} Service members should be reassured and encouraged that their condition is transient and that full recovery is expected. Typically, recovery is seen within hours to days, with a small portion taking longer.^{9,41} In a small minority, symptoms may persist⁴⁴ beyond 6 months to a year.⁹ In the civilian sector, it has been shown that educating individuals regarding this positive expectation for recovery is associated with positive outcomes.⁴⁵

Many free educational resources are offered online. The Defense and Veterans Brain Injury Center (DVBIC) website, dvbic.org,⁴⁶ offers resources about mTBI and include symptom management for memory, sleep, mood changes, and headache difficulties. The Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE),⁴⁷

traumaticbraininjuryatoz.org, brainlinemilitary.org, and afterdeployment.org also offer many resources available to service members and providers. Some education materials are meant to be provided in combination with verbal review of the information with their health care provider.⁹

As stated earlier, most service members with recent onset of symptoms following a single mTBI can be successfully managed in the primary care setting. For the majority, referral to specialty care for mTBI is not required.⁹ However, because many service members sustain an mTBI in the context of combat, their care can be complex and multifaceted, requiring consultation with rehabilitation therapists, neurologists, pharmacists, mental health, and social support.^{9,41,48,49}

Service members who are in-garrison and have suffered an mTBI can be cared for using the VA/DoD CPGs.⁹ In April 2009, an evidence-based CPG was created through the collaborative efforts of the Defense Department and VA to establish guidelines for treating service members with ongoing symptoms following mTBI injury. The intent of these in-garrison guidelines is for the service member to receive care from their primary care provider at their home duty station. The following are the three algorithms contained in this CPG: (1) initial presentation, (2) management of symptoms, and (3) follow-up of persistent symptoms. The most up-to-date version of the VA/DoD CPG guidelines with algorithms can be found online at www.dcoe.health.mil.⁹

Algorithm A of the CPG describes next steps that a provider should follow once a service member has been diagnosed with an mTBI. If he or she has no concussion-related symptoms at the time of diagnosis, then mTBI education is to be provided. The service member should also be screened for stress, substance use, and mental health conditions. If the service member is symptomatic, algorithms B, C, or in-theater guidelines can be used depending on the situation.⁹

Algorithm B of the CPG outlines management of symptoms of mTBI in steps (Table IV). Steps are explained in further detail in the full version of the CPG.⁹

Algorithm C is used when a concussed service member continues to have persistent symptoms beyond 4 to 6 weeks

TABLE IV. Steps Outlined in Algorithm B of the CPG for Management of Symptoms

<ol style="list-style-type: none"> (1) History and physical exam (labs, MSE, psychosocial evaluation) (2) Clarify symptoms and build therapeutic alliance (3) Evaluate and treat co-occurring disorders (4) Determine treatment plan (5) Educate patient and family on symptoms and expected recovery (6) Provide early (nonpharmacologic) interventions (7) Sleep hygiene, relaxation techniques, limit caffeine/tobacco/alcohol, graded exercise, monitored progressive RTD/work/activity (8) Initiate symptom-based treatment (consider case management) (9) Follow-up and reassess in 4–6 weeks (10) If symptoms are unresolved, proceed to Algorithm C: follow-up of persistent symptoms (11) If symptoms are resolved, follow-up with patient as needed and address: RTD, community participation, and family/social issues
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and is not responding to initial treatment. Reassessment of symptoms and functional status is recommended as well as a complete psychosocial evaluation.⁹ If symptoms such as mood, behavior, or sleep difficulties have not improved, the service member is assessed for possible alternative causes for the persisting symptoms. It has been found that a service member may not demonstrate psychological impairment in the immediate time frame following a concussion and may arise as a result of returning home and readjusting from a combat deployment.^{20,50} Alternative causes should be treated according to VA/DoD guidelines, and the service member should be considered for a referral to mental health for evaluation and treatment. If persisting symptoms are physical, cognitive, or emotional, they may also need a specialty referral for services.⁹ Available interventions for mTBI patients throughout the services can be found in Table V.⁴¹

A useful tool for any clinician caring for a service member with mTBI is the Mild Traumatic Brain Injury Pocket Guide created by the Defense Department, DCoE and DVbic (Fig. 1). This pocket guide includes management guides for common mTBI symptoms such as headache, dizziness, fatigue, vision difficulties, irritability, and appetite changes. It also provides guidance for physical examination, medication management, and referrals. A mobile application of this guide is available to the provider at <http://t2health.org/apps/mtbi>. Table VI describes the information contained in this pocket guide.

The Co-occurring Conditions Toolkit: mTBI and Psychological Health, is another tool that can be accessed online from the DCoE website. This toolkit has additional management guides for sleep, mood, attention, and chronic pain. A companion video is available, which is designed to show the provider how to use the toolkit. A copy of both of these pocket guides can be found online (www.dcoe.health.mil/ForHealthPros/TBIInformation.aspx)⁵¹ or obtained by contacting info@dvbic.org or calling 1800-870-9244.

In addition to the CPG, another resource to consider is the Clinical Guidance for Evaluation and Management of Concussion/mTBI management for both acute and subacute nondeployed care. This guide was updated in May 2008. It was created by an interdisciplinary work group through the DVbic. The work group included both U.S. military services

TABLE V. Core TBI Therapies and Interventions Available Throughout the Services¹²

<ul style="list-style-type: none"> Medication Management Vestibular Rehabilitation Vision Therapy Cognitive Rehabilitation Driving Rehabilitation Balance Training Life skills Training Assistive Technology Tinnitus Management Complementary and Alternative Medicine Interventions

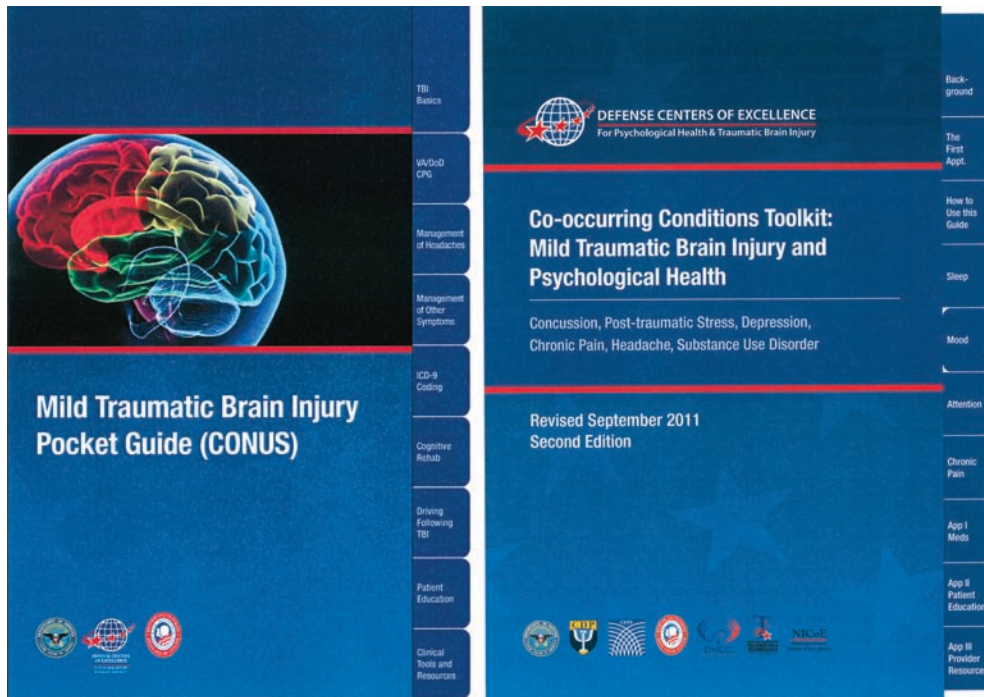


FIGURE 1. Pocket guides that are available to help clinicians caring for mTBI service members.

and civilian representation. The group provided expert guidance regarding appropriate management of symptomatic concussed service members in a military setting. The full report with algorithms for the clinician can be found online (www.dcoe.health.mil).⁵¹

Regarding concussion management in the Deployed setting, the Concussion Management in the Deployed Settings

pocket guide was updated in 2012 (Table II) and offers three algorithms which include:

- 1) Combat Medic/Corpsman Algorithm
- 2) Initial Provider Algorithm
- 3) Comprehensive Concussion Algorithm

This pocket guide can be obtained by submitting a request online at: <http://www.dvbic.org/material/concussion-management-algorithm-cma-pocket-cards>.

