



# Army Medicine Peer-Reviewed Publications

August 2013

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## **Executive Summary**

Aug 2013 – Journal coverage for August is similar to July in that a range of research conducted was featured in prominent media outlets. However, coverage of the research differed from the previous month in that it was disseminated in balanced and positive tones, rather than critical, while discussing children and PTSD.

Multiple outlets featured media mentions of Lt. Gen. Patricia Horoho while discussing a study on programs for children with a deployed caregiver. August reporting featured a majority of articles with a positive tone highlighting the Army's need to address child stress management. Reporting on the study by Military Medicine commonly noted the Ready and Resilient Campaign while featuring initiatives from the Army Surgeon General.

Research from the Journal of the American Medical Association (JAMA) discussing the topics of suicide, behavioral health and PTSD was featured in a range of print media outlets with high circulations. The studies reflected common storylines from the month of August that noted the need for the Army to reduce Soldier stigma on requesting medical assistance for behavioral health complications.

JAMA provided results in multiple studies that contradicted the outcomes of previous research and medical expert advice. Research on behavioral health and suicide disproved previous notions, which suggested a link between combat and Soldier suicide while highlighting that none of the deployment-related factors were associated with increased service member suicide risk. The Journal's research also contradicted previous medical advice not to simultaneously treat those suffering from PTSD and alcoholism, while providing results of the benefits of the combined treatment.

## **Medical Journal Coverage**

### ***Behavioral Health***

### **JAMA: Suicide, Mental Disorders, and the US Military**

The Journal of the American Medical Association highlighted Leard Mann and colleagues' research that proved service members are likely to experience many of the same broad pressures, forces and trends as civilians. Therefore, results contradict previous research, noting that military combat did not have as high of a consequence on troops' behavioral health disorders and suicide. Army Medicine has the opportunity to apply the advice from the recent results by addressing "long-standing military ambivalence toward the medical model of mental illness—an ambivalence affecting service members, military clinicians, and senior leaders alike." The research appeared in a range of high profile print media outlets, broadcast and newswires such as the *Associated Press*, *Bloomberg News*, *CNN*, *IVN*, *The New York Times*, *USA Today* and *The Washington Post*. Reporting on the study was also seen in trade publications such as *HealthDay*, *Internal Medicine News* and *MedPage Today*.

### **JAMA: Risk Factors Associated With Suicide in Current and Former US Military Personnel**

A prospective longitudinal study conducted by the Journal of the American Medical Association sought to identify and quantify risk factors associated with suicide in current and former US military personnel including demographic, military, mental health, behavioral and deployment

characteristics. Results proved that none of the deployment-related factors, including combat experience, cumulative days deployed and the number of times a service member is deployed, were associated with increased suicide risk in any of the models. The research is relevant to Army Medicine in how it suggests to separate service members with behavioral health complications that are also suicidal from those that are exclusively suicidal while investigating treatment options. The research appeared in a range of high profile print media outlets, broadcast and newswires such as the *Associated Press*, *Bloomberg News*, *CNN*, *IVN*, *The New York Times*, *USA Today* and *The Washington Post*. Reporting on the study was also seen in trade publications such as *HealthDay*, *Internal Medicine News* and *MedPage Today*.

### ***Disease***

#### **JAMA: Asthma Drug Improves Cognitive Function in Down Syndrome Model**

The Journal of the American Medical Association provided research on the effect of formoterol, an asthma drug, on mice with Down syndrome. The results indicated strengthened nerve connections and improved cognitive function, with post-mortem observations that included a more complex cognitive structure. Developments in the understanding of cognitive complexity and improvements may offer Army Medicine insight into brain disorders.

#### **JAMA: Early Detection and Intervention in Schizophrenia**

Analysis of detection and intervention into the treatment of schizophrenia discussed a comprehensive strategy developed over two decades that was aimed at minimizing and/or preventing the morbidity of the illness. Based on two distinct approaches, the analysis looked at the pharmacologic and psychosocial treatment options. Information on schizophrenia can be useful to Army Medicine due to the increased interest in cognitive disorders and treatment.

#### **Military Medicine: Psychological Health of Military Children: Longitudinal Evaluation of a Family-Centered Prevention Program to Enhance Family Resilience**

Research conducted by Military Medicine evaluated the impact of a family-centered prevention program, Families OverComing Under Stress Family Resilience Training (FOCUS), on the psychological adjustment of military children to a care provider's deployment. The research promoted its uniqueness by noting that although multiple studies have documented the salience of these family processes to adaptive responses to stress, trauma and loss, most have been cross-sectional or qualitative in design and/or have not been conducted with military populations. Army Medicine has the opportunity to apply the suggestions from the results in treating children negatively affected by a caregiver's deployment by using interventions to support family resilience processes such as effective communication, emotional awareness and regulation, collaborative problem-solving, and development of shared meaning about stressful experiences. The Office of the Surgeon General also can continue citing the research conducted while discussing the Ready and Resilient Campaign. Coverage of this study was disseminated by the *American Forces Press Service*, *Army News Service* and *Patch*, and included media mentions of Lt. Gen. Patricia Horoho.

#### **Military Medicine: Management of Seizure Disorders in the Deployed Environment: A Treatment Guide for the Non-Neurologist in Theater**

Focusing on the deployed environment, the article noted the lack of research into the difficulty for medical professionals in treating those suffering from seizures. Two case studies served as the basis for guidelines on how non-neurologists in a deployed environment could address various issues, including management of pharmacological drugs and evacuation concerns. Information related to seizure care can allow Army Medicine to highlight state-of-the-art responses for Soldiers suffering from regular seizures.

### **Military Medicine: Update: Community-Acquired Methicillin-Resistant Staphylococcus aureus Skin and Soft Tissue Infection Surveillance Among Active Duty Military Personnel at Fort Benning GA, 2008–2010**

Looking at methicillin-resistant staphylococcus (MRSA), the article detailed the rates of infection at Fort Benning, Ga. Male Soldiers under the age of 25 comprised the majority MRSA SSTI cases, according to two different methods of data collection – the Martin Army Community Hospital and the HL7 laboratory. Results suggested that Army Medicine has the potential to learn from and control for MRSA in recruits at Fort Benning.

#### ***Medical Protocol and Training***

### **JAMA: Implications of Combat Casualty Care for Mass Casualty Events**

The evaluation of Combat Casualty Care highlighted care during transport, hospital-based care and various lessons from wartime trauma care. The article summarized lessons learned from combat and applied them to mass casualty events, highlighting the potential life-saving of civilians. Army Medicine can continue, as with the Boston Marathon bombing, to highlight the positive impact of lessons learned from combat on civilian care.

### **NEJM: On Access and Accountability — Two Supreme Court Rulings on Generic Drugs**

The New England Journal of Medicine’s discussion on the Supreme Court’s ruling regarding generic drug availability focused on practices that pharmaceutical companies pursue to further monopolize the market. The resulting decisions affected the administration of generic versus name-brand drugs, thus indirectly disturbing Soldier care.

### **NEJM: Taking Our Medicine — Improving Adherence in the Accountability Era**

The entry highlighted the average American’s reluctance to adhere to medication or medical care, detailing the \$100 billion to \$290 billion annually of cost to the U.S. In focusing on efforts to improve adherence and quality of life, the New England Journal of Medicine turned to the Affordable Care Act as a model, shifting reimbursement from fee for service toward rewarding improved quality, outcomes and efficiency. The patient-centered medical home (PCMH), an effort pursued by military medicine, is lauded as an example of accountability measures aimed at improving care.

## **Military Medicine: A Comparison of Deployed Occupational Tasks Performed by Different Types of Military Battalions and Resulting Low Back Pain**

The study aimed to determine certain tasks required by a Brigade Combat Team, the resulting impact on low back pain (LBP) and noted which tasks predict LBP in the team. Military Medicine employed 805 Soldiers who were deployed to Afghanistan for a year in the survey. The study results indicated a direct correlation between a history of LBP, time wearing body armor and the possibility of LBP while deployed. Army Medicine can use the information to develop policy related to LBP and body armor wear.

## **Military Medicine: Field-Based PCR for Rapid Diagnosis of Cutaneous Anthrax in the Deployed Setting Using the Joint Biological Agent Identification and Diagnostic System**

Military Medicine published research that consisted of determining methods for a rapid diagnosis of cutaneous anthrax in a combat setting. The research presented a case using a ruggedized polymerase chain reaction in combat conditions. Research offered details on the Army's process of detecting anthrax as a potential biowarfare agent and concluded that the Army's methodology for detection can help with diagnosis; however, initial clinical responses are key. Army Medicine has the opportunity to capitalize on clinical training to avoid diagnostic delays and distractions.

## **Military Medicine: Intra-Articular Synovial Sarcoma Treated With a Transfemoral Amputation: A Case Report and Review of the Literature**

This study from Military Medicine discussed a case of monophasic intra-articular synovial sarcoma in the knee of a service member who was treated with a transfemoral amputation. This case is of an active duty serviceman who had pain and fullness in his right knee and opted for amputation instead of continued surgery, which resulted in no further evidence of recurrence or metastatic disease. Army Medicine has the opportunity to use this case report to consider amputation as a potential surgical treatment for intra-articular synovial sarcoma.

## **Military Medicine: A Culture of Patient Safety in Military Medicine**

Military Medicine published a study on preventable medical errors that led to patient deaths and identifies that these problems occur in "stovepipes." The study then identifies that improving health care standards, identifying specific roles and responsibilities to team members, executing the mission, and being accountable for ones actions would improve overall patient safety. Army Medicine has the opportunity to use the findings in the study and apply them to medical teams.

## **Military Medicine: When Will Acupuncture Become a First-Line Treatment for Acute Pain Management?**

This study published by Military Medicine discussed the possibly use of acupuncture as a first-line treatment for pain management. The study showed multiple cases of success in acupuncture being effective in managing pain and that an advantage to this method over drugs is that there are no unintended consequences. Army Medicine has the opportunity to further study the effectiveness of acupuncture in combat settings.

## **PTSD**

### **JAMA: Mental Health Response to Community Disasters: A Systematic Review**

This study from the Journal of the American Medical Association highlighted exposure to a disaster that could potentially result in post-traumatic stress and other mental health problems. The study organized disaster mental health literature into an operational framework for the implementation of mental health services for individuals affected by disasters. The study concluded that the integration of preventative and responsive services in public health and clinical systems of care is important to counter mental health issues surrounding disasters. Army Medicine has the opportunity to review the study and identify areas in which to improve on disaster relief efforts and how this applies to combat situations.

### **JAMA: Management of Acute Stress, PTSD, and Bereavement WHO Recommendations**

The Journal of the American Medical Association published a study that addressed the treatment gap for mental disorders in low and middle income countries. The study notes the World Health Organization's (WHO) efforts to develop a new module on conditions specifically related to stress and PTSD. The WHO outlines several recommendations for the treatment of PTSD in both children and adults. Army Medicine has the opportunity to use this information to conduct further research on treatment of PTSD in local areas affected by combat.