Telemedicine services are currently being used for mTBI identification, management of symptoms in theater, and improving the overall care of TBI throughout the Defense Department and VA. TBI.consult@us.army.mil is an electronic consultation service specifically for deployed military health care providers. It is monitored 7 days a week, staffed by TBI medical specialists, and offers a response within hours. This service provides consultation on a variety of TBI-related questions including how to screen for a TBI, RTD decisions, strategies for symptom management, and TBI and psychological health overlap questions. The tele-TBI clinic⁵² uses neurologists, neuropsychologists, pain management specialists, and rehabilitation therapists via video teleconferencing to assist service members in more remote sites.⁵²

Duty restrictions after mTBI vary among the services. RTD status should be based upon the service members symptoms and allow for progressive return to full duty.⁹ The service member may need to restrict some work and other activities to allow for healing and to decrease risk of further injury. When a service member has recovered from symptoms that

TABLE VI. Information Contained in the mTBI Pocket Guide (CONUS)

TBI Basics
A Summary of the CPG
A Management Guide to mTBI
A Management Guide to Headaches
A Management Guide to Other Symptoms: dizziness, fatigue, vision, irritability, appetite changes
DoD ICD-9 Coding Guidance
Cognitive Rehabilitation for mTBI Consensus Conference Clinical Recommendations
Patient Education
Clinical Tools and Resources
Dizziness Handicap Inventory
Epworth Sleepiness Scale
GCS
Multidimensional Assessment of Fatigue
Neurobehavioral Symptom Inventory
Patient Health Questionnaire
PTSD Checklist (PCL-M)
Other Tools
Additional Resources

were previously functionally limiting, exertion testing should be performed.⁹ This includes a brief period of aerobic activity followed by re-evaluation for both physical symptoms and cognitive function. Before full duty status, the service member should be able to

- Pass a physical fitness test
- Pass “warrior training” if needed for duty
- Have psychological health issues controlled and monitored by a primary care clinician
- Have neuropsychological testing that is within functional limits if cognitive impairment was noted after injury.⁹

In 2008, the National Defense Authorization Act HR 4986 was signed into law, which led to the Defense Department to establish a Neurocognitive Assessment Tool (NCAT) program.⁵³ The program establishes and monitors a pre-deployment neurocognitive battery of tests to assess and document cognitive functioning of service members before deployment. The Automated Neurocognitive Assessment Metrics (ANAM) was the tool chosen by a Defense Department expert consensus panel as an interim program pending further evaluation of other NCATs. The Army Neurocognitive Assessment Branch office has distributed to OEF and OND numerous laptops loaded with ANAM capability for postinjury assessments by theater providers. Following injury, the ANAM can be repeated and compared to the individuals own baseline when considering cognitive function and RTD.^{53,54} It is important to note that the ANAM is not intended to be a diagnostic tool for TBI (as many other conditions may cause decreased cognitive function), but is meant to assist providers in making medical and report-to-duty decisions. Capabilities are developing for web-based access to predeployment ANAM scores, but currently providers in need of an individual’s baseline ANAM to compare with a postinjury assessments should submit the request with demographic information to anam.baselines@amedd.army.mil.

There are numerous opportunities available for more in-depth training regarding mTBI. Some of the learning opportunities available include:

- DVBIC’s Annual Defense and Veterans Military TBI Summit
 - Annual training conference held annually since 2007 in Washington, DC area
- Annual Blast Conference
 - Held annually since 2004 hosted by DVBIC and the James A. Haley Veterans’ Hospital
- TBI modules via Military Health System Learning Portal
 - Defense Department personnel may access online training courses
- Staff lecture series (WRNMMC)

TABLE VII. Resources for TBI Information

Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE); http://www.dcoe.health.mil DVBIC; http://www.dvbic.org Deployment Health Clinical Center (DHCC); http://pdhealth.mil/TBI.asp The Center of Excellence of Medical Multimedia; http://www.traumaticbraininjuryatoz.org Brain Injury Association of America; http://www.biausa.org Brainline (WETA); http://www.brainlinemilitary.org
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- First Thursday of every month 2 to 3 p.m. (EST)
- Available through tele/video conference
- TBI Grand Rounds
 - Second Tuesday of each month
 - Access via tele/video conference from participating sites

Table VII lists other TBI information resources in addition to those included in this article.

CONCLUSIONS

Since 2006, many initiatives have been implemented to improve care for service members with TBI, specifically mTBI. Surveillance efforts aimed at identifying the incidence and prevalence of combat-related TBI have improved the availability of TBI-specific resources both in-theater and in-garrison. This is largely attributable to enhanced screening methods, which occur at various locations throughout the deployment cycle. Mandated CPGs standardize care and provide both evaluation and treatment recommendations to those on the battlefield as well as stateside. Opportunities for TBI education have expanded, now including regional/national conferences, online case studies, training modules and instruction at some deployment platforms. The evolution of telehealth capabilities allows providers the ability to treat injured service members in-theater, which may minimize the need for evacuation from theater or transfer to major MTF. Finally, ongoing research seeks to identify ways to mitigate blast exposure and effects, determine similarities/differences between blunt and blast TBI, and establish treatment paradigms to enhance TBI care.

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Diagnosis and Management of Moderate and Severe Traumatic Brain Injury Sustained in Combat

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ABSTRACT Traumatic brain injury exists in a spectrum of severity among wounded personnel. The evaluation and clinical presentation, initial management, and treatment interventions to prevent secondary injury processes for combat-associated moderate and severe traumatic brain injury are reviewed. Promising therapies are discussed, and a current review of the literature is provided.

INTRODUCTION

Traumatic brain injury (TBI) is principally classified by either mechanism (closed vs. penetrating) or clinical severity. Severity classification ranges from mild, moderate, to severe and is based largely on the presenting Glasgow Coma Scale (GCS) score postinitial resuscitation and the duration of typical post-TBI neurologic findings (Tables I and II). Patients with mild TBI have an admission GCS score of 13 to 15. A further discussion of the management of mild TBI is included elsewhere in this supplement. Moderate TBI is defined as an admission GCS score of 9 to 12, and is often associated with prolonged loss of consciousness, abnormal neuroimaging, and neurological deficits.¹ Patients with moderate TBI will require rapid removal from the area of operations, subsequent theater hospitalization, and may need neurosurgical evaluation or intervention. Patients with GCS scores of 8 or less have significant neurological injury and are classified as having a severe TBI. Typically, these patients have abnormal neuroimaging to include computed tomography (CT) scan findings, such as a skull fracture, traumatic intracranial hemorrhage, or contusional injury.² These patients require rapid evacuation from the point of injury to the combat support hospital (CSH) and admission to the intensive care unit for immediate airway control, mechanical ventilation, neurosurgical evaluation, and consideration for intracranial pressure (ICP) monitoring.

The U.S. Army and the Institute of Surgical Research publishes clinical practice guidelines for the management

of severe head injury as part of the Joint Theater Trauma System, which is updated annually.³ This is available for public distribution at usaisr.amedd.army.mil/clinical_practice_guidelines.html. Guidelines for the management of severe TBI published by the Brain Trauma Foundation have been instrumental in improving care through guiding therapy with evidence-based recommendations.⁴ Guidelines are also available for the prehospital management of severe TBI, field management of combat-related head trauma, and surgical management of TBI. All guidelines can be obtained online from the Brain Trauma Foundation at braintrauma.org. The latest version of the Guidelines for the Management of Severe Traumatic Brain Injury will be published in an updated online version. An interactive guideline compliance tool is available at tbiclickandlearn.com.

Goals in the theater management of a patient who sustains a moderate or severe TBI include the arrest of any ongoing injury, preservation of neurological function, prevention of medical complications of critical illness, and improvement in overall outcome. The presence of a brain injury must be suspected in any case of severe trauma, especially with a blast-related mechanism of injury. TBI patients should be recognized early and evacuated to the CSH or trauma center with available specialized neurological care, such as neurosurgery and neurointensivist care. Once evacuated and clinically stable, TBI patients are transitioned to a posture of in-hospital rehabilitation with physical therapy, occupational therapy, and speech–cognitive therapy.

CLINICAL EVALUATION

The clinical examination of a patient with a suspected TBI is critically important. The examination has both prognostic and management implications, particularly in the early treatment of TBI.⁴ Treatment begins in the field or combat setting with the first responder and continues to the CSH. Decisions made in the hyperacute period after brain injury are essential for optimal outcome. The Guidelines for Field Management of Combat-Related Head Trauma and Advanced Trauma Life Support are both excellent resources for providers who treat TBI.⁵ The Brain Trauma Foundation also publishes guidelines, including the surgical

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The opinions and views expressed herein belong solely to those of the authors. They are not nor should they be implied as being endorsed by the Uniformed Services University of the Health Sciences, Department of the Army, Department of Defense or any other branch of the Federal Government of the United States.

TABLE I. Glasgow Coma Scale¹²

Eye		Motor		Verbal	
Eyes Open Spontaneously	4	Follows Commands	6	Oriented, Alert	5
		Localizes	5		
		Withdraws	4	Confused, Appropriate	4
Eyes Open to Voice	3	Flexion	3	Disoriented, Inappropriate	3
Eyes Open to Pain	2	Extension	2	Incomprehensible Speech	2
No Response	1	No Response	1	No Response	1

management of TBI and prehospital management of TBI (both are available at braintrauma.org).

In keeping with the care of all trauma patients, stabilization of circulation, airway, and breathing is followed by a rapid initial neurological evaluation and determination of the GCS score^{1,6} (Table I). The GCS score is important for triage and is a quantifiable measure of impairment, which can help decide early management sequences. A more detailed neurological assessment also helps prognosticate outcome of moderate and severe TBI and is important to document in the trauma record before paralysis or sedation if possible.^{7,8}

Initial Emergency Department and Field Management

First responders must recognize the importance of circulation, airway, and breathing to optimize cerebral oxygenation and perfusion. It is well established that the duration and severity of hypoxia and hypotension in this critical early period has dramatic consequences on ultimate clinical outcome.^{4,8} Published guidelines support goals of oxygen saturation greater than 90% and avoiding hypotension of systolic blood pressure (SBP) <90 mmHg. Airway protection and ventilator support are needed in many moderate and in most severe TBI patients. Attention is directed to maintaining normoxemia to mild hyperoxemia as recent work has shown extreme hyperoxemia to be associated with an increased risk of mortality in severe TBI.⁹ Support of circulation starts with hemorrhage control and is followed by fluid resuscitation with blood products or crystalloids.