### **RAND Corporation: The Role and Importance of the 'D' in PTSD**

Reporting by the RAND Corporation discussed the American Psychiatric Association (APA) board of trustees deciding to retain the word "disorder" in the term "posttraumatic stress disorder" (PTSD), despite U.S. Army leadership's request to change the terminology. Army officials requested to alter the naming of the disease due to their opinion that stating the word "disorder" is inducing a stigma of the disease and removing it would encourage more Soldiers suffering from symptoms to access care. Army Medicine has the opportunity to note that while there is a difference in labeling of the disorder between its own Force and the APA, the disease still remains one in the same. Reporting on this study was disseminated by *USA Today*, which was then reprinted in a range of local news outlets.

### **JAMA: Treatment of Comorbid Substance Dependence and Posttraumatic Stress Disorder**

An article by the Journal of the American Medical Association highlights research conducted that showed the benefits of combining the treatment of comorbid PTSD and alcohol dependence simultaneously. While the research discussed both issues, the article focused more on the effects of the combined treatment on PTSD. While previous research advised against the dual treatment of the separate diseases, the current results showed benefits from the combined use of psychotherapy and pharmacotherapy for the treatment of comorbid PTSD and substance use disorder. Army Medicine has the opportunity to further the existing research by comparing the relative efficacy of integrated versus parallel approaches to treatment. Coverage of the research was disseminated by a range of trade publications, including *MedPage Today*, *HealthDay* and *Internal Medicine News*, and prominent media outlets, such as the *Associated Press*, *Bloomberg News*, *CNN*, *The New York Times* and *USA Today*.

## **JAMA: Recovery After Violence and Human Rights Abuses**

The study published by the Journal of the American Medical Association focused on quality of life after a trauma based on the treatment received to help with recovery and healing. The case study discussed a patient who experienced pain and PTSD from a trauma experienced as a refugee and mentioned recommendations from the World Health Organization. The study suggested a need for stronger levels of evidence from other studies and clinical trials to support recovery-aimed interventions. Army Medicine has an opportunity the further the study with providing help to civilians affected by warzones.

## **Military Medicine: A Yoga Program for the Symptoms of Post-Traumatic Stress Disorder in Veterans**

Research conducted by Military Medicine was designed to evaluate the feasibility and effectiveness of a yoga program as an adjunctive therapy for improving PTSD symptoms. While researching veterans with military-related PTSD, the results noted a significant improvement in PTSD hyperarousal symptoms and overall sleep quality, as well as daytime dysfunction related to sleep. However, the application of yoga did not show a significant improvement in the symptoms of overall PTSD, anger or quality of life outcome scores. Army Medicine has the opportunity to conduct further research into the application of yoga as a treatment for PTSD if it should prove to be a feasible, equally effective alternative treatment. Coverage of this study was disseminated by *Army Times*.

### ***Sexual Assault***

## **JAMA: An Evidence-Based Response to Intimate Partner Violence**

Reporting by the Journal of the American Medical Association detailed guidelines provided by the World Health Organization's *Responding to Intimate Partner Violence and Sexual Violence Against Women*. The evidence-based recommendations to guide clinicians are relevant to Army Medicine in that clinicians may be the first professional contact for persons exposed to intimate partner violence (IPV). Army Medicine has the opportunity to adapt recommendations from the *Care for Survivors of IPV* to its treatment plan due its discussion of trauma and PTSD.

### ***Substance Abuse***

## **NEJM: Abusive Prescribing of Controlled Substances — A Pharmacy View**

The study published by the New England Journal of Medicine highlighted the public's focus on illness and death caused by inappropriate use of controlled substances, specifically opioids. The study focused on the growing number of prescriptions being given out for treatment of chronic pain. The study outlined the necessary steps that clinics and pharmacists need to take in order to ensure the proper use of prescriptions for controlled substances. Army Medicine has the opportunity to use the study as a platform to curb controlled substance abuse by Soldiers upon returning from deployment.

## **JAMA: Concurrent Naltrexone and Prolonged Exposure Therapy for Patients With Comorbid Alcohol Dependence and PTSD**

Research conducted by the Journal of the American Medical Association sought to compare the efficacy of evidence-based treatment for alcohol dependence (naltrexone) plus evidence-based treatment for PTSD (prolonged exposure therapy), their combination and supportive counseling. The research highlighted the need for medical professionals to address the two diseases in a combined manner, but that alcohol addiction did not always occur in those that suffered PTSD. However, while those that suffered PTSD frequently were dependent on alcohol, the combined treatment showed positive results on those suffering exclusively from alcoholism. Army Medicine has the opportunity to further the research conducted to discover if large-scale, dual treatment would be a more feasible option to provide help to those that suffer from the diseases. Coverage of the research was disseminated by a range of trade publications, including *MedPage Today*, *HealthDay* and *Internal Medicine News*, and prominent media outlets, such as the *Associated Press*, *Bloomberg News*, *CNN*, *The New York Times* and *USA Today*.

### **TBI**

## **JAMA: Traumatic Brain Injury: An International Knowledge-Based Approach**

The Journal of the American Medical Association featured a study on Traumatic brain injuries that highlighted the lack of knowledge and when serious injuries occur and are dismissed by medical professionals. The study noted that awareness for TBI has increased, however, there is a need for a new way to classify injuries to better understand how to treat TBI. Research also indicated that there is a need for cooperation between national and international organizations, including the BRAIN Initiative, to ensure proper clinical care for TBI. Army Medicine has the opportunity to provide research on TBI from combat related injuries in order to provide competent care for those outside of the military.

### **Other**

## **JAMA: Researchers Use Human Stem Cells to Build a Functional Liver**

This study published by the Journal of the American Medical Association highlighted Japanese researchers that coaxed human stem cells to form into a fully functioning liver. The research indicated that the potential for transplanting organ buds grown from stem cells for the treatment of organ failure. Army Medicine has the opportunity to further research the scope of treatment involving organ transplants.

## **JAMA: Perspectives on Complementary and Alternative Medicine Research**

Reporting discusses examples of alternative medicine and its effective and ineffective applications. A few examples of effective mind-body approaches, such as yoga and massage, were cited in emerging evidence is reflected in practice guidelines from the American College of Physicians, the American Pain Society and the Department of Defense. However, the article continued on to highlight ineffective alternative medicine applications, such as St John's wort for major depression, noting that those receiving treatment who cited alleviated symptoms were only experiencing placebo effects. Army Medicine has the opportunity to conduct further research on alternative medicine, which could foster a wider

range of research partnerships and improve the dialogue between health care professionals and patients. Coverage discussing the study highlighted the effects of yoga and was disseminated by *Army Times*.

## **JAMA: Cancer-Causing Infections Decline After HPV Vaccine Introduced**

The Journal of the American Medical Association published a study on the decline of cancer-causing infections after the HPV vaccination was introduced. The study focused on investigations conducted by the CDC on the decline of HPV among girls and women aged 14 to 59 years. Investigators concluded that there needs to be an increase in vaccination rates in order to protect against cancer caused by HPV. Army Medicine has the opportunity to disseminate this information to female Soldiers to help prevent cancer-causing infections from HPV.

### **Medical Journal Clips**

#### ***Behavioral Health***

## **Suicide, Mental Disorders, and the US Military**

Journal of the American Medical Association  
Charles C. Engel, MD, MPH  
7 August 2013

Suicide in the US military has been the recent focus of controversy and misunderstanding. The disappointing lack of valid and generalizable epidemiologic research from which to confidently ground clinical and policy decisions has only helped to fuel debates about the magnitude and causes of the problem and how best to approach it. Military suicides are sometimes characterized as epidemic in proportion, and many observers appear to assume that the incidence is escalating out of control as a consequence of prolonged combat and associated stress. Although a worrisome increase in the rate of military suicide has occurred since 2005, suicide in the military remains rare, a fact that leads to many challenges when trying to predict, study, and prevent suicide.

In this issue of *JAMA*, LeardMann and colleagues follow up Millennium Cohort Study participants to investigate prospective, longitudinal factors associated with suicide among US Armed Forces personnel serving between 2001 and 2008. The study included 151 560 active and reserve component service members across all branches of service who were observed a collective 707 493 person-years. During the study period, 83 suicides occurred and the authors estimated a suicide rate of 11.73 per 100 000 person years. A range of potential deployment-related and clinical risk factors were evaluated using self-report and administrative data sources. Suicides were identified using the National Death Index and the Department of Defense Medical Mortality Registry. Several treatable mental health disorders known to be associated with suicide in civilian studies (manic-depressive disorder, depression, and alcohol-related problems) were significantly related to suicide risk, whereas deployment-

related factors (combat experiences, cumulative days deployed, and number of deployments) were not. The findings proved robust across 2 major methods of analysis, Cox proportional hazards modeling and a nested case-control design.

These findings offer some potentially reassuring ways forward: the major modifiable mental health antecedents of military suicide—mood disorders and alcohol misuse—are mental disorders for which effective treatments exist. Furthermore, evidence-based service delivery models, particularly those involving primary care, are well known, supported by randomized trial evidence of lasting improvements in suicidal ideation among patients with depression, and designed to overcome population stigma and barriers to care. Collaborative primary care management is a strategy strongly recommended by the National Institute of Mental Health to military senior leaders as perhaps the most promising suicide prevention strategy. This strategy has been embraced and implemented worldwide for nearly 3 million primary care visits across the US Army health system since 2007 using a team care approach to screening, care management, and enhanced specialist involvement. Additionally, this strategy uses an online decision support system offering worldwide and real-time capacity to measure individual patient symptom status and create an illness registry to enhance, monitor, and benchmark facility and system-level continuity of care, intervention fidelity, and treatment outcomes.

However, lasting military success in the identification and treatment of the mental illness antecedents of suicide will require overcoming current overreliance on outdated combat and operational stress models of suicide prevention. Such success will also require addressing long-standing military ambivalence toward the medical model of mental illness—an ambivalence affecting service members, military clinicians, and senior leaders alike. Service members are leery of the diagnosis of a mental disorder because of its potential career implications. Patient confidentiality for service members must be enhanced to approximate civilian standards except when there is an imminent threat to combat-related mission. Military mental health clinicians must leave behind the age-old and empirically unsupported military mental health view that a diagnostic label reduces service members' will to recover and function. To alleviate the illness, it must first be recognized, then treated using evidence-based approaches, and reassessed using reliable and valid methods of measurement to ensure treatment is accountable and effective. Moreover, military leaders must trust and empower the mental health service system, reduce pressure on unit commanders to prevent suicides and other adverse mental health outcomes for which there is no evidence they can control, and respect service members' confidentiality except in narrow, well-defined, and specific circumstances.