The head should be kept in midline position and elevated to 30°. This is to allow optimal venous drainage which, if compromised, can exacerbate intracranial hypertension. It is wise to assume an occult cervical spine injury in any TBI patient with altered mental status or blunt injury above the clavicle until ruled out by radiographic imaging.¹ Spinal inju-

ries concomitant with TBI are not uncommon, as a recent retrospective review of head injury casualties from the conflicts in Iraq and Afghanistan included a 16% incidence of spinal column trauma of various types.¹⁰

Secondary Survey and Neuroimaging

The secondary survey in Advanced Trauma Life Support guidance includes a more detailed but rapid neurologic or disability examination. The presence of a TBI is made based on clinical grounds, with neuroimaging offering hypothesis testing for clinical suspicion of a brain injury. Altered mental status or obtundation may be a result of other causes, including oxygenation or ventilatory insufficiency, glycemic derangement, medication/toxin exposure or hypoperfusion, sometimes concomitant with obvious or occult head injury.¹

Neuroimaging is clearly integral to the complete evaluation of patients with moderate and severe TBI. CT imaging of the brain will generally provide sufficient information to initiate appropriate initial clinical management. CT imaging is based on the attenuation of X-rays by tissue density and, subsequently, is most effective in identifying acute blood products. Given the high frequency of hemorrhage after traumatic injury and the rapid acquisition time of CT scanning, it is considered the first-line imaging technique for TBI patients. Hemorrhage appears hyperdense or bright on CT and can be detected extra-axially (epidural hematoma, subdural hematoma, subarachnoid hemorrhage) or intra-axially (hemorrhagic contusions, intracerebral hemorrhage, petechial hemorrhage from traumatic axonal injury). CT can also detect bland contusions, which are common after closed head injury, and help identify embedded fragments resulting from penetrating injuries. Figures 1–5 demonstrate some typical CT findings in patients with combat-related TBI. Magnetic resonance imaging (MRI) can be helpful during the evaluation of TBI, but generally in the subacute or chronic phases of

TABLE II. TBI Severity

Severity	GCS	LOC	AOC	PTA
Mild	13–15	<30 minutes	<24 hours	<24 hours
Moderate	9–13	>30 minutes <24 hours	>24 hours	>24 hours <7 days
Severe	3–8	>24 hours	>24 hours	>7 days

LOC, loss of consciousness; AOC, alteration of consciousness; PTA, post-traumatic amnesia.

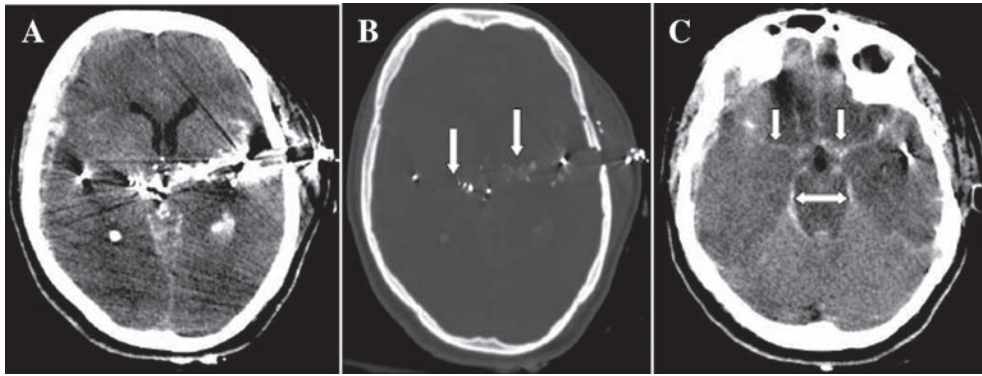


FIGURE 1. Traumatic subarachnoid hemorrhage (tSAH). (a) Penetrating supratentorial injury to the left temporal and parietal lobes with subsequent bihemispheric injury. (b) Axial bone windows of same image, which help delineate projectile (arrows) from primary intracerebral hemorrhage. (c) Subarachnoid blood layering in the basal cisterns (arrows). This mechanism of tSAH would result in a high risk of subsequent vasospasm and delayed cerebral ischemia. This patient did not survive.

injury. MRI should not be used in the imaging of unstable patients or acute penetrating TBI (pTBI) from metallic projectiles secondary to potential displacement of retained foreign bodies by the MRI magnetic field. MRI is clearly more sensitive to the detection of traumatic axonal injury and provides better ability to quantify chronic sequelae of TBI.¹¹ Currently, MRI capabilities exist at multiple sites in the Afghanistan theater (A. Larsen, personal communication). If a vascular injury is suspected, then cerebral angiography is indicated as the incidence of vasospasm in the setting of blast-related pTBI has been reported as high as 50%.¹² Thus, it is recommended that patients with acute pTBI from explosives undergo surveillance assessment via transcranial Doppler and CT angiography or catheter angiography for definitive diagnosis and endovascular-based treatments.¹²

CLINICAL SYNDROMES

The clinical presentation of moderate–severe TBI can be as heterogeneous as the underlying tissue injuries seen. Patients

with pTBI often have focal deficits referable to the location of the projectile’s path, whereas closed TBI patients can have both focal and diffuse deficits. The biomechanics of closed injuries (acceleration–deceleration and rotational forces) place the fibers of the ascending reticular activating system and thalamic projections at particular risk. Damage to these structures is what typically results in disorders of consciousness such as coma. Classically, epidural hematomas, often seen in association with skull fractures, result in the classic “talk-then-die” phenomenon in which a patient has a precipitous decline after build up of arterial blood compressing the brain focally. Traumatic intracerebral hematomas can present with focal neurologic deficits such as unilateral motor or sensory findings.

Patients with brain injury who develop intracranial hypertension may progress to a cerebral herniation event. The clinical manifestations of increased intracranial pressure (ICP) are important to recognize while managing these

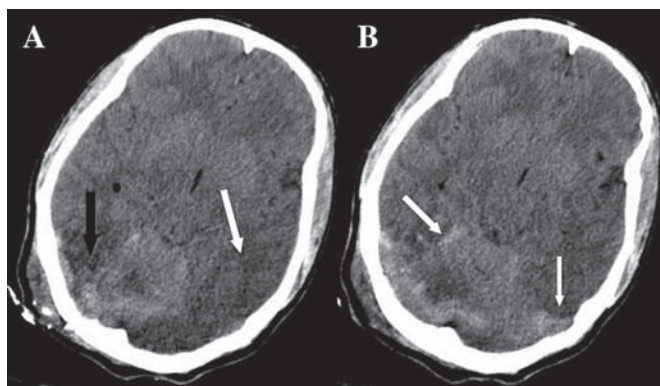


FIGURE 2. Nonpenetrating blast TBI. (a) Cytotoxic edema in the occipital lobes (white arrow) and hemorrhagic occipital contusion (black arrow). (b) In this, more caudal image note the subdural layering of hemorrhage over the tentorium (white arrows).

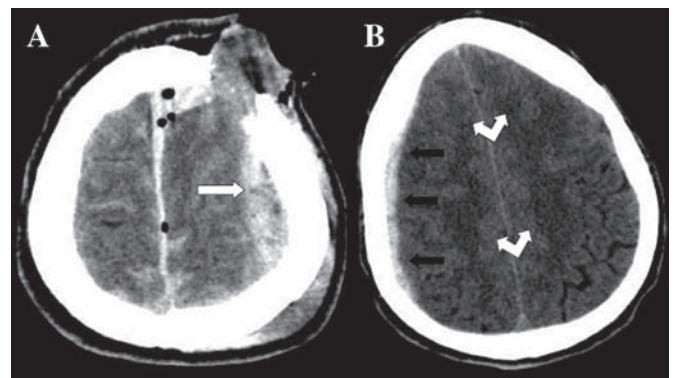


FIGURE 3. Traumatic subdural hematoma. (a) This patient suffered a low velocity penetrating head injury with resultant subdural hematoma (arrow) near the vertex and traumatic craniectomy. (b) This patient suffered an acute right subdural hematoma (black arrows) after a blast exposure. There is resultant cerebral edema and loss of sulcation over the bifrontal regions (white arrows).

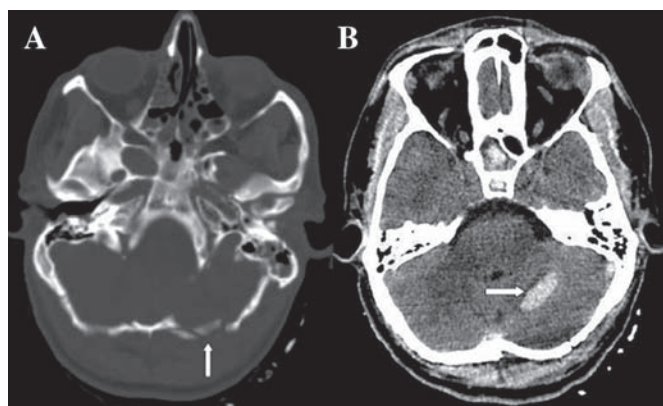


FIGURE 4. Traumatic intracerebral hematoma. (a) This patient suffered a nonpenetrating blast injury resulting in multiple suboccipital skull fractures (arrow). (b) The blast injury resulted small left hemisphere cerebellar hematoma (arrow) with focal edema and mild effacement of the fourth ventricle. The patient was able to be managed nonoperatively with serial computed tomography scans showing no progression of the fourth ventricle effacement or hydrocephalus.

patients. When compensatory mechanisms are exceeded, a herniation may occur, which will manifest in a variety of neurologic syndromes. Although specific clinical presentations and focal findings may occur, many patients simply begin to become more lethargic and may drop points in their GCS score. Herniation syndromes, which should be recognizable at the bedside, include the transtentorial or uncal herniation syndrome where the medial portion of the tempo-

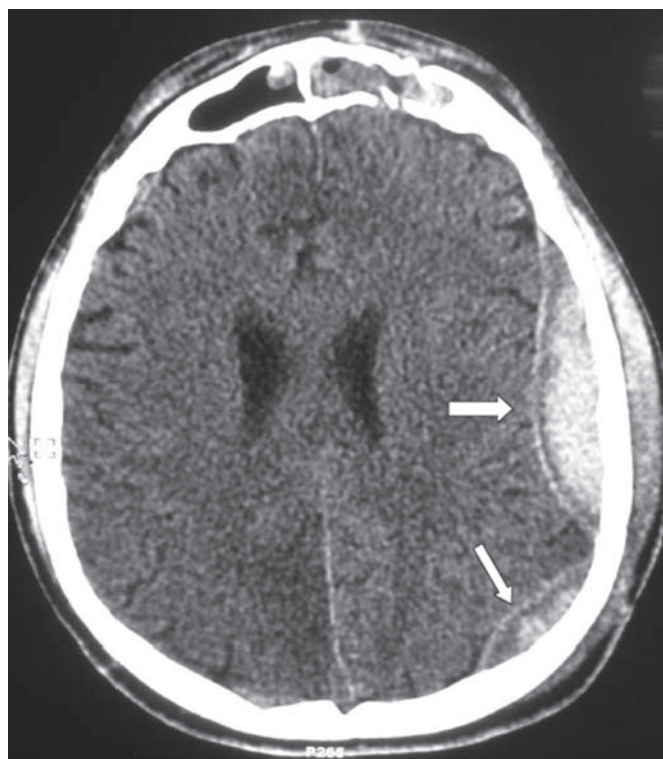


FIGURE 5. Epidural hematoma.

ral lobe compresses the lateral midbrain and third nerve. Because of the anatomic organization of this nerve, parasympathetic fibers are compressed initially, which results in unilateral pupillary dilation. Additionally, patients can develop weakness/paralysis affecting the body ipsilateral to the herniation. With more diffuse edema, central herniation can occur where the dorsal midbrain is compressed, resulting in forced downward gaze or other alterations of vertical gaze control. As elevations in ICP progress or with posterior fossa lesions, cerebellar tonsillar herniation can occur whereby the caudal medulla is compressed, often a terminal event caused by disruption of brainstem cardiorespiratory centers. A specific type of herniation bears mention because of the large number of military patients treated with decompressive craniectomy (DC). Paradoxical herniation has been reported during lumbar puncture in this setting and occurs by downward movement of brain in the setting of an overall lowered ICP.¹³ This can also follow severe sodium dysregulation and hypernatremia. If the pressure change is a result of lumbar drainage and subsequent cerebral spinal fluid (CSF) leak, the use of a blood patch has been reported to be lifesaving.¹⁴ In addition to the brain parenchymal damage, which can occur from herniation, herniation syndromes can result in cerebral infarcts secondary to compression of proximate vessels, e.g., posterior cerebral artery infarction associated with uncal herniation. These infarcts further increase edema and impact long-term morbidity.

It is an important point to emphasize that numerous authors have published reports regarding outcome data of patients with clinical and radiographic herniation who have survived to discharge with variable disability.¹⁴⁻¹⁸ Poor prognostic assessment of these patients who have not had aggressive medical management may be inappropriate.

MANAGEMENT OF TBI

Blood Pressure and Fluid Management

Maintenance of euvolemia and adequate brain perfusion is the overall objective of hemodynamic therapy in TBI. Cerebral perfusion pressure (CPP) is a measure of the overall adequacy of global brain perfusion and is calculated by the mean arterial pressure (MAP) minus ICP. Recommended treatment goals are SBP >90 mmHg and CPP >60 mmHg.⁴

The patient with TBI may be in hemorrhagic shock because of accompanying polytrauma and hypotension. As such, hypotension (SBP < 90 mmHg) in the setting of TBI is independently associated with poor outcome and mortality from TBI.¹⁹⁻²¹ When compared to hypoxia, low SBP is associated relatively with an even worse outcome.¹⁹ Autoregulation of the neurovasculature is impaired, and regional cerebral blood flow becomes directly dependent on systemic blood pressure.²² Experimental models show that the injured brain is highly susceptible to even subtle ischemic states.²¹ Current evidence grows for the practice of hypotensive resuscitation in the care of trauma

patients; however, it should be noted that TBI patients are often specifically excluded from studies examining this practice.¹⁶

Limited amounts of crystalloid fluids are used by U.S. Army medic and Navy corpsmen protocols for field resuscitation in TBI/polytrauma. Once the patients are evaluated in field hospital facilities, blood products are the preferred resuscitation fluid. From the conflicts in Afghanistan and Iraq, it has been reported that hemorrhagic shock is ideally treated with red blood cells and plasma using a 1:1 ratio based on volume.^{23,24} Colloid fluids are relatively contraindicated in TBI.²⁵ Hypotonic fluids, such as 1/2 normal saline and Lactated Ringer's, have the potential of exacerbating cerebral edema and should be avoided.²² Fluid balance of TBI patients is important as patients with TBI who were fluid balance negative by approximately 600 cc had worse proximal outcomes in an often referenced study.²⁶ The Lund Concept is a practice contrary to this premise, which advocates fluid restriction as a means to control cerebral edema and normalize ICP.²⁷

CPP goals may initially be satisfied with intravenous (IV) fluids, but if CPP cannot be maintained with IV fluids alone, vasoactive pharmacologic agents may be considered. Norepinephrine and phenylephrine are commonly used. Continuous hemodynamic monitoring is needed with both a central venous pressure catheter and a peripheral arterial pressure catheter with pressor therapy.²⁸ Aggressive use of these agents has been associated with increased incidence of acute respiratory distress syndrome (ARDS); however, this complication potentially could have been the result of exceeding CPP levels of 70 mmHg.²⁹ Beneficial effects of the Lund Concept may be attributed to the lower incidence of pulmonary complications, such as ARDS, in patients with more judicious fluid management.³⁰

Ventilation and Airway Management

Oxygenation and ventilation goals are established early to maintain adequate oxygenation with the partial pressure of oxygen in arterial blood (PaO₂) remaining above 60 mmHg, and normocarbida.^{3,4,31} Avoidance of hypoxemia or extreme hyperoxemia (PaO₂ > 487 mmHg) reduces mortality in TBI.⁹ In the field, oxygen saturation should be less than 90%.³² Indications for placement of an artificial airway are a GCS score of 8 or less or clinical concern that the patient's ability to ventilate or protect his or her airway is in jeopardy.²² Overaggressive hyperventilation should be avoided because of the potential for decreased cerebral perfusion at PCO₂ <25 mmHg.^{4,33} Newer ventilator management strategies, such as airway pressure release ventilation (APRV) aimed at improving oxygenation at the expense of ventilation, require further study for use in the setting of head injury and must be used with caution because of the possibility of hypercapnea. A review of APRV is referenced.³⁴

Intracerebral Pressure (ICP) Management

Much of neurocritical and neurosurgical care of TBI is concerned with ICP. If ICP progresses unchecked, it can result in herniation and ischemia. Conservative measures should be instituted in moderate and severe TBI patients to minimize elevations in ICP. Simple interventions include raising the head of the bed to 30°, keeping the head midline, avoiding any circumferential neck dressings for securing the endotracheal tube, and avoiding placement of internal jugular (IJ) central venous lines into the dominant IJ. All these will optimize venous outflow from the head. Central lines that require the Trendelenburg position should not be used for central access during a herniation event as placing the patient in Trendelenburg may increase ICP further.³⁵ Alternatively, femoral lines may be temporarily appropriate. Aggressive treatment of fever, seizures, pain, and agitation can help prevent elevations in ICP.⁴

Indications for ICP Monitoring

Severe TBI patients with a strong clinical suspicion of increased ICP should have a monitor placed. There are a number of options that include the extraventricular drain (EVD), intraparenchymal fiber optic monitor, subdural bolt, and epidural fiber optic catheters. If hydrocephalus is seen on imaging, an EVD is obviously the best option. Clear indications exist for placing an ICP monitor. If the patient has a GCS score of 8 or less (after resuscitation) and an acute abnormality on CT, such as traumatic intracerebral hemorrhage, compression of the basal cisterns, evidence of contusion or herniation, then an ICP monitor should be placed.⁴ If a patient has two of the following: SBP ≤90 mmHg, motor posturing on examination, and/or is 40 years of age or older, then an ICP monitor should likewise be placed or strongly considered.⁴

Other invasive monitoring devices, such as brain tissue oxygenation monitors, microdialysis catheters, and jugular venous saturation monitors, can be used to tailor therapy. Routine application of these devices awaits further study.⁴ The use of brain tissue oxygen monitors have recently been reported to be associated with increased fluid and vasopressor use and pulmonary complications such as ARDS.³⁰

ICP Treatment Goals

The goal ICP in TBI is to maintain a normal pressure state, which is generally less than 20 cmH₂O or 15 mmHg. Elevations to more than 25 mmHg are associated with poor outcome. Current guidelines recommend instituting measures to control ICP when pressures of 20 mmHg are reached and aggressive means employed to prevent ICP elevations to more than 25 mmHg.⁴ Awareness of CPP is important as many interventions to decrease ICP may also have systemic effects on peripheral hemodynamics. The maintenance of a CPP of at least 60 mmHg with

IV fluids or vasopressors is strongly recommended.⁴ Pulmonary complications, including higher incidence of ARDS, may result from overshooting the goal CPP to greater than 70 mmHg.^{29,30}

Medical Treatment Options for Elevated ICP

Hyperventilation

Hyperventilation for ICP reduction may be used only as an emergent and temporary intervention. Prolonged hyperventilation has been clearly associated with exacerbation of cerebral ischemia.³⁶ Short durations of hyperventilation are acceptable as a temporizing measure until other methods of managing ICP are available. If hyperventilation is continued for longer than 12 hours, metabolic compensation negates any helpful effects of hyperventilation. The recommended goal for a chronic PCO₂ is 35 to 40 mmHg. During a herniation event, hyperventilation will acutely and reliably lower PCO₂, as well as ICP, within seconds. The current recommended PCO₂ is to strictly avoid levels below 25 mmHg.^{4,22}