While the study by LeardMann et al provides important information about suicide in the military, there are no vaccines to prevent mental disorders, and the study findings suggest the need to remain circumspect about the capacity to reduce suicide rates in practice. The population attributable risk percent (PAR%) reported by LeardMann et al is an estimate of the percentage of military suicides that might be prevented by eliminating a given risk factor assuming a causal link between the risk factor and suicide. The estimated PAR%s for depression (11.2%), manic-depressive disorder (4.8%), and alcohol-related problems (18.4%) suggest only a modest reduction under ideal conditions. However, depression, manic-depressive disorder, and alcohol problems often occur concurrently, are difficult to identify, and respond only partially to treatment. Linkages between suicide events and these disorders are also variable, complex, and involve multiple factors.

Because the analysis for the study by LeardMan et al ended in 2008, some may misinterpret the findings as evidence that 12 years of war is not to blame for the recent increase in military suicide rates. In addition, the study did not compare civilian with military populations and it remains possible that the broad organizational consequences of prolonged conflict have resulted in increases in mental disorders and suicide across both deployed and nondeployed personnel. In addition, these data should be considered in light of recently published evidence of increases in the suicide rate among the general US population, from 13.7 per 100 000 population in 1999 to 17.6 per 100 000 in 2010. In this context, it should be

noted that the military is but one sector of society, and service members are likely to experience many of the same broad pressures, forces, and trends as do civilians. For example, upward trends in the general US suicide rate have been recently linked to changes in the status of the national economy and unemployment rates. The downturn in the national economy was associated with increased military enlistment, and with the current plan to reduce the size of the military, there is little reason to think that the effect of future economic prospects on the incidence of service member suicide will be different than for comparable civilians.

The Millennium Cohort Study, the large rolling enrollment longitudinal cohort study that comprised the basis for the study by LeardMann et al, was recommended by the US Institute of Medicine during efforts in the 1990s to understand the health issues associated with 1991 Gulf War service. This study continues to be an invaluable tool for understanding a range of physical and mental health risk factors and outcomes among US service members and must be sustained into the foreseeable future. A similar evolution is needed in the way the military health system studies clinical interventions and evaluates clinical programs. Particularly in the mental health arena, the military cannot afford to rely on evidence generated from settings and contexts vastly different from its own. Developing a sound organizational infrastructure and cadre of personnel with the appropriate expertise and experience that enables ongoing clinical testing, implementing, evaluating and monitoring of new interventions and programs in real time (perhaps in collaboration with the Department of Veterans Affairs), may help ensure that rigorous longitudinal studies of risk factors, important though they are, will not serve as the final scientific word on suicide and other mental health issues in the US military.

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## **Risk Factors Associated With Suicide in Current and Former US Military Personnel**

Journal of the American Medical Association

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7 August 2013

### **ABSTRACT**

**Importance** Beginning in 2005, the incidence of suicide deaths in the US military began to sharply increase. Unique stressors, such as combat deployments, have been assumed to underlie the increasing incidence. Previous military suicide studies, however, have relied on case series and cross-sectional investigations and have not linked data during service with postservice periods.

**Objective** To prospectively identify and quantify risk factors associated with suicide in current and former US military personnel including demographic, military, mental health, behavioral, and deployment characteristics.

**Design, Setting, and Participants** Prospective longitudinal study with accrual and assessment of participants in 2001, 2004, and 2007. Questionnaire data were linked with the National Death Index and the Department of Defense Medical Mortality Registry through December 31, 2008. Participants were current and former US military personnel from all service branches, including active and Reserve/National Guard, who were included in the Millennium Cohort Study (N = 151 560).

August 2013

**Main Outcomes and Measures** Death by suicide captured by the National Death Index and the Department of Defense Medical Mortality Registry.

**Results** Through the end of 2008, findings were 83 suicides in 707 493 person-years of follow-up (11.73/100 000 person-years [95% CI, 9.21-14.26]). In Cox models adjusted for age and sex, factors significantly associated with increased risk of suicide included male sex, depression, manic-depressive disorder, heavy or binge drinking, and alcohol-related problems. None of the deployment-related factors (combat experience, cumulative days deployed, or number of deployments) were associated with increased suicide risk in any of the models. In multivariable Cox models, individuals with increased risk for suicide were men (hazard ratio [HR], 2.14; 95% CI, 1.17-3.92;  $P = .01$ ; attributable risk [AR], 3.5 cases/10 000 persons), and those with depression (HR, 1.96; 95% CI, 1.05-3.64;  $P = .03$ ; AR, 6.9/10 000 persons), manic-depressive disorder (HR, 4.35; 95% CI, 1.56-12.09;  $P = .005$ ; AR, 35.6/10 000 persons), or alcohol-related problems (HR, 2.56; 95% CI, 1.56-4.18;  $P < .001$ ; AR, 7.7/10 000 persons). A nested, matched case-control analysis using 20:1 control participants per case confirmed these findings.

**Conclusions and Relevance** In this sample of current and former military personnel observed July 1, 2001-December 31, 2008, suicide risk was independently associated with male sex and mental disorders but not with military-specific variables. These findings may inform approaches to mitigating suicide risk in this population.

Despite universal access to health care services, mandatory suicide prevention training, and other preventive efforts, suicide has become one of the leading causes of death in the US military in recent years.<sup>1-3</sup> Suicide rates across the population of active-duty US military personnel began to increase sharply in 2005 from a baseline rate of 10.3 to 11.3 per 100 000 persons to a rate of 16.3 per 100 000 persons in 2008, with the highest rates among Marine Corps and Army personnel (19.9 and 19.3 per 100 000 persons). Since 2009, suicide rates among those on active-duty status have stabilized at approximately 18 per 100 000.

Despite this increase, suicide remains a rare outcome that is challenging to study. Studies among military populations have not been able to adequately examine the association between deployment characteristics and suicide following military discharge. Military separations due to medical or administrative reasons (eg, mental disorders, substance misuse, misconduct) are likely to bias incidence figures and risk-factor estimates in studies that fail to link records between active service and postmilitary periods. Separation of service members with mental disorders, for example, could lead to underestimates of incidence or risks associated with these conditions in studies based only on active-duty members, and possibly overestimates in studies that only involve veterans. Previous studies have not linked US Department of Defense data with national death records, thus limiting the ability to conduct comprehensive studies across inservice and postservice time periods.

Understanding the circumstances and factors leading to suicide in military members and identifying appropriate interventions is of high priority to military and civilian leaders. This study prospectively examined and quantified factors associated with suicide risk in a large population of active, Reserve, and National Guard members across all branches of the military during and following service.

## **METHODS**

### **Study Population**

Launched in 2001, the Millennium Cohort Study is the largest longitudinal US military study. Designed to prospectively evaluate the health impact of serving in the military, it is a study drawn from randomly selected samples of US military service members on rosters as of October 2000 (panel

1, July 2001-June 2003), October 2003 (panel 2, June 2004-February 2006), and October 2006 (panel 3, June 2007-December 2008) including members from all service branches and components. Panel 1 was a probability-based sample of the entire military population with oversampling for women, Reservist/National Guardsmen, and those who had previously deployed. Designed to augment panel 1, personnel invited to join panels 2 and 3 had 1 to 3 years of military service and were oversampled for Marines and women. Of those contacted (n = 491 659), a baseline questionnaire and consent to volunteer was provided by 151 597 service members, resulting in a 31% cumulative baseline response rate. The cohort has been shown to have minimal response bias and although similar to the US military population in 2008, members of the cohort are proportionately more likely to be women and younger (17-24 years old) ( $\geq 10\%$  likely); and college educated, of white non-Hispanic race/ethnicity, and serving in the Air Force ( $>5\%$  likely) at baseline. Cohort participants are requested to complete a survey approximately every 3 years regarding mental, behavioral, and functional health, regardless of their current military status. Detailed descriptions of the study population and methods have been published elsewhere. For this analysis, the population included eligible participants from the first 3 panels who completed a baseline questionnaire and did not have missing or undetermined cause of death information (99.9% of all participants). Due to the relatively low number of suicides in the cohort, data from these 3 panels were combined for all analyses. This research has been conducted in compliance with all applicable federal regulations governing the protection of human subjects in research (Protocol [Naval Health Research Center] NHRC.2000.0007).

### **Suicide**

Suicide deaths were identified, during and following military service, using mortality data from the National Death Index and the Department of Defense Medical Mortality Registry (DoD MMR). The DoD MMR, maintained in the Mortality Surveillance Division of the Armed Forces Medical Examiner System, contains detailed information on all US military active-duty deaths, including Reserve and National Guard members in an activated status, regardless of geographic location. The DoD MMR also includes detailed information on any former military members who died while serving as civilians or contractors during the current operations. A previous study found that National Death Index together with DoD MMR captured 99% of deaths in this cohort. Consistent with this previous study, a participant was identified as a decedent if the cohort data and information provided by the mortality data sources had an exact agreement on at least 2 personal identifiers consisting of Social Security number, first and last name, and full date of birth. Deaths as a result of suicide were identified using *International Classification of Diseases, 10th Revision* codes X60-X84, Y87, and U03.

### **Deployment**

Deployment, a time-dependent variable, was based on DoD personnel files obtained from the Defense Manpower Data Center. Service members were identified as deploying in support of operations in Iraq and Afghanistan from September 11, 2001, through December 31, 2008 (ie, Operation Iraqi Freedom [OIF] and Operation Enduring Freedom [OEF]), based on direct report from personnel offices of the service branches or report of receiving imminent danger pay, hardship duty pay, or combat zone tax exclusion benefits. Participants who did not deploy in support of OIF/OEF prior to December 31, 2008 were classified as not deployed for the entire study period. Others were classified as not deployed until the first date of deployment, at which time they were classified as deployed (with or without combat experience) for the remaining follow-up time. Combat experience was assessed using data from the Millennium Cohort and the Post-Deployment Health Assessment (PDHA) surveys. Data from the PDHA, a survey administered to all service members within 30 days of returning from deployment, were obtained from the Armed Forces Health Surveillance Center for members from all service branches. The PDHA asks respondents about encountering dead bodies or seeing people killed, discharging a weapon, and feeling in great danger of being killed during their most recent deployment. The Millennium Cohort survey includes a

question that asks, “During the past 3 years, have you been personally exposed to any of the following? (do not include TV, video, movies, computers, or theater): (1) witnessing a person’s death due to war, disaster, or tragic event, (2) witnessing instances of physical abuse (torture, beating, rape), (3) dead and/or decomposing bodies, (4) maimed soldiers or civilians, and (5) prisoners of war or refugees.” Among those deployed, combat experience was identified by an affirmative response to 1 or more of these experiences from either questionnaire. Cumulative days deployed and number of deployments were based on the total number of days deployed and number of deployments, respectively, in support of OIF/OEF from 2001 through 2008. Deployment experience to the 1991 Gulf War or to Bosnia, Kosovo, or Southwest Asia between 1998 and 2000 was assessed as a separate variable referred to as “pre-2001 deployment experience.”

### **Covariates**

Self-reported physical functioning was assessed at baseline using the physical component score of the Medical Outcomes Study Short Form 36-Item Survey for Veterans (SF-36V). In order to examine if those at the extremes of the scale were at increased or decreased risk for suicide, physical functioning was categorized into 3 levels (<15th percentile, 15th-85th percentiles, and >85th percentile), consistent with previous publications.

Previous research has indicated that individuals who die by suicide are more likely to have experienced adverse life events. Consequently, the presence of stressful life events was assessed using Millennium Cohort Study questions and a modified version of the Social Readjustment Rating Scale scoring system. Based on severity, each type of stressful life event, such as experiencing divorce or severe illness, was assigned a point value (between 48 and 83 points) and then collectively scored. Based on the summation of baseline scores, participants were categorized as having either low/mild (<200 points) or moderate/major (≥200 points) life stress.

The mental and behavioral covariates (including posttraumatic stress disorder [PTSD], depression, manic-depressive disorder, panic/anxiety syndromes, heavy or binge drinking, and alcohol-related problems) were analyzed using 2 distinct methods: (1) assessed using only baseline data and (2) assessed using all available data for each individual (responses from 1-3 questionnaires).

PTSD was assessed using the PTSD Checklist-Civilian Version (PCL-C), a 17-item self-reported measure and a question that asked participants if they had ever been diagnosed with PTSD from a health professional. A positive PTSD screen was based on reporting a moderate or higher level of at least 1 intrusion symptom, 3 avoidance symptoms, and 2 hyperarousal symptoms, criteria established by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*). Participants who screened positive or reported ever being diagnosed with PTSD were classified as having PTSD.

Similarly, depression was assessed using the 9 depression items of the Patient Health Questionnaire (PHQ). The scoring algorithm that corresponds to the depression diagnosis from the *DSM-IV* was used to identify individuals with a positive depression screen. Participants who screened positive or reported ever having a depression diagnosis were classified as having depression. Similarly 15 panic items and 6 generalized anxiety items from the PHQ were used to assess presence of panic or other anxiety syndromes. Manic-depressive disorder was identified by those who reported that a doctor or other health professional ever diagnosed them with manic-depressive disorder.

Heavy weekly drinking was defined as consumption of more than 14 drinks per week for men or 7 drinks per week for women. Binge drinking was defined as reporting of drinking 5 or more drinks for men or 4 or more drinks for women on at least 1 day or occasion during the past year. Participants who met the threshold for either drinking condition were classified as heavy or binge drinkers. Assessed using questions from the

PHQ, alcohol-related problems were determined by endorsement of at least 1 of 5 problems (eg, driving after having several drinks or drinking alcohol even though a physician suggested stopping) in the last 12 months.

Demographic and military-specific data were obtained at baseline from electronic personnel files maintained by the Defense Manpower Data Center including sex, date of birth, educational level, marital status, race/ethnicity, military rank, service component, service branch, occupation, and date of separation from the military. Age and military service status were assessed as time-dependent variables. Those participants who did not separate from the military were classified as current service members. All others were classified as current service members until their date of separation, at which time they were classified as former service members for the remaining follow-up time.

### **Statistical Analysis**

The overall crude suicide rate as well as the age- and sex-adjusted (direct standardization based on the 2000 US population) suicide rate per 100 000 person-years were calculated. Characteristics by suicide deaths were compared using crude suicide rates and  $\chi^2$  tests. Person-years for OIF/OEF deployment and military service status were calculated using the time-varying status for the crude suicide rates. Attributable risk (AR), also referred to as risk difference, was calculated by subtracting the incidence of suicide in the unexposed group from the incidence of suicide in the exposed group, presented as the number of suicide cases per 10 000 persons. The population AR percent was calculated as the prevalence of the risk factor among the suicide deaths multiplied by the hazard ratios (HRs) minus 1 divided by the HR multiplied by 100 (prevalence among cases  $\times [(HR-1)/HR] \times 100\%$ ). Cox proportional hazards modeling was used to estimate unadjusted and age- and sex-adjusted HRs and 95% CIs for suicide. Multivariable Cox proportional hazards models to assess the association between deployment and suicide completion were built using a backwards elimination algorithm that initially included all variables significantly associated with suicide ( $P < .05$ ) after age and sex adjustment (sex, depression, manic-depressive disorder, heavy or binge drinking, alcohol-related problems). Deployment was forced into these models, with covariates removed sequentially until the final model included only significant ones ( $P < .05$ ). The multivariable Cox proportional hazards models were performed 2 ways: (1) factors were assessed at baseline with the inclusion of deployment as a time-dependent variable; and (2) factors were assessed as time-dependent variables, except sex. For example, using the latter method, participants who screened positive for a mental or behavioral condition on their second (or third) questionnaire were classified as having that condition for the remaining time of their follow-up period. For all Cox models, participants were censored at the date of a nonsuicide death or the end of the study period (December 31, 2008). Person-days for each participant were calculated from the date of baseline survey completion to the date of death (suicide or nonsuicide death) or end of study. For inclusion into each Cox model, participants had to have complete data for all variables in that model. The proportionality assumption for recent deployment was verified by assessing the correlation between the Schoenfeld residuals and person-days.

In an effort to further investigate the military-specific risk factors and underlying mental disorders, a nested case-control analysis was conducted that matched each suicide case to 20 control participants on birth year (within 2 years), sex, race/ethnicity, marital status, enrollment (within 180 days), service branch, and military rank. Similar to the multivariable Cox model, deployment and variables that were significantly ( $P < .05$ ) associated with suicide were entered into a conditional logistic regression model (deployment, depression, manic-depressive disorder, heavy or binge drinking, and alcohol-related problems). Covariates were removed in the same manner as the multivariable Cox model, yielding a final model that included only significant variables ( $P < .05$ ). To be considered for inclusion into the nested case-control analysis, participants had to have complete data on all the matching characteristics as well as the variables that were significantly associated with suicide after age and sex adjustment. All reported  $P$  values were 2 sided. Data management and statistical analyses were performed using SAS software version 9.3 (SAS Institute, Inc).

## RESULTS

Of the 151 597 Millennium Cohort participants (77 047 in panel 1, 31 110 in panel 2, and 43 440 in panel 3), 151 568 were eligible for analysis. Eight participants were excluded due to missing or undetermined cause of death data. The study population was composed of the remaining 151 560 participants (99.9% of all participants), of whom 646 (0.4%) died between 2001 and 2008. Of the decedents, 83 (12.8% of total deaths) were the result of suicide, during a total of 707 493 person-years of observation, yielding a crude rate of 11.73 (95% CI, 9.21-14.26) suicides per 100 000 person-years or an age- and sex-adjusted rate of 9.60 (95% CI, 7.10-12.10) suicides per 100 000 person-years. Crude suicide rates (per 100 000 person years) were highest among those with manic-depressive disorder (87.55, 95% CI, 10.84-164.30; n = 5), alcohol-related problems (27.67, 95% CI, 16.83-38.52; n = 25), and depression (26.94, 95% CI, 14.83-39.05; n = 19). Those with a suicide death were proportionately more likely, compared with all other participants, to have the following characteristics: fewer cumulative deployment days, combat specialist occupation, pre-2001 deployment experience, male sex, depression, manic-depressive disorder, heavy or binge drinking, and alcohol-related problems (Table 1 and Table 2).

Table 1. Military Characteristics of Millennium Cohort Participants by Suicide Death

Table 1. Military Characteristics of Millennium Cohort Participants by Suicide Death

Characteristic <sup>a</sup>	Crude Suicide Rate/100 000 Person-Years (95% CI)	No. (%) <sup>b</sup>	
		Nonsuicide (n = 151 477)	Suicide Death (n = 83)
OIF/OEF deployment <sup>c</sup>			
Not deployed	10.70 (7.67-13.72)	72 635 (48.0)	48 (57.8)
Deployed without combat	12.80 (5.84-19.76)	32 657 (21.6)	13 (15.7)
Deployed with combat	12.39 (6.82-17.96)	45 435 (30.0)	19 (22.9)
No. of deployments <sup>c</sup>			
0	13.13 (9.41-16.84)	72 635 (48.0)	48 (57.8)
1	11.32 (6.59-16.05)	46 291 (30.6)	22 (26.5)
>1	8.81 (4.02-13.60)	32 551 (21.5)	13 (15.7)
Cumulative days deployed <sup>d</sup>			
0	13.13 (9.41-16.84)	72 635 (48.0)	48 (57.8)
1-90	14.62 (1.81-27.43)	6950 (4.6)	5 (6.0)
91-180	18.36 (7.97-28.74)	14 833 (9.8)	12 (14.5)
181-365	9.77 (4.46-15.08)	31 230 (20.6)	13 (15.7)
>365	4.58 (0.57-8.59)	25 829 (17.1)	5 (6.0)
Military rank <sup>d</sup>			
Junior enlisted	13.43 (9.22-17.65)	82 362 (54.4)	39 (47.0)
Noncommissioned officer	10.98 (7.05-14.91)	42 793 (28.3)	30 (36.1)
Officer	9.73 (4.63-14.82)	26 322 (17.4)	14 (16.9)
Service component			
Reserve/National Guard	10.62 (6.88-14.35)	54 560 (36.0)	31 (37.3)
Active	12.52 (9.11-15.92)	96 917 (64.0)	52 (62.7)
Service branch			
Army	12.98 (9.10-16.86)	67 209 (44.4)	43 (51.8)
Navy/Coast Guard	8.59 (3.51-13.67)	27 437 (18.1)	11 (13.3)
Marine Corps	11.24 (1.39-21.09)	13 310 (8.8)	5 (6.0)
Air Force	11.78 (7.07-16.50)	43 521 (28.7)	24 (28.9)
Occupation			
Combat specialist	15.08 (8.47-21.69)	26 851 (17.7)	20 (24.1)
Health care	9.16 (2.38-15.95)	16 250 (10.7)	7 (8.4)
Functional support, service and supply	9.43 (5.19-13.67)	42 603 (28.1)	19 (22.9)
Mechanical or electrical repair	17.97 (11.54-24.40)	36 526 (24.1)	30 (36.1)
Other	5.39 (1.40-9.39)	29 214 (19.3)	7 (8.4)
Pre-2001 deployment experience <sup>e</sup>			
No	11.77 (8.79-14.75)	122 613 (80.9)	60 (72.3)
Yes	11.63 (6.88-16.38)	28 864 (19.1)	23 (27.7)
Military service status <sup>f</sup>			
Current service member	11.04 (8.24-13.83)	108 869 (71.9)	60 (72.3)
Former service member	14.04 (8.30-19.77)	42 608 (28.1)	23 (27.7)

Abbreviations: OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom.

<sup>a</sup> Assessed at baseline except participants' deployment and military service status. Cumulative days deployed, occupation, and pre-2001 deployment status were statistically significant ( $P < .05$ ).

<sup>b</sup> Percentages are based on the population size for each group but exclude individuals with missing data, therefore, percents may not sum to 100.

<sup>c</sup> Based on OIF/OEF deployment September 11, 2001-December 31, 2008. Crude suicide rates for OIF/OEF deployment were based on time-varying status, whereas, the status was fixed for number of deployments and cumulative days deployed.