Hyperosmolar Therapy

Pharmacologic creation of an osmotic gradient causes movement of water from intracellular and extracellular compartments of the brain into the vasculature where it reduces the volume of the overall cranial compartment.³⁵ Several agents have been used for this purpose in the past but, currently, mannitol and hypertonic saline (HTS) are the mainstays of hyperosmolar therapy. Mannitol should be given intravenously via a peripheral or central IV line at a dose of 0.25 to 1.0 g/kg. Small doses of mannitol (0.25 g/kg) have been shown to effectively reduce ICP in patients with TBI.³⁷ Earlier data shows that mannitol use in TBI correlates with decreased ICP and improvements in cerebral blood flow and CPP.³⁸ Mannitol can be given while following serum osmolality, where a serum osmolality of 320 mOsm/L is generally accepted as a treatment endpoint. Some investigators advocate that slightly higher levels can be obtained with caution.³⁹

Another option for hyperosmolar therapy is HTS. Studies using 7.5 and 23.4% HTS provide evidence of efficacy. Recent evidence supports the use of bolus doses of 30 to 60 mL of 23.4% HTS to emergently reverse a herniation event.¹⁸ About 23.4% HTS ameliorative effect on ICP lasts longer than mannitol.⁴⁰ High concentrations of HTS must be administered via a central venous line during a 10 to 15 minutes time period to prevent phlebitis and hypotension. A commonly used initial treatment goal is to achieve serum sodium levels 145 to 155 mEq/L, equivalent to a serum osmolality of 300 to 320 mOsm/L in most patients.³⁵ Recent evidence shows 23.4% HTS to be effective in reducing ICP by a mean value of more than 8 mmHg when given for ICP >20 mmHg and can increase CPP values by 6 mmHg when pretreatment values are <70 mmHg.⁴¹ A continuous IV infusion of 2 or 3%

HTS can be used to maintain high serum osmolality, and solutions of 3% or higher HTS should be given via a central line. If continuous infusions of HTS are used, serum sodium should be monitored every 4 hours although avoiding rapid changes in serum sodium so as not to precipitate cerebral edema or central pontine myelinolysis.³⁵ A recent review discusses frequent questions clinicians have regarding the use of HTS in the setting of intracranial hypertension.⁴²

Agents to Reduce the Cerebral Metabolic Rate of Oxygen (CMRO₂)

If ICP remains poorly controlled, then reduction in the metabolic rate of the brain via pharmacologic coma can be considered. The postulated effect by which ICP is reduced is though a reduction in cerebral metabolism, resulting in reductions in cerebral blood flow and reduced tissue oxygen demand. Pentobarbital is the most widespread agent in use for induction of pharmacological coma. Pentobarbital is administered intravenously at a loading dose of 10 mg/kg during a 30-minute time period, followed by a 5 mg/kg/h infusion for 3 hours, and maintenance therapy of 1 mg/kg/h titrated to therapeutic goals of either burst suppression on continuous electroencephalography (EEG) monitoring or a satisfactory reduction in ICP.²⁸ If burst suppression is not obtained with this dose, then a smaller loading dose and increased rate can be given until an EEG tracing consistent with burst suppression is seen or ICP is controlled. In the past, other barbiturates such as the much shorter acting thiopental were used for acute exacerbations of ICP.³⁸ This medication is not currently available in the United States but may be available to deployed forces overseas (A. Holley, personal communication).

Propofol represents an alternative therapy. Propofol is given at an IV loading dose of 2 mg/kg, followed by a titrated infusion of up to 100 µg/kg/min. The use of propofol for this clinical indication is controversial, and this drug has several side effects, including severe systemic hypotension. A study using propofol for ICP reduction showed a failure of an improvement in 6-month outcome, and long-term and high-dose propofol infusions have been associated with the development of propofol infusion syndrome, which consists of renal failure, rhabdomyolysis, hyperkalemia, myocardial failure, metabolic acidosis, lipemia, hepatomegaly, and often death.⁴³ Vigilance for this condition is wise for any patient receiving an infusion for more than 48 hours.⁴ Continuous EEG monitoring may be helpful to monitor for burst suppression or better control of ICP.

FUTURE DIRECTIONS

Induced hypothermia to improve outcomes in TBI is promising but controversial. Recent animal data show induced hypothermia to be associated with improved neurophysiologic metrics in an hypoxic brain injury model.⁴⁴ There is data in brain trauma that induced mild hypothermia may

improve outcome post-TBI.⁴⁵ Current use of induced hypothermia for treatment of ICP in severe TBI is a second-tier therapy but may be helpful in refractory cases.³⁵ The goal of maintaining normothermia and avoiding hyperthermia in TBI patients is strongly recommended.⁴⁶ The potential of coagulopathy and antiplatelet effects of induced hypothermia should be considered, especially in the setting of hemorrhagic TBI.⁴⁷⁻⁵¹

Older preclinical data suggests a difference between outcomes of models of brain injury based on gender.⁵² Further work defined high levels of progesterone as potentially protective from the standpoint of developing cerebral edema, and as supportive data began to accumulate, interest in investigating the potential benefits of progesterone therapy in TBI grew.⁵³ A synopsis of both preclinical and epidemiologic studies regarding progesterone is provided.⁵⁴ Currently, there are two ongoing clinical trials attempting to clarify the benefit of progesterone therapy in TBI, the ProTECT III (Progesterone for Traumatic Brain Injury, Experimental Clinical Trial III), and SYNAPSE (Study of the Neuroprotective Activity of Progesterone in Severe Traumatic Brain Injury). Both have a planned enrollment of more than 1,100 patients and expected completion dates are 2015 and 2012, respectively.⁵⁵

SURGICAL TREATMENT OPTIONS

Decompressive Craniectomy

DC represents another clinical approach to the early intervention and management of TBI. The reported experience to date is conflicting.⁵⁶⁻⁵⁸ The role of DC in treating brief elevations in ICP in the setting of diffuse non-pTBI was evaluated in the recently published Decompressive Craniectomy (DECRA) trial.⁵⁹ ICP control was significantly improved in the surgical treatment arm, but 6-month outcomes were worsened compared with medical therapy. The surgical procedure performed was a bilateral DC, and patients with focal space occupying lesions were excluded from the study. Of note, patients in the surgical arm had a statistically significant difference in loss of pupil reactivity compared with the medically treated patients. This fundamental difference in the treatment arm, combined with the fact that bilateral DC is not the most often used surgical procedure in treatment of refractory elevations in ICP, appears to limit the ability to generalize the study's conclusions. The Randomized Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intra-Cranial Pressure (RESCUEicp) may help further define the role DC may have in the management of severe TBI.⁶⁰ RESCUEicp recently completed its enrollment of approximately 400 patients comparing DC to medical management (including barbiturates) in severe TBI.

The U.S. military neurosurgical experience in Operation Enduring Freedom and Operation Iraqi Freedom used early hemicraniectomy for treating some cases of severe TBI with concerns for imminent elevations in ICP, whether from pen-

etrating, blunt injury, or blast induced.^{61,62} This population is unique because of long, fixed-wing evacuation flights and exposure to relative altitude proximal to the incident trauma. In a recent study of this population comparing GCS scores of patients at the time of head trauma and at discharge, TBI patients who underwent a craniectomy had a lower initial GCS score than those who underwent craniotomy, but at discharge their GCS score was not significantly different.¹² A similar article with a smaller sample size and follow-up at 11 months and the use of the Extended Glasgow Outcome Scale (GOSE) as the outcome metric is referenced.⁶³ Anticipated randomized studies on large cohorts of patients may clarify the role of this treatment option.

Common Clinical Approach for Elevated ICP Management

The management of acute elevations in ICP initially involves ensuring that the waveform and ICP reading is accurate. Seizures, fever, metabolic and respiratory derangements need to be ruled out if suspected. Brain CT imaging should be considered in any new episode of increased ICP without explanation. Maneuvers such as repositioning the head to midline, sitting the patient up at 30°, establishing normothermia and cessation of suctioning or other noxious stimuli may help lower temporary spikes in ICP. If this is unsuccessful and the ICP is felt to be accurate, very brief hyperventilation of intubated patients may be performed. If central access exists, then 30 cc of 23.4% HTS may be given via a central line during a 10-minute period. If given faster, CPP may need to be augmented with small doses of phenylephrine. As an alternative to HTS, mannitol may be given via a peripheral line with the dose tailored to the clinical situation. A dose of 1 g/kg is given for clinical signs of herniation and doses of 0.25 to 0.5 g/kg for less severe increases in ICP. In a herniation event, central access should be obtained with consideration of a femoral central venous catheter or avoidance of extreme Trendelenburg positioning for subclavian lines.³⁵ If ICP continues to be elevated after these maneuvers, then additional HTS can be given as well as further boluses of mannitol, treating up to a serum osmolality of approximately 320 mOsm/L. Standing infusions of 3% HTS can be used, with goal sodium values that may exceed 155 to 160 mEq/L if required. Further medical management includes use of bolus doses of propofol, and consideration given to pharmacologic coma induced hypothermia or surgical intervention.