<sup>d</sup> Ranks include junior enlisted (E1-E4), noncommissioned officer (E5-E9), and officer (O1-O10 and W1-W5).

<sup>e</sup> Deployed to the 1991 Gulf War or to Bosnia, Kosovo, or Southwest Asia 1998-2000.

<sup>f</sup> Based on status at the end of follow-up (December 31, 2008). Crude suicide rates were based on time-varying status.

Table 2. Characteristics of Millennium Cohort Participants by Suicide Death

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Baseline Characteristics <sup>a</sup>	Crude Suicide Rate/100 000 Person-Years (95% CI)	No. (%) <sup>b</sup>	
		Nonsuicide (n = 151 477)	Suicide Death (n = 83)
<b>Sex</b>			
Men	13.69 (10.44-16.94)	103 420 (68.3)	68 (81.9)
Women	7.12 (3.52-10.72)	48 057 (31.7)	15 (18.1)
<b>Age, y</b>			
<25	15.03 (9.56-20.49)	58 151 (38.4)	29 (34.9)
25-34	11.12 (6.93-15.31)	51 988 (34.3)	27 (32.5)
35-44	9.32 (5.01-13.62)	29 917 (19.8)	18 (21.7)
≥45	11.47 (3.98-18.96)	11 421 (7.5)	9 (10.8)
<b>Education</b>			
≤Some college	13.26 (10.20-16.33)	120 387 (79.5)	72 (86.7)
≥Bachelor's degree	6.68 (2.73-10.63)	31 070 (20.5)	11 (13.3)
<b>Marital status</b>			
Not married	11.32 (7.62-15.02)	78 623 (51.9)	36 (43.4)
Married	12.07 (8.62-15.52)	72 854 (48.1)	47 (56.6)
<b>Race/ethnicity</b>			
White non-Hispanic	12.27 (9.19-15.35)	107 038 (70.7)	61 (73.5)
Black non-Hispanic	6.50 (1.30-11.69)	19 101 (12.6)	6 (7.2)
Other	13.64 (6.96-20.32)	25 231 (16.7)	16 (19.3)
<b>Physical component score, percentile<sup>c</sup></b>			
<15th	12.11 (5.53-18.69)	22 211 (14.7)	13 (15.7)
15th-85th	10.67 (7.77-13.57)	103 647 (68.4)	52 (62.7)
>85th	16.09 (8.21-23.98)	22 227 (14.7)	16 (19.3)
<b>Life stressors<sup>d</sup></b>			
Low/mild	11.30 (8.61-13.99)	130 345 (86.0)	68 (81.9)
Moderate/major	15.16 (7.49-22.84)	19 148 (12.6)	15 (18.1)
<b>PTSD<sup>e</sup></b>			
No	11.22 (8.66-13.77)	139 328 (92.0)	74 (89.2)
Yes	19.97 (6.92-33.02)	11 252 (7.4)	9 (10.8)
<b>Depression<sup>f</sup></b>			
No	10.09 (7.62-12.57)	134 275 (88.6)	64 (77.1)
Yes	26.94 (14.83-39.05)	16 304 (10.8)	19 (22.9)
<b>Manic-depressive disorder<sup>g</sup></b>			
No	11.08 (8.59-13.58)	146 327 (96.6)	76 (91.6)
Yes	87.55 (10.84-164.30)	1222 (0.8)	5 (6.0)
<b>Panic or other anxiety<sup>h</sup></b>			
No positive screen	11.35 (8.82-13.89)	144 109 (95.1)	77 (92.8)
Positive screen	20.70 (2.56-38.84)	5962 (3.9)	5 (6.0)
<b>Heavy or binge drinking<sup>i</sup></b>			
No positive screen	8.01 (5.04-10.98)	69 368 (45.8)	28 (33.7)
Positive screen	15.76 (11.59-19.92)	79 696 (52.6)	55 (66.3)
<b>Alcohol-related problems<sup>j</sup></b>			
No positive screen	9.53 (7.08-11.98)	128 722 (85.0)	58 (69.9)
Positive screen	27.67 (16.83-38.52)	20 389 (13.5)	25 (30.1)

Abbreviations: DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth ed; PCL-C, PTSD Patient Checklist-Civilian Version; PHQ, Patient Health Questionnaire; PTSD, posttraumatic stress disorder; SF-36V, Short Form 36-Item Questionnaire for Veterans.

<sup>a</sup> Sex, depression, manic-depressive disorder, heavy or binge drinking, and alcohol-related problems were statistically significant ( $P < .05$ ).

<sup>b</sup> Percentages are based on the population size for each group but exclude individuals with missing data, therefore, percents may not sum to 100.

<sup>c</sup> Computed using the SF-36V at baseline.

<sup>d</sup> Using a similar scoring mechanism,<sup>20</sup> life stress was based on major financial problems, violent or sexual assault, sexual harassment, severe illness or death of family member or loved one, and disabling illness or injury.

<sup>e</sup> Self-reported for ever being diagnosed or screened positive for PTSD (PCL-C) using the DSM-IV criteria or for depression using the PHQ-9.

<sup>f</sup> Self-reported for ever being diagnosed with manic-depressive disorder.

<sup>g</sup> Screened positive for panic or other anxiety syndrome (PHQ).

<sup>h</sup> Self-reported weekly consumption (>14 drinks for men, >7 for women); or per day or per occasion (>4 drinks for women, >5 drinks for men).

<sup>i</sup> Participants affirmed at least 1 of the 5 items from the PHQ alcohol questions.

Unadjusted proportional hazards models revealed that those deployed to the current operations with or without combat were not significantly more likely to have a suicide death than those who did not deploy (HR, 1.15; 95% CI, 0.68-1.96 with combat experience; HR, 1.17; 95% CI, 0.63-2.16

without combat experience;  $P=.82$ ) (Table 3 and Table 4). Unadjusted significant risk factors for suicide included occupation, male sex, educational attainment of some college or less, depression, manic-depressive disorder, heavy or binge drinking, and alcohol-related problems. After adjusting for age and sex, the same factors were significantly associated with suicide except that occupation and education were no longer significant and deployment for more than 365 days was inversely associated with suicide (Table 3 and Table 4). The magnitude of the HRs for deployment further diminished.

Table 3. Hazard Ratios for Suicide Among Millennium Cohort Participants by Military Categories

Characteristics <sup>a</sup>	Unadjusted HR (95% CI)	P Value	Age- and Sex-Adjusted HR (95% CI)	P Value
<b>OIF/OEF deployment<sup>b</sup></b>				
Not deployed	1 [Reference]		1 [Reference]	
Deployed without combat	1.17 (0.63-2.16)	.82	1.04 (0.56-1.93)	.98
Deployed with combat	1.15 (0.68-1.96)		0.97 (0.56-1.68)	
<b>No. of deployments<sup>b</sup></b>				
0	1 [Reference]		1 [Reference]	
1	0.88 (0.53-1.45)	.46	0.75 (0.45-1.25)	.14
>1	0.68 (0.37-1.26)		0.55 (0.29-1.02)	
<b>Cumulative days deployed<sup>b</sup></b>				
0	1 [Reference]		1 [Reference]	
1-90	1.12 (0.44-2.80)		1.01 (0.40-2.55)	
91-180	1.41 (0.75-2.66)	.10	1.22 (0.64-2.03)	.04
181-365	0.76 (0.41-1.40)		0.63 (0.34-1.17)	
>365	0.36 (0.14-0.89) <sup>c</sup>		0.28 (0.11-0.70) <sup>c</sup>	
<b>Military rank<sup>d</sup></b>				
Junior enlisted	1 [Reference]		1 [Reference]	
Noncommissioned officer	0.76 (0.47-1.23)	.37	0.84 (0.45-1.58)	.80
Officer	0.68 (0.37-1.26)		0.79 (0.38-1.64)	
<b>Service component</b>				
Active	1 [Reference]		1 [Reference]	
Reserve/National Guard	0.84 (0.54-1.31)	.44	0.96 (0.61-1.52)	.86
<b>Service branch</b>				
Army	1.10 (0.67-1.82)		1.06 (0.64-1.76)	
Navy/Coast Guard	0.73 (0.36-1.49)	.68	0.71 (0.35-1.45)	.63
Marine Corps	0.97 (0.37-2.56)		0.77 (0.29-2.04)	
Air Force	1 [Reference]		1 [Reference]	
<b>Occupation</b>				
Combat specialist	1.64 (0.69-3.87)		1.23 (0.51-3.00)	
Health care	1 [Reference]		1 [Reference]	
Functional support, service and supply	1.03 (0.43-2.44)	.02	0.93 (0.39-2.22)	.07
Electrical or mechanical repair	1.96 (0.86-4.46)		1.49 (0.64-3.49)	
Other	0.59 (0.21-1.68)		0.46 (0.16-1.33)	
<b>Pre-2001 deployment experience<sup>e</sup></b>				
No	1 [Reference]		1 [Reference]	
Yes	0.94 (0.58-1.53)	.82	0.88 (0.54-1.46)	.63
<b>Military service status<sup>f</sup></b>				
Current service member	1 [Reference]		1 [Reference]	
Former service member	1.19 (0.72-1.97)	.49	1.24 (0.75-2.05)	.40

Abbreviations: HR, hazard ratio; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom.

<sup>a</sup> Assessed at baseline except participants' deployment and military service status.

<sup>b</sup> Based on OIF/OEF deployment September 11, 2001-December 31, 2008. OIF/OEF deployment was assessed as a time-varying covariate, whereas, the number of deployments and cumulative days deployed were assessed as fixed covariates based on status at the end of follow-up.

<sup>c</sup> HR and 95% CI were significant ( $P < .05$ ).

<sup>d</sup> Ranks include junior enlisted (E1-E4), noncommissioned officer (E5-E9), and officer (O1-O10 and W1-W5).

<sup>e</sup> Deployed to the 1991 Gulf War or to Bosnia, Kosovo, or Southwest Asia 1998-2000.

<sup>f</sup> Military service status was assessed as a time-varying covariate.