OTHER ASPECTS OF CARE

Anticonvulsants

TBI patients, both penetrating and nonpenetrating, are at risk for both early (less than 7 days) and late (more than 7 days) post-traumatic seizures. A seizure in the acute phase can exacerbate the injury. Phenytoin, a well-established anti-epileptic drug (AED), has been shown to be beneficial in reducing the risk of seizures during the first week after

TBI.^{64,65} Carbamazepine, phenobarbital, and valproate are also effective AEDs.⁶⁴ Unfortunately, no AED has been shown to prevent the development of late post-traumatic seizures. The recommended approach is to stop AED therapy after the first 7 days, and only reinstitute treatment should late seizures manifest.⁴ Data regarding cognitive side effects of phenytoin make prolonged prophylactic use of this medication, in particular, less attractive.⁶⁶ If a patient requires IV medications, alternatives include valproate, lacosamide, and levetiracetam. Levetiracetam has been shown to be highly effective in preclinical TBI models, and in randomized trials it has been shown to be as effective as phenytoin with improved GOSE at 6 months.^{67,68} The American Academy of Neurology has published guidelines for the use of AEDs in the setting of severe TBI recommending treatment with AEDs prophylactically for the first 7 days following injury.⁶⁹

Secondary Complications of the Critically Ill

Prevention of secondary complications of critical illness includes consideration of venous thromboembolism (VTE), stress ulceration, and skin breakdown. Any critically ill and immobilized patient is at high risk for developing deep venous thrombosis (DVT) with subsequent VTE. The optimal approach for VTE/DVT prophylaxis in severe TBI complicated by intracranial hemorrhage is unclear. Sequential compression devices (SCD) on the lower extremities are minimally invasive and are not associated with worsening intracranial hemorrhage. The timing for introduction of unfractionated or low molecular weight heparin (LMWH) for VTE prophylaxis in this population is an individualized decision. Lacking a contraindication to pharmacologic DVT prophylaxis, heparin, or LMWH should be started ideally within the first 36 hours after injury.⁷⁰ The routine placement of inferior vena cava filters currently has limited support.^{70,71} Gastric stress ulcers may be prevented using either H₂ receptor antagonists or proton pump inhibitors (PPIs). Potential comorbidities, resulting from the indiscriminate use of PPIs and drug-to-drug interactions, require consideration of alternative means of gastric ulcer prophylaxis, particularly in the setting where a TBI patient requires an antiplatelet regimen.⁷² Either one of these medications should be considered for gastric stress ulceration prophylaxis in severe TBI patients, although the tendency for H₂ blockers to cause thrombocytopenia may limit their usefulness.⁷³ Also, prevention of skin breakdown is important in all severe trauma patients, and care must be taken to reduce the likelihood of such by appropriate skin hygiene and proper nursing care with scheduled repositioning.

CONCLUSIONS

The management of patients with combat-related moderate and severe brain injury is challenging, and medical and surgical means of treatment are indicated to reduce secondary injury from brain trauma. Maintaining brain perfusion, con-

trolling ICP, and preventing morbidity associated with critical illness are principle to care. As new medical and surgical approaches are introduced, there will be increasing opportunity to better manage these patients and improve neurologic outcomes in the near and long term.

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Traumatic Brain Injury: Next Steps, Research Needed, and Priority Focus Areas

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ABSTRACT Traumatic brain injury (TBI) has been not only a major focus of concern during the recent conflicts in Afghanistan and Iraq, but also among our garrison service members. The prevalence of these injuries has compelled the nation and Congress to invest in the development of policies and programs that support evidence-based care for the full continuum of TBI, from mild (otherwise known as concussion) to severe and penetrating brain injuries. Although, the Department of Defense has made great strides in the areas of TBI clinical care, education, and research, there remains a great need to leverage scientific, policy, and clinical advancement to maximize care of the service member. The purpose of this article is to outline the 7 major areas of work currently being undertaken to help advance the field of TBI. The 7 areas include: (1) eliminating undetected mild traumatic brain injury through prompt early diagnosis, (2) ensuring force readiness and addressing cultural barriers, (3) improving collaborations with the Department of Veterans Affairs, other federal agencies, and academic and civilian organizations, (4) improving deployment-related assessments, (5) deploying effective treatments, (6) conducting military-relevant and targeted research, and (7) enhancing information technology systems.

INTRODUCTION

As discussed in previous articles within this special edition of Military Medicine, traumatic brain injury (TBI) prevalence has been steadily increasing over the past 10 years of combat operations. The incidence of blast-related brain injuries, numerous deployments, and long combat engagements led to a critical need to train, treat, and track service members with TBI. The paucity of literature has driven the military to seek advancement in the science of blast-related brain injury pathophysiology to better understand enduring sequelae from TBI and to develop mitigation strategies that improve recovery. Simultaneously, there has been unprecedented attention to TBI in the sports realm resulting in a need for sharing of best practices between military and athletic communities. The Department of Defense (DoD), however, is a large enterprise with more than 2.2 million in the Armed Forces, including the National Guard and reserve components, more than 1.8 million deployments since September 11, 2001, and serving a health care system of more than 9.6 million beneficiaries.¹⁻³ In the DoD system, similar to the civilian sector, TBI remains a subspecialty of care within the neurological rubric. It also represents numerous challenges, of greater consequence to the military, crossing the entire continuum of care from prevention to reintegration. Thus, defining priority areas and identifying resources are vital to elucidating the best way forward. The purpose of this article is to outline the seven major areas of work currently being undertaken to help advance the field of

TBI. The seven areas include: (1) eliminating undetected mild TBI (mTBI) through prompt early diagnosis, (2) ensuring force readiness and addressing cultural barriers, (3) improving collaborations with the Department of Veterans Affairs (VA), other federal agencies, and academic and civilian organizations, (4) improving deployment-related assessments, (5) deploying effective treatments, (6) conducting military-relevant targeted research, and (7) enhancing information technology systems.

UNDETECTED mTBI AND DIAGNOSIS OF mTBI

The military faces unique challenges related to screening and diagnosis of mTBI in the combat setting, including delayed screening because of mission requirements, geographically dispersed medics and corpsmen, and the necessity to manage other life-threatening situations before addressing mTBI. Brigadier General Richard Thomas, Assistant Surgeon General of the Army for Force Projection has stated, "War is a catalyst for medical innovation." Numerous advances such as lifesaving surgical techniques, critical interventions during aeromedical evacuation, and new rehabilitation technologies have greatly improved medical care throughout the spectrum of combat operations. Presently, one of the highest priorities of the DoD, TBI research efforts involves the objective diagnosis of mTBI. Without objective diagnostic tools, clinicians rely on aggressive screening, beginning at the point of injury, followed by a timely diagnostic evaluation that should include a history and focused clinical exam, and can be augmented by a battery of supplemental assessments. However, the diagnosis of mTBI relies heavily on subjective information. As scientists continue to validate promising diagnostic technologies, current screening and evaluation tools are also being revised to improve TBI detection and facilitate early intervention.

The military has recently made significant policy changes, developed clinical guidance, and created tools to improve

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screening and evaluation of mTBI. Although many of these efforts are primarily focused in-theater, there have been substantial improvements in redeployment screening, surveillance, and garrison clinical management as well. Other recent efforts by the DoD to improve mTBI systems of care involve training, standardized educational materials, point-of-injury care and documentation, and aggressive pursuit of new diagnostic technologies. By way of these collective efforts, the DoD is working to mitigate the effects of mTBI and prevent subsequent injuries.

Consistency of the screening process is an essential element in accurate data capture. Medical care, far forward, is largely dependent on well-trained medics and corpsmen to conduct point-of-injury screening, care, and documentation. Enlisted medical staff performs TBI screenings on the battlefield with limited oversight, while balancing significant demands on their time triaging other injuries. The DoD recognized these impediments to proper and consistent mTBI screening and, in 2006, fielded the Military Acute Concussion Evaluation (MACE) to both screen for and then assess cognitive and neurological function in the concussed patient. When a Corpsman or Medic utilizes the MACE, the history portion serves as the initial screening tool, requiring confirmation from a licensed provider, for all potentially concussed service members. When a concussion is confirmed, then the remainder of the MACE, including the cognitive and neurological portions, is completed to provide a first line assessment. The MACE has undergone multiple revisions to better reflect the scope of concussion in the theater environment and to maximize standardization of the screening process at the point of injury.

In 2010, a new DoD level policy was implemented to improve mTBI screening and detection in the deployed environment. This policy, Directive-Type Memorandum (DTM) 09-033,⁴ entitled "Policy Guidance for the Management of Concussion/Mild Traumatic Brain Injury in the Deployed Setting" has changed care in three major ways: (1) decreased stigma associated with concussion care in battle; (2) required mandatory documentation of the injury event, screening, and diagnosis; (3) standardized treatment practice and patient movement to higher echelons of care with treatment failure. The DTM, first and foremost, requires mandatory screening and rest for any service member exposed to a potentially concussive event. This incident-based screening occurs regardless of whether or not the service member has the actual diagnosis of concussion. The policy change helps eliminate concerns over any stigma involved with seeking medical care during combat since all service members are screened and treated as necessary. Second, the DTM mandated significant data collection processes to help assess current needs and inform future efforts. The nonmedical leaders are required to conduct a basic "eyes on screening" of all exposed service members and report results in a database. Simultaneously, corpsmen and medics have increased screening requirements utilizing the MACE. The MACE results, now required to be docu-

mented in the electronic medical record, was also updated to focus on the screening section. The third change came with the release of updated clinical practice guidelines for mTBI in the deployed setting. Among other important changes, these guidelines provided simple and effective standardized instructions for screening, treatment, and documentation of mTBI from point of injury to comprehensive concussion and recurrent concussion evaluation.

To further increase sensitivity of the overarching screening process, the DoD has implemented screenings at a number of points in time: point of injury, before medical evacuation to continental United States facilities, and upon redeployment. TBI screening also occurs throughout the VA system. Service members now have an opportunity both near and far from the fight to provide information related to potentially concussive events. Upon redeployment, efforts are underway to improve the Postdeployment Health Assessment (PDHA)⁵⁻⁹ and Postdeployment Health Reassessment (PDHRA)⁶⁻¹⁰ process. This screening provides an additional opportunity to identify service members who may have sustained mTBI while deployed. The questions, therefore, are designed to be sensitive with a follow-up diagnostic evaluation to ensure specificity.

As the DoD, in partnership with the VA, continues to address mTBI, future efforts involving mTBI screening in the deployed and garrison setting will coexist with emerging technologies to improve injury detection. mTBI screening remains an enormous challenge for the military because of the absence of an objective diagnostic tool. The military is addressing the paucity of diagnostic technologies with research portfolios investigating the spectrum of possibilities from biomarkers to the latest neuroimaging techniques. Point-of-injury tests will not only have to prove sensitive and specific, but also need to be portable for use in austere environments. Until a time when sensitive and specific diagnostic tests are ready to be fielded into combat environments, the military must continue to pursue a number of initiatives to help providers better identify mTBI.

FORCE READINESS/CULTURAL BARRIERS

Total Force Fitness has been defined by the Chairman of the Joint Chiefs of Staff as supporting the social, physical, environmental, medical and dental, spiritual, nutritional, psychological, and behavioral needs (Fig. 1) so that the nation's Armed Forces can function at optimal levels while securing our national defense. To create this type of environment, certain ethos or values become relevant. Unit cohesion, a sense of mission, honor, and courage make up a few of these tightly held values. Sometimes, these values can interfere with a service member's interest in accessing health care, including the evaluation and treatment of mTBI, otherwise known as concussion. Seeking treatment for a concussion may take a service member away from his/her mission and perhaps impact unit cohesion. Therefore, to ensure early detection and treatment for concussion, these cultural barriers

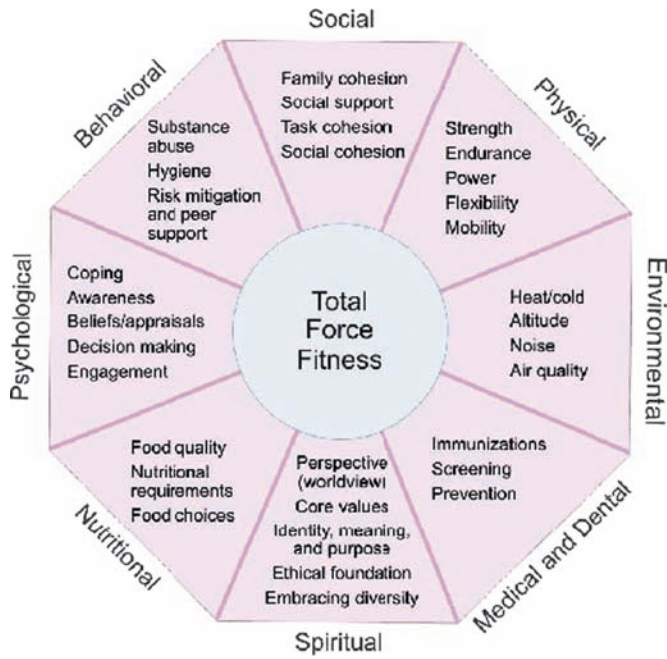


FIGURE 1. Chairman of the Joint Chief of Staff Guidance for 2011: Total Force Fitness initiative. Chairman Joint Chiefs of Staff Instruction 3405.01 1 September 2011.

to care need to be explored. This is done through increasing awareness of the signs and symptoms of concussion, and the impact of these symptoms not only on performance but also on unit safety when the concussed service member remains in the fight (Fig. 2). Skills and capabilities important to operating in combat such as poor marksmanship or decreased situational awareness can be hampered if a service member has a concussion that is left untreated.

A commander’s commitment to ensure his unit receives prompt medical attention is the target of current TBI educa-

tional and awareness initiatives. Education is a key for the treatment of mTBI; in fact, providing an educational intervention after concussion has the highest level of evidence in the medical literature (Class I evidence). Work from Ponsford et al shows that early educational interventions that include expectations of a positive recovery, reintegration to normal activity, and strategies to help facilitate recovery are predictive factors in the pediatric and adult concussion civilian populations.⁷

There is easy access to educational resources to help highlight the importance of early detection and early intervention (see Fig. 3 for examples of resources available for TBI in the military).

Finally, a structured DoD campaign is being developed to help address access to care issues in mTBI. A better understanding of the barriers to seeking health care will be necessary to implement the cultural changes needed to ensure early detection and prompt treatment for mTBI. Suggestions about perceived effect on career, what other people in their unit may think of them as they seek out health care or letting down a unit by not being available to serve a vital function have all been postulated as examples of the barriers that exist. To help address the perceived barriers, the DoD has partnered with other agencies, including the professional sports community. The DoD and the National Football League have joint strategic messaging initiatives promoting the need to get checked out after a possible concussion.

IMPROVING COLLABORATIONS WITH VA, OTHER FEDERAL AGENCIES AND ACADEMIA/ CIVILIAN ORGANIZATIONS

The DoD and Congress have communicated the expectation that the solution to many of the challenges related to TBI lies in effective partnerships that can be leveraged across the nation.



FIGURE 2. Impact of TBI on the Warfighter.

Electronic Resources	Print Resources	Contact Points
<ul style="list-style-type: none"> ▪ www.dvbic.org ▪ www.dcoe.health.mil ▪ www.Afterdeployment.org ▪ DCoE Social Media: Facebook, Twitter, YouTube, Scribd and Blog ▪ DCoE Newsletter & Webinars ▪ Real Warriors Campaign ▪ Web-Based Case Studies for mTBI on www.mhslearn.mil: <ul style="list-style-type: none"> ▪ Diagnosing mTBI ▪ Assessing the Individual with Persistent Symptoms ▪ Use, Administration and Interpretation of the MACE ▪ Assessing the Individual with Headache 	<ul style="list-style-type: none"> ▪ TBI Family Caregiver Guide (electronic version available) ▪ mTBI and Co-Occurring Disorders Toolkit ▪ mTBI Pocket Guide ▪ Major Depressive Toolkit (MDD) ▪ Handbook for Family & Friends of Service Members Before, During, and After Deployment 	<ul style="list-style-type: none"> ▪ National Resource Library ▪ Military OneSource ▪ DCoE 24/7 Outreach Call Center ▪ Yellow Ribbon Reintegration Programs

FIGURE 3. Available resources for providers, service members, and families.

There is an abundant amount of work being conducted within the VA system of care to tackle TBI-related issues. The Defense and Veterans Brain Injury Center (DVBIC) is a congressionally mandated, multisite consortium established in 1991 to ensure state-of-the-art care, research, education, and care coordination of service members and veterans who sustain a TBI. Five of the 17 DVBIC sites in the consortium are embedded with VA medical centers. They include the 4 polytrauma rehabilitation centers: Richmond, Virginia; Tampa, Florida; Minneapolis, Minnesota; and Palo Alto, California as well as one polytrauma network site, in Boston Mass. There are currently more than 65 research studies being conducted by DVBIC to advance the science of TBI and advance the work across the VA and other federal agencies.

The Centers for Disease Control and Prevention (CDC) as well as the National Institutes of Health (NIH) are also leading agencies that are involved in advancing the science and care for those who sustain TBI. The DoD has partnered with both on numerous initiatives to include the development of common data elements (CDE)⁸ for research studies, re-examining the definition of mTBI through the concussion definition consortium, and defining gaps in research to guide future studies.

Common Data Elements

The CDE project began from an interagency collaborative effort involving more than 50 American and European universities and several U.S. federal agencies. The main goal of this project was to be able to compare similar data fields across studies. With the vast amount of TBI-related research occurring around the world, the challenge is being able to do comparative effectiveness research and make conclusions

from similar studies that capture different data fields. The CDE project provides definitions and guidelines to standardize the kinds of data that should be collected in studies and how to collect these data. As academic and civilian partners adhere to these CDEs, direct comparison with disparate studies will be possible. The research bank will be greater, and the study implications and conclusions can be drawn quicker through this combined process.

Concussion Definition Consortium

The current DoD definition of TBI⁹ has limitations and is under review. The defining characteristics of concussion are reflective of the current state of knowledge of military and civilian medical science; however, they do not adequately describe the natural history of injuries, nor indicate a patient's prospects for full recovery or long-term deficits. In addition, the definition of mTBI is not standardized throughout the research community. This creates variable study populations, limiting the ability to draw conclusions when analyzing the aggregate body of research. There is a current workgroup, led by the Brain Trauma Foundation, re-evaluating the literature with the goal of refining the current accepted definitions of concussion or mTBI.

DEPLOYMENT-RELATED ASSESSMENTS

The military TBI community continues to be challenged by a lengthy engagement in Afghanistan and Iraq to include multiple deployments, changing combat warfare and significant deployment time with decreasing dwell time. An understanding of deployment-related exposures and injuries, to include concussion, continue to challenge the military health system. Some promising instruments that may assist in providing

objective data related to deployment-related concussion are neurocognitive assessment tools (NCAT). Currently, the DoD is utilizing the automated neuropsychological assessment metric (ANAM) to perform predeployment baseline neurocognitive assessment¹⁰. Enticement for usage of these tools is that they supply objective, nonbiased data of ongoing cognitive deficits for those who sustain concussion, thus minimizing reliance on mainly subjective information. Their utility is in assessment of the cognitive changes frequently caused by concussion. Returning service members to duty, before resolution of cognitive changes (or other neurological deficits), might result in increased vulnerability to subsequent injury, protracted neurological recovery, or reduced performance in critical situations. Obtaining a baseline, then using the same test instrument postinjury for comparison, produces more accurate assessments of cognitive change following a concussive event than does assessment based only on normative data. For this reason, more than 1 million deploying service members have received a predeployment baseline ANAM. If any of these service members are diagnosed with a concussion in the deployed setting, they can retake the ANAM test battery, and these scores can be compared to their own predeployment baseline scores to help determine if there are ongoing cognitive deficits. This piece of objective data contributes to the whole clinical picture and provides additional information by which to make more informed return to duty determinations. This program is evolving, and next steps include fully executing a neurocognitive assessment tool (NCAT) program in the deployed setting.