Table 4. Hazard Ratios for Suicide Among Millennium Cohort Participants

Table 4. Hazard Ratios for Suicide Among Millennium Cohort Participants

Characteristics <sup>a</sup>	Unadjusted HR (95% CI)	P Value	Age- and Sex-Adjusted HR (95% CI)	P Value
<b>Sex</b>				
Men	1.90 (1.09-3.33) <sup>b</sup>	.02	2.03 (1.15-3.56) <sup>b</sup>	.01
Women	1 [Reference]		1 [Reference]	
Age per 5-y increase	0.91 (0.80-1.03)	.13	0.89 (0.78-1.01)	.07
<b>Education</b>				
≤Some college	2.02 (1.07-3.81) <sup>b</sup>	.03	1.82 (0.94-3.51)	.07
≥Bachelor's degree	1 [Reference]		1 [Reference]	
<b>Marital status</b>				
Not married	0.97 (0.63-1.50)	.88	0.85 (0.52-1.39)	.52
Married	1 [Reference]		1 [Reference]	
<b>Race/ethnicity</b>				
White non-Hispanic	1 [Reference]		1 [Reference]	
Black non-Hispanic	0.53 (0.23-1.22)	.27	0.59 (0.26-1.38)	.40
Other	1.11 (0.64-1.93)		1.12 (0.65-1.95)	
<b>Physical component score, percentile<sup>c</sup></b>				
<15th	1.13 (0.62-2.08)		1.21 (0.66-2.22)	
15th-85th	1 [Reference]	.34	1 [Reference]	.37
>85th	1.52 (0.87-2.66)		1.48 (0.84-2.59)	
<b>Life stressors<sup>d</sup></b>				
Low/mild	1 [Reference]		1 [Reference]	
Moderate/major	1.33 (0.76-2.33)	.32	1.73 (0.97-3.08)	.06
<b>PTSD<sup>e</sup></b>				
No	1 [Reference]		1 [Reference]	
Yes	1.81 (0.91-3.62)	.09	1.80 (0.90-3.60)	.10
<b>Depression<sup>f</sup></b>				
No	1 [Reference]		1 [Reference]	
Yes	2.70 (1.62-4.50) <sup>b</sup>	<.001	3.03 (1.80-5.08) <sup>b</sup>	<.001
<b>Manic depressive disorder<sup>g</sup></b>				
No	1 [Reference]		1 [Reference]	
Yes	7.92 (3.20-19.60) <sup>b</sup>	<.001	7.92 (3.20-19.60) <sup>b</sup>	<.001
<b>Panic or other anxiety<sup>h</sup></b>				
No positive screen	1 [Reference]		1 [Reference]	
Positive screen	1.85 (0.75-4.58)	.18	1.96 (0.79-4.85)	.15
<b>Heavy or binge drinking<sup>i</sup></b>				
No positive screen	1 [Reference]		1 [Reference]	
Positive screen	1.99 (1.26-3.14) <sup>b</sup>	.003	1.72 (1.07-2.76) <sup>b</sup>	.02
<b>Alcohol-related problems<sup>j</sup></b>				
No positive screen	1 [Reference]		1 [Reference]	
Positive screen	2.93 (1.83-4.69) <sup>b</sup>	<.001	2.64 (1.63-4.26) <sup>b</sup>	<.001

Abbreviations: DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth ed; HR, hazard ratio; PCL-C, PTSD Patient Checklist-Civilian Version; PTSD, posttraumatic stress disorder; PHQ, Patient Health Questionnaire; SF-36V, Short Form 36-Item Questionnaire for Veterans.

<sup>a</sup> Assessed at baseline except age (which was time-varying).

<sup>b</sup> HR and 95% CI were significant ( $P < .05$ ).

<sup>c</sup> Computed using the SF-36V at baseline.

<sup>d</sup> Using a similar scoring mechanism,<sup>20</sup> life stress was based on major financial problems, violent or sexual assault, sexual harassment, severe illness or death of family member or loved one, and disabling illness or injury.

<sup>e</sup> Self-reported for ever being diagnosed or screened positive for PTSD (PCL-C) using the DSM-IV criteria or for depression using the PHQ-9.

<sup>f</sup> Self-reported for ever being diagnosed with manic-depressive disorder.

<sup>g</sup> Screened positive for panic or other anxiety syndrome (PHQ).

<sup>h</sup> Self-reported weekly consumption (>14 drinks for men, >7 for women); or per day or per occasion (>4 drinks for women, >5 drinks for men).

<sup>i</sup> Participants affirmed at least 1 of the 5 items from the PHQ alcohol questions.

A total of 145 387 participants were included in the final Cox model, including 78 suicide deaths. The final multivariable Cox model included the following statistically significant covariates: male sex (HR, 2.14; 95% CI, 1.17-3.92;  $P = .01$ ; AR, 3.5/10 000; population attributable risk percent

[PAR%, 43.6%), depression (HR, 1.96; 95% CI, 1.05-3.64;  $P = .03$ ; AR, 6.9/10 000; PAR%, 11.2%), manic-depressive disorder (HR, 4.35; 95% CI, 1.56-12.09;  $P = .005$ ; AR, 35.6/10 000; PAR%, 4.8%), and alcohol-related problems (HR, 2.56; 95% CI, 1.56-4.18;  $P < .001$ ; AR, 7.7/10 000; PAR%, 18.4%) (Table 5). Deployment, assessed as a 3-level variable, was not associated with suicide in this final model. When the 3-level deployment variable was replaced first with cumulative days deployed and then the number deployments in the final model, neither deployment factor was associated with suicide; all other factors remained unchanged. Results were also consistent in the alternate final Cox model with the mental and behavioral factors assessed as time-dependent variables. Depression (HR, 2.05; 95% CI, 1.15-3.65;  $P = .01$ ; AR, 5.0/10 000), manic-depressive disorder (HR, 4.18; 95% CI, 1.64-10.63;  $P = .003$ ; AR, 26.9/10 000), and alcohol-related problems (HR, 2.28; 95% CI, 1.40-3.72;  $P < .001$ ; AR, 5.5/10 000) were significantly associated with suicide in addition to male sex (HR, 2.19; 95% CI, 1.20-4.02;  $P = .01$ ; AR, 3.5/10 000).

Table 5. Multivariable Cox Proportional Hazards Model for Suicide Among Millennium Cohort Participants, 2001-2008 (n = 145 387)<sup>1</sup>

Characteristic	Adjusted HR (95% CI)	P Value
OIF/OEF deployment <sup>b</sup>		
Not deployed	1 [Reference]	
Deployed without combat	1.22 (0.65-2.26)	.82
Deployed with combat	1.00 (0.58-1.73)	
Sex		
Men	2.14 (1.17-3.92) <sup>c</sup>	.01
Women	1 [Reference]	
Depression <sup>d</sup>		
No	1 [Reference]	
Yes	1.96 (1.05-3.64) <sup>c</sup>	.03
Manic depressive disorder <sup>e</sup>		
No	1 [Reference]	
Yes	4.35 (1.56-12.09) <sup>c</sup>	.005
Alcohol-related problems <sup>f</sup>		
No positive screen	1 [Reference]	
Positive screen	2.56 (1.56-4.18) <sup>c</sup>	<.001

Abbreviations: HR, hazard ratio; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom; PHQ, Patient Health Questionnaire.

<sup>a</sup> Model adjusted for all shown variables.

<sup>b</sup> Based on OIF/OEF deployment September 11, 2001-December 31, 2008.

<sup>c</sup> HR and 95% CI were significant ( $P < .05$ ).

<sup>d</sup> Self-reported diagnosis or screening positive for depression using the PHQ-9 at baseline.

<sup>e</sup> Self-reported for ever being diagnosed with manic-depressive disorder.

<sup>f</sup> Participants affirmed at least 1 of the 5 items from the PHQ alcohol questions.

Results from the final conditional logistic model of the nested case-control analysis (Table 6, n = 1617 including 77 suicide deaths) were also consistent with the final Cox model (Table 5). Depression (OR [odds ratio], 2.68; 95% CI, 1.46-4.93;  $P = .002$ ), manic-depressive disorder (OR, 7.38; 95% CI, 2.13-25.61;  $P = .002$ ), and alcohol-related problems (OR, 2.30; 95% CI, 1.35-3.91;  $P = .002$ ) were significantly and independently associated with suicide. Again, there was no significant association between deployment and suicide.

Table 6. Conditional Logistic Regression for Suicide Among Matched Millennium Cohort Participants, 2001-2008 (n = 1617)<sup>1</sup>

Table 6. Conditional Logistic Regression for Suicide Among Matched Millennium Cohort Participants, 2001-2008 (n=1617)<sup>a</sup>

Characteristic	Adjusted OR (95% CI)	P Value
OIF/OEF deployment <sup>b</sup>		
Not deployed	1 [Reference]	
Deployed without combat	1.16 (0.60-2.26)	.86
Deployed with combat	0.95 (0.51-1.75)	
Depression <sup>c</sup>		
No	1 [Reference]	
Yes	2.68 (1.46-4.93) <sup>e</sup>	.002
Manic-depressive disorder <sup>d</sup>		
No	1 [Reference]	
Yes	7.38 (2.13-25.61) <sup>e</sup>	.002
Alcohol-related problems <sup>f</sup>		
No	1 [Reference]	
Yes	2.30 (1.35-3.91) <sup>e</sup>	.002

Abbreviations: OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom; OR, odds ratio; PHQ, Patient Health Questionnaire.

<sup>a</sup> Each suicide case was matched to 20 nonsuicide control cases matched on sex, race/ethnicity, marital status, birth year (within 2 y), enrollment (within 180 d), service branch, and rank. Model was adjusted for all shown variables.

<sup>b</sup> Based on OIF/OEF deployment September 11, 2001-December 31, 2008.

<sup>c</sup> Self-reported diagnosis or screening positive for depression using the PHQ-9 at baseline.

<sup>d</sup> Self-reported for ever being diagnosed with manic-depressive disorder.

<sup>e</sup> OR and 95% CI are significant ( $P < .05$ ).

<sup>f</sup> Participants affirmed at least 1 of the 5 items from the PHQ alcohol questions.

In a subanalysis among Army personnel only, manic-depressive disorder (HR, 5.96; 95% CI, 1.82-19.49;  $P = .003$ ; AR, 37.6/10 000) and alcohol-related problems (HR, 3.86; 95% CI, 2.05-7.27;  $P < .001$ ; AR, 11.3/10 000) remained significantly associated with suicide in a reduced model. There was no evidence that deployment was associated with suicide ( $P = .54$ ). However, this was based on 41 suicide cases, so lack of

significance among other factors such as depression may have been due to a deficiency of power, a shared variance between the mental health variables, or both combined. When manic-depressive disorder was removed and replaced with depression in the reduced model, depression became significant (HR, 2.34; 95% CI, 1.16-4.72;  $P = .02$ ; AR, 7.4/10 000), and alcohol-related problems remained significantly associated with suicide.

## DISCUSSION

The US military combat deployments in Iraq and Afghanistan have been associated with a notable upward trend in suicides since 2005 that has led to considerable speculation as to the cause. Using national and military mortality records, this study is the first, to our knowledge, to prospectively follow US service members from all military branches and components to assess suicide during and after military service.

The findings from this study are not consistent with the assumption that specific deployment-related characteristics, such as length of deployment, number of deployments, or combat experiences, are directly associated with increased suicide risk. Instead, the risk factors associated with suicide in this military population are consistent with civilian populations, including male sex and mental disorders. Studies have shown a marked increase in the incidence of diagnosed mental disorders in active-duty service members since 2005, paralleling the incidence of suicide. This suggests that the increased rate of suicide in the military may largely be a product of an increased prevalence of mental disorders in this population, possibly resulting from indirect cumulative occupational stresses across both deployed and home-station environments over years of war. In addition to screening for and addressing mental health problems, further research is needed to more clearly understand the interrelationship of multiple risk factors leading to suicidal behaviors and the types and timing of interventions that may reduce or prevent death by suicide.

Since data collection ended in 2008, we did not capture suicides in the most recent time period when the rates were the highest.<sup>2</sup> However, the study did include the 3 years with the sharpest statistically significant increases in suicides (seen especially in the Army and Marine Corps). It is possible that the cumulative strain of multiple and lengthy deployments only began to be reflected in suicide rates toward the later stages of the conflicts, although the overall evidence points to the lack of any specific deployment-related effects.

The most important finding was that mental health problems, including manic-depressive disorder, depression, and alcohol-related problems, were significantly associated with an increase in the risk of suicide. These findings suggest that current prevention initiatives in the DoD and the Department of Veterans Affairs that address previous mental health disorders and involve screening and facilitation of high-quality treatment for mental and substance use disorders in primary care, specialty mental health care, and postdeployment settings have the greatest potential to mitigate suicide risk. However, there are limited studies that validate prevention initiatives and well-conducted program effectiveness trials should remain a high priority.

The PAR% indicates that suicide deaths could potentially be reduced (by approximately 18% and 11%) in this population as a whole, by preventing or eliminating alcohol-related problems and depression, respectively (assuming that these observed associations are causal and that elimination of these risk factors do not affect distribution of other covariates). Despite the larger magnitudes of the HRs for manic-depressive disorder, the PAR% shows that preventing or eliminating this disorder would have a smaller effect ( $\approx 5\%$  reduction) due to the very low prevalence of this disorder in this population. In addition, male sex was also a strong contributing factor to suicide deaths (44%) in this population. These findings provide further evidence that the prevention and quality treatment of these mental health disorders may prevent suicide deaths.

This study has several limitations. The findings are based on 83 suicide deaths so the study may have lacked statistical power to produce a stable and reproducible multivariable model. As with any prospective cohort study, nonresponse on the initial survey or loss to follow-up may introduce bias. However, objective national registry-based mortality data obtained for all cohort members minimizes bias due to loss to follow-up. Additionally, a previous study examining weighting for nonresponse among panel 1 members of this cohort indicated that prevalence rates are comparable to results of unweighted analysis for PTSD, depression, and eating disorders. Although the study relied on the PHQ and PCL-C self-report screening measures, these measures are standardized validated instruments shown to be reliable in this cohort. The questions used to assess combat experience were also self-reported and based on 2 different instruments, but combat experience based on self-report has consistently been shown to be associated with a variety of adverse health outcomes. This study could also be influenced by misclassification of suicide on death certificates. There is some evidence that suicides are underreported on death certificates; however, this method of cause-specific mortality ascertainment has been widely accepted and there is no reason to believe that cause-of-death reporting on death certificates would be influenced by the risk factor variables that were studied. The main findings were based on baseline data that were assessed an average of 3 years (mean [SD] 3.23 [2.03] years) prior to suicide; however, results using all available survey data were consistent. This study was only able to cover the first 3 years of an increasing trend in suicides occurring in military service members that began around 2005, therefore additional research will be needed to confirm these results using data from later years. Lastly, data from the first 3 panels of the Millennium Cohort, which consisted of different enrollment criteria, were combined due to the low numbers of suicides in this study population.

Key strengths of the study that reinforce the validity of the findings include the linkage of records with national registry-based mortality data, the consistency of results between Cox modeling and the nested case-control methods, and the fact that the study spanned the 3-year time period when the greatest increase in military suicides occurred. In addition, this study included individuals from all service branches including active and Reserve members, as well as those who have retired or are no longer serving in the military.

In conclusion, this study prospectively quantified military-specific risk factors associated with suicide in a cohort of military members who were followed-up for as long as 7 years. In this sample of current and former US military personnel, mental health concerns but not military-specific variables were found to be independently associated with suicide risk. The findings from this study do not support an association between deployment or combat with suicide, rather they are consistent with previous research indicating that mental health problems increase suicide risk. Therefore, knowing the psychiatric history, screening for mental and substance use disorders, and early recognition of associated suicidal behaviors combined with high-quality treatment are likely to provide the best potential for mitigating suicide risk.

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***Disease***

## **Asthma Drug Improves Cognitive Function in Down Syndrome Model**

Journal of the American Medical Association  
Tracy Hampton, PhD  
7 August 2013

August 2013

Treating mice with Down syndrome with the asthma drug formoterol strengthened nerve connections in the hippocampus and improved cognitive function and the brain's ability to integrate spatial and sensory information (Dang V et al. Biol Psychiatry. doi:10.1016/j.biopsych.2013.05.024 [published online July 2, 2013]). Postmortem analyses revealed more synapses and a more complex structure of nerve endings in the hippocampus in affected mice treated with the drug than in control animals, report investigators from the Stanford University School of Medicine in Palo Alto, Calif.

Previous research showed derioration of the brain center that manufactures norepinephrine in persons with Down syndrome and in the mouse model of the disease. Formoterol is also known to partially cross the blood-brain barrier and activate receptors that respond to norepinephrine.

The study's findings suggest that improving signaling through these receptors may be an effective strategy for treating cognitive disabilities in persons with Down syndrome. However, the authors cautioned that the dose of formoterol used in this study was many times higher than that used for asthma treatment.

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## **Early Detection and Intervention in Schizophrenia**

Journal of the American Medical Association

Jeffrey A. Lieberman, MD; Lisa B. Dixon, MD, MPH; Howard H. Goldman, MD, PhD

21 August 2013

Schizophrenia is a brain disorder with lifetime prevalence near 1%. This disorder is clinically manifested by psychotic, negative, and cognitive symptoms that typically emerge in adolescence and early adulthood (peak age for males, 20 years; for females, 25 years) and follows a course characterized by recurrent exacerbations and remissions, resulting in a chronic state of residual symptoms and functional impairment.

The annual cost of schizophrenia in the United States is approximately 60 billion dollars, including direct medical costs, non–health care costs, and lost productivity. This is because individuals become ill early in life and have high rates of unemployment and psychiatric and medical comorbidities.

Historically, schizophrenia was thought to have devastating consequences. However, the advent of antipsychotic drugs, the development of psychosocial treatments, and the accounts from individuals diagnosed with schizophrenia who have recovered have begun to change the perspectives and expectations of clinicians and the public. In addition, an increasing body of research in the last 2 decades has inspired optimism for development of a comprehensive strategy that has the potential to minimize (if not prevent) the cumulative morbidity of this once-debilitating illness.

This strategy crystallized from 2 lines of investigation: research on the natural history and pathophysiology of schizophrenia, and studies of treatments geared toward symptom suppression and psychosocial recovery. The integration of this research has led to a reconceptualization of schizophrenia, the development of an ambitious and innovative therapeutic strategy, and a redefinition of health policy and financing approaches.

NATURAL HISTORY AND PATHOPHYSIOLOGY

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Numerous studies have demonstrated that longer duration of the initial episode of illness prior to treatment intervention is associated with poorer treatment response and outcomes. This has been interpreted as suggesting that psychosis reflects the phenotypic expression of the illness, which, if persistent or recurrent, can diminish patients' capacity to respond to treatment and result in residual impairment. Although abnormalities in brain morphology may be present at (or even prior to) the first psychotic episode, there is subsequent progression in brain pathomorphology, particularly reduction in cortical gray matter volume, that may reflect the loss of cell processes and synapses.

Other research has shown that subgroups of individuals diagnosed with schizophrenia may experience only limited disability or have positive outcomes in spite of substantial symptoms.<sup>1</sup> Resilience, coping skills, and peer and family support also contribute. Nevertheless, regardless of the variation in coping skills, environmental supports, and range of outcomes observed, all patients who develop schizophrenia would benefit from prompt, effective treatment to limit the disruption to their lives caused by the symptoms of their illness and the potential for progression and lasting disability.

Collectively, these findings have suggested the value of early detection, intervention, and sustained engagement with treatment to enhance recovery and prevent disability.

#### EFFECTIVENESS OF TREATMENT

Pharmacologic treatment of schizophrenia has targeted reducing symptoms and preventing relapse, whereas psychosocial approaches have focused on fostering treatment engagement and adherence as well as enhancing self-efficacy and social and occupational functioning. Studies reveal that patients with first-episode psychosis have greater therapeutic responses and require lower doses of medication than patients in the chronic stages of illness, indicating an overall greater pharmacologic sensitivity. However, the greater response to pharmacological treatment among patients with first-episode illness has not led to high rates of recovery. Rather, high rates of dropout and medication discontinuation frequently follow initial treatment and reduction in symptoms. Studies of patients with first-episode schizophrenia indicate that only 58% filled their prescriptions during the first 30 days of hospital discharge, and only 46% continued their initial treatment for 30 days or longer. In addition, more than 40% of patients with first-episode psychosis are nonadherent and discontinue medication during the first 9 months of treatment.

Patients with first-episode schizophrenia have been found to benefit from psychosocial treatments including cognitive behavioral therapy, social skills training, family support, and supported employment and education services, which increase rates of work and school participation and social functioning. However, in the United States, psychosocial and recovery-oriented services have not been available to patients with first-episode psychosis. Treatment approaches in the early stages of the illness have historically focused on reduction of symptoms with antipsychotic medication, whereas psychosocial and rehabilitative treatments have predominantly been provided to patients after their accrual of residual morbidity and disability.

#### HEALTH CARE POLICY AND FINANCING CONSIDERATIONS

Comprehensive services for patients with early-stage psychosis are being implemented in Australia, Europe, Canada, and Asia at a more rapid pace than in the United States. An important reason for the slow US adoption of this treatment model is a lack of adequate financing. Health insurance does not pay for psychosocial and rehabilitative services recommended for individuals in the earliest stages of psychosis; moreover, many such individuals in the United States do not have health insurance. Furthermore, funding and service delivery priorities for the public mental health system, designed to serve individuals without health insurance and to provide services not covered by insurance, favor individuals who

have already become disabled by mental illness. These factors have limited the availability of services for patients with first-episode schizophrenia.

#### NEW CARE MODEL FOR COMPREHENSIVE CARE OF FIRST-EPISODE SCHIZOPHRENIA

A new conceptualization of schizophrenia has led to a new care model developed for patients with first-episode schizophrenia that fosters recovery and prevents disability. Effective treatment targeting this early stage of illness has the greatest potential to limit the progression of the illness and minimize the association between the disease and failure to achieve age-appropriate advances in social development, education, and work functioning. Interruption of the developmental trajectory and introduction of self-stigma and diminished self-efficacy at this critical stage of life is particularly difficult to overcome, even if treatment is provided subsequently.

The new therapeutic model involves a team-based approach focused on recovery and requires financing schemes that are seamless across the transition from adolescence to adulthood, a time frame often characterized by interruption in insurance coverage. In addition, activities targeting engagement and maintenance of community functioning must be covered by insurance benefits.