EFFECTIVE TREATMENTS

Deploying effective treatments for TBI have been more successful for severe brain injuries than what is available for mTBI. Evidence-based treatments for severe and penetrating brain injuries include neurosurgical intervention and incorporating numerous strategies to decrease intracranial pressure. The DoD, along with civilian partners, has been rather successful in ameliorating the effects of secondary cerebral edema and ischemia in this cohort because of advanced diagnostics and a mature combat casualty care system, which has focused on hemorrhagic control and management of shock. This is not the case for mTBI. Currently, there are very few evidence-based treatments for concussion. As mentioned previously, an educational intervention holds the highest evidence in the literature for an effective strategy. In addition, rest to prevent another concussion while allowing time to recover is a cornerstone of treatment. There are no Food and Drug Administration (FDA) approved treatments for mTBI. To fill this gap, the DoD TBI research portfolio has a significant investment focused on identifying effective treatments for mTBI. Areas of interest, include, but are not limited to the following:

- Assess several potential TBI therapies that are currently FDA approved for other indications

- Develop and validate more effective, technology-enhanced cognitive and behavioral rehabilitation tools
- Consider the role and effectiveness of complementary and alternative medicines as part of an integrative health approach model for TBI
- Explore effective treatments in the context of TBI and other co-occurring conditions such as visual impairments, pain, amputations, hearing issues, and mental health conditions such as post-traumatic stress disorder, depression, and substance use disorder
- Study the role of hyperbaric oxygen in the treatment of chronic symptoms after mTBI

In addition to the large DoD research portfolio studying effective treatments for TBI, there is significant work being done in the civilian sector. It has been a challenge for the DoD to evaluate all the work that has been accomplished worldwide to further the field of TBI care. In addition, many of the studies are not done in military cohorts nor with blast brain injury, therefore, translation of findings is another challenge. Rapid field testing programs are underway to deploy promising technologies or treatments to the military community so that efforts are fast tracked to influence care now.

The challenge now in front of us is to translate as quickly as possible when a treatment is considered safe and effective. Furthermore, it is imperative to keep the commitment to the advancement of military medical capabilities at the forefront so that the current TBI studies are finished and those that are deemed promising are allowed to flourish to create solutions to the problem of TBI and advance the field.

RESEARCH

TBI research in the DoD is particularly complex because the military is responsible for a patient population with high levels of three challenging patient types: penetrating injuries, polytrauma, and blast-related mTBI. The scenario is further complicated by the constraints of a war zone, which impacts the type of solutions that the researchers are able to seek. The military also faces unique challenges in that it is solely responsible for all aspects of care, from prevention of injury to reintegration, thereby needing an expansive portfolio of research covering everything from personal protective equipment to advanced ruggedized diagnostics. As a result of these challenges and the need to often address more than one of these issues within a single patient, the military has had to develop a comprehensive and yet focused research portfolio. This research, which parallels the military continuum of care, falls into the following categories: basic science, prevention/environmental monitoring, screening, assessment, treatment, rehabilitation, and reintegration. Once the military identifies promising research in a given area, the final challenge is to expedite the process from proposal to field. This task requires coordination at many levels, internally and externally, but most important is the coordination with the FDA to fast track key initiatives.

The DoD has placed significant emphasis on finding reliable diagnostics and effective interventions for TBI. To support this push, more than 450 studies with more than 400 million dollars were allocated, starting in 2007, through DoD research organizations, such as the U.S. Army Medical Research and Materiel Command (USAMRMC). TBI research programs and direction were further honed as USAMRMC added neurotrauma portfolio managers to better handle the significant quantities of research being conducted. The key areas of investigation are highlighted here. Basic science funded by the DoD is currently looking at multiple aspects of subcellular changes related to concussion. The potential role of biomarkers as indicators of dysfunction is among the priorities in this category. Prevention of TBI is being addressed by focusing on improvement of personal protective equipment, neuroprotective agents, and developing a better understanding of blast exposure. This category includes the environmental monitors that help determine forces that impact the brain; the data is being collected using blast dosimeters from the Defense Advanced Research Projects Agency (DARPA). Other studies are using a number of modalities to try and elucidate whether blast concussion is different than nonblast concussion. The screening and assessment tools currently in use are being investigated in order to determine continued effectiveness. The ANAM is undergoing comparison to determine efficacy in this population and against the leading products on the market. In the diagnostics area, initiatives are underway to see if a combination of tools for assessments could be useful in screening and/or diagnosis of mTBI. Tests such as biomarkers or eye tracking are among those under consideration for individual and combination use. A number of assessment and imaging improvements are being analyzed to include diffusion tensor imaging for its ability to detect diffuse axonal injury in blast-related concussion. Research impacting treatment of TBI must focus on comparative effectiveness studies. Continued study of medications, hypothermia, and hyperbaric oxygen therapy are among treatment interventions currently being funded. In rehabilitation and reintegration, the current studies are looking at cognitive rehabilitation therapies as well as uses for technological assistive devices. There are also investigations looking at short- and long-term impact of brain injury to include such areas as chronic traumatic encephalopathy and co-occurring disorders.

Going forward, the DoD will have to work with the FDA to ensure rapid and safe movement through clinical trials. Advances made thus far as a result of combat have demonstrated a need and benefit to moving quickly while maintaining appropriate patient safety measures. Other challenges that need to be overcome across all DoD TBI research include the ability to conduct trials in-theater in the rugged environment that is typical of the military TBI population.¹¹ The research is further challenged by the need to have operational solutions. Once tests are proven in labs and relatively stable environments, they will need to be rapidly ruggedized and made field deployable. This process will likely have to

occur simultaneously with the actual investigations as additional delays to make diagnostics or interventions field-ready will not fit with the military timeline. Lastly, the DoD will need to ensure continued funding after the drawdown of combat troops in Operation Enduring Freedom/Operation New Dawn to ensure progress that is being rapidly made does not wane.

INFORMATION TECHNOLOGY

As mentioned previously, the DoD is a very large enterprise that supports active duty and reserve components as well as beneficiaries. The Military Health System is the largest health system in the world. This makes transfer of information and communications challenging. As we strive to track patient progress and clinical/support needs, enhancements in telecommunications and technology are vital. In addition, as we partner with the VA as well as other health care providers and organizations, the need to support private yet important communications is critical. Tracking patients with TBI across the continuum of care, from deployed settings to stateside facilities and beyond, remains a challenge. Bidirectional data sharing with the VA is one initiative that has helped to enhance these capabilities. As mentioned throughout this article, there are numerous DoD programs that support TBI screening, assessment, and treatments. We want to ensure that our health care partners have access to this information. In addition, theater capabilities related to information technology issues has been problematic. Theater bandwidth issues, difficulty with computerized medical records documentation in a war zone as well as time zone differences are but just a few challenges that we face. There are a few teleconsultation services that have been developed to support theater care with expert TBI clinicians. In addition, video conferencing has been pilot tested to deliver health care in rural and underserved settings. There are some telecommunication models being studied in TBI populations to help leverage this capability across sites and with specialty clinicians that are not found readily across the enterprise, such as neuropsychologists. Information technology encompasses a vast array of systems that can help to deliver state-of-the-art care, whether through tracking mechanisms, transfer of clinical information to providers, or teleconsultation. Next steps will be to leverage these capabilities across the continuum to help enhance care for those who have TBI.

CONCLUSIONS

TBI has received unprecedented attention, highlighted by the current conflicts in Afghanistan and Iraq and increased awareness throughout the sports community. The DoD has taken the issue very seriously and in co-operation with other federal agencies, including the VA, DVBIC, NIH and CDC, strives to lead the way in advancing evaluation and treatment of mTBI. Steps have been taken to improve point-of-injury screening with widespread use of the MACE in the deployed setting.

Guidelines for the management of mTBI in the deployed setting require recognition of potentially concussive events so that service members get appropriate evaluation promptly and are afforded the opportunity to recover before returning to duty. Additional opportunities to identify service members who may have persistent problems as a result of mTBI are offered in the PDHA and VA TBI clinical reminder. Despite these screening mechanisms, there is great need for an objective diagnostic tool. Efforts to fill this gap are underway with promising research in the area of biomarkers, portable non-invasive neurodiagnostic tools, and advanced neuroimaging techniques. Although not a diagnostic tool, neurocognitive assessment tests such as ANAM provide objective information regarding one's cognitive performance following a concussion. When used postinjury and compared to a predeployment baseline, the ANAM provides an objective piece of information that adds to the entire clinical assessment when determining readiness to return to duty. Much remains to be discovered for effectively treating mTBI and resulting symptoms. Education on the natural course of recovery is currently the only Level 1 evidence-based intervention. Research is underway to evaluate the effectiveness of pharmaceuticals for treatment or neuroprotection, complementary and alternative medicine approaches such as acupuncture and yoga, and novel therapeutics such as hyperbaric oxygen. Education of the total force on causes and consequences of mTBI is also a key to the overall strategy to improve TBI evaluation and treatment by increasing recognition and willingness to seek care for potentially concussive events. As the Chairman of the Joint Chiefs of Staff has supported a Total Force Fitness paradigm, the strength of our nation relies on maintaining fighting strength to preserve our most sacred value of freedom. Adequate detection and treatment of mTBI helps to achieve this goal. The DoD is fully committed to stay on course in the advancement of the field of TBI to help both the military and worldwide TBI populations. These clinical issues are and will remain a serious threat to our service members and to civilians in war and at peace. The DoD is on the verge of significant scientific advancements in these areas that will directly

impact care for our service members and our civilian counterparts for decades to come.

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