The elements of this care model for proactive treatment of early psychosis include (1) reducing the duration of active symptoms through rapid diagnosis and treatment of patients with first-episode psychosis (ensuring adherence to the pharmacologic regimen is critical); (2) sustaining treatment and preventing psychotic relapse following the acute treatment response in the context of maintenance medication or supported discontinuation; (3) integrating pharmacologic management with psychosocial therapies and recovery-oriented approaches that involve other mental health professionals in the context of a disease-management approach to the illness; and (4) offering social and vocational services, substance abuse treatment, family education and support, and assistance with coping with past trauma and the trauma of psychosis, as well as suicide prevention and safety planning.

All components of the plan must use active strategies to address the stigma associated with seeking and receiving treatment.

#### CONCLUSION

More than a century after Kraepelin initially defined schizophrenia as a progressive illness leading to clinical deterioration and 60 years since the introduction of antipsychotic drugs, the first effective treatment for schizophrenia, psychiatry has within its grasp the potential to limit the morbidity and disability associated with this disorder. However, to do so requires the application of existing knowledge and methods in a new care model. To take full advantage of this capability, mental health care services and reimbursement schemes must be reorganized. Emerging knowledge and the prospect of health care reform render this initiative timely and important.

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## **Psychological Health of Military Children: Longitudinal Evaluation of a Family-Centered Prevention Program to Enhance Family Resilience**

Military Medicine

August 2013

Patricia Lester, MD; Judith A. Stein, PhD; William Saltzman, PhD; Kirsten Woodward, LCSW; Shelley W. MacDermid, PhD; Norweeta Milburn, PhD; Catherine Mogil, PsyD; William Beardslee, MD  
August 2013

## **ABSTRACT**

Family-centered preventive interventions have been proposed as relevant to mitigating psychological health risk and promoting resilience in military families facing wartime deployment and reintegration. This study evaluates the impact of a family-centered prevention program, Families OverComing Under Stress Family Resilience Training (FOCUS), on the psychological adjustment of military children. Two primary goals include (1) understanding the relationships of distress among family members using a longitudinal path model to assess relations at the child and family level and (2) determining pathways of program impact on child adjustment. Multilevel data analysis using structural equation modeling was conducted with deidentified service delivery data from 280 families (505 children aged 3–17) in two follow-up assessments. Standardized measures included service member and civilian parental distress (Brief Symptom Inventory, PTSD Checklist—Military), child adjustment (Strengths and Difficulties Questionnaire), and family functioning (McMaster Family Assessment Device). Distress was significantly related among the service member parent, civilian parent, and children. FOCUS improved family functioning, which in turn significantly reduced child distress at follow-up. Salient components of improved family functioning in reducing child distress mirrored resilience processes targeted by FOCUS. These findings underscore the public health potential of family-centered prevention for military families and suggest areas for future research.

## **INTRODUCTION**

A decade of war has underscored the challenges and sacrifices imposed upon children by a parent's military service. By the Fall of 2010, more than 2.1 million service members, almost half of them parents, had deployed to support Operation Enduring Freedom and Operation Iraqi Freedom. Of these, about 48% had deployed at least twice, with many serving multiple times. For many military children in the last decade, an entire childhood has been defined by at least one parent leaving and returning in the context of dangerous duties. A growing research literature has documented heightened risk for psychological health problems among service members, spouses, and children associated with these challenges. Increasingly, military, veteran, and national leadership have recognized the urgent need to support military families both to maintain readiness and mitigate the impact of deployment stress. Adapting, implementing, and evaluating preventive programs for military families have emerged as an important public health need. This study uses a multilevel path analysis to evaluate the impact of a family-centered preventive service program designed to promote family resilience on military child emotional and behavioral outcomes and to provide an initial test of targeted family resilience mechanisms as pathways of psychological health promotion for military children.

Research on the impact of wartime deployments on military families indicates the reverberations of stress across family members and the family system. The critical role of individual and family resilience in managing deployment challenges have been identified within scientific, clinical, and policy communities. In particular, strategies that draw upon current models of resilience have underscored the importance of family-level processes and relationships to the reduction of distress in children. Development and implementation of effective family prevention programs will be enhanced by identifying and testing the specific impact of resilience-enhancing interventions on family processes and by examining the impact of enhanced family functioning on child adjustment.

Decades of child development and prevention science provide strong evidence for the benefits of family-centered interventions in supporting positive parent and child psychological health and suggest promise for military and veteran families. Convergent research has consistently identified key factors that contribute to child resilience in the context of adversity, including parent psychological health, parent–child relationships, parenting/co-parenting, and environmental support. Family-level characteristics and interactions have been identified as potential mediators of children's ability to adapt and thrive following exposure to stress. Initial studies support these factors as relevant for military children negotiating deployment stress.

These findings suggest the potential benefit of interventions that are consistent with current models of psychological resilience and designed to enhance family functioning and relationships for reducing distress in children. In particular, interventions that target family functioning theorized to support family resilience processes such as effective communication, emotional awareness and regulation, collaborative problem-solving, and development of shared meaning about stressful experiences hold promise for supporting military families affected by stress. Although multiple studies have documented the salience of these family processes to adaptive responses to stress, trauma, and loss, most have been cross-sectional or qualitative in design or have not been conducted with military populations. Evaluation of a family-centered prevention program implemented at scale with military families offers the opportunity to examine whether changes in child psychological health symptoms are significantly mediated by improvements in resilient family processes.

Since 2008, the U.S. Navy Bureau of Medicine and Surgery contracted with a team from UCLA and Harvard to implement the family-centered prevention program Families OverComing Under Stress Family Resiliency Training (FOCUS) and a suite of related services at active duty military installations known as the FOCUS Project. Adapted from the team's established evidence-based family-centered preventive interventions shown to improve psychological health and family functioning over longitudinal follow-up in other settings,<sup>16,25</sup> FOCUS was customized for military families affected by deployment and reintegration challenges in partnership with military providers and community members. During its first 20 months of operation, this tiered public health implementation provided a “suite” of integrated prevention services based on core evidence-based practices. FOCUS delivered family resiliency training for individual families, as well as parent and child resilience skills building groups to over 5,000 military children, spouses, and service members. The FOCUS Project also provided family-centered consultations, briefings, and educational workshops to over 100,000 family members, providers, and other community members. All of these services were designed to enhance specific family processes theorized to support resilience in the context of stress. The FOCUS program evaluated in this report includes individual family assessment, education and skill enhancement, and the construction of individual and family narrative time lines, an activity designed to develop increased understanding within the family regarding their experiences.

Prior evaluation of the FOCUS program delivery from the initial implementation period showed significant reductions in service member, spouse, and child distress and concurrent improvements in family functioning. Although these initial findings indicated positive impact, an important next step was to identify whether reductions in child distress were mediated by theorized improvements in family functioning, and if one or more of the resilient family functioning processes would be more central to distress reduction than others. This information would help inform preventive programs for military families, as well as contribute to our understanding of transmission of deployment and reintegration stress among family members.

Previous research has identified the sources of family stress as “direct,” for example, the worry attendant to having a loved one at risk, the reductions in available emotional and financial resources across the family, or “indirect” when stress burdens are due to interactions with a family member who is highly distressed, symptomatic, or engaging in uncharacteristic or stress-inducing behaviors. Such is the case with the studies of

military families from the Vietnam War era forward that have documented the impact of parental post-traumatic stress disorder (PTSD) on spouses and children. This research examining the family impact of deployment stressors suggest that most are mediated by parent and family factors and may be considered primarily indirect or “secondary.” Signs of distress among children are also significantly linked to levels of distress among parents, both caretaker and service member. A primary shortcoming of current literature, however, is that most studies focus on the individual prevalence of psychological disorders among service members, spouses, and children with limited information on the concordance of difficulties among family members. Even studies that explicitly look at the relationship of distress levels between parents and children generally do not capture the systemic view of distress concordance across the family system.

The first goal of this study was to develop a systemic understanding of the relationships of distress among active duty families facing deployment stress that attended the FOCUS program. To do this, we used a multilevel path model that describes the relationships between levels of distress measured at program entry among service member parents, civilian parents, and children. We anticipated significant correlations among service member distress (anxiety and depression), service member post-traumatic stress symptoms, civilian spouse adjustment, child adjustment, and family functioning.

The second goal of the study was to evaluate the pathways of program impact on child psychological health symptoms using longitudinal assessment data following program participation. Consistent with the underlying theoretical model of family resilience, we hypothesized that improvement in family functioning would mediate improvements in child psychological health outcomes. In addition, we anticipated that the specific family functioning processes that are associated with resilience and targeted by FOCUS (e.g., emotional awareness and regulation, problem-solving, and communication in families) might account for greater variance in child outcomes.

## **METHODS**

### **Participants**

Data are from a secondary analysis of deidentified data originally collected (July 2008–February 2010) for the purpose of customized delivery and program quality improvement of the family-centered preventive intervention for military families. Participating families included families with at least one active duty military parent and at least one dependent child age 3 and older. Data presented here are from 11 U.S. Marine Corps and U.S. Navy installations located in California (4 sites), North Carolina, Hawaii, Okinawa (Japan), Virginia (2 sites), Mississippi, and Washington State. The final sample for this analysis consists of 280 families with at least one service member parent and one 1 or more children (505 children: 44% female child; average child age, 7.5 years; range 3–17 years). Of this sample, 35.4% participated at U.S. Navy installations and 65.6% at U.S. Marine Corps installations. Both the military and civilian/caretaker self-report parent provided data for this analysis; primary caretaker (280 civilian parents) child report data were used for child outcomes. This study of program evaluation data was approved by the UCLA Institutional Review Board.

### **Procedures**

The manualized prevention program, FOCUS Family Resilience Training, is delivered to individual families including the service member and civilian/caretaker parent, and children ages 3 to 18. Delivered in eight modularized sessions, FOCUS includes parent-only, child-only, and family sessions. The program provides family-level education about (1) stress reactions, including helping the family to identify reminders that trigger unhelpful responses, and linking specific stress reactions to breakdowns in family cohesion, communication, routines, and parenting activities; (2)

family communication, such as similarities and differences among family members' understanding of and reactions to deployment and reintegration experiences; (3) identifying and using family strengths; and (4) guidance about child development and common stress reactions. FOCUS also trains parents and children in family-level cognitive behavioral skills designed to promote resilience, including emotional regulation, goal setting, problem-solving, trauma/separation/loss stress reminder management, and communication.

FOCUS providers, identified as “resiliency trainers,” are master- or doctoral-level child and family mental health providers who complete in-person and web-based training. UCLA provides weekly model supervision, reviews fidelity measures and delivery notes, conducts site visits, and provides emergency support and technical assistance. Centralized management ensures program standardization and quality improvement processes.

## **Measures**

The program uses a web-based family assessment at time of entry, completion, 1 month, and 4 to 6 months after completion. The full assessment protocol includes standardized psychological health, family functioning, and coping measures completed by children and parents to identify areas of strength and challenge, make timely referrals, and conduct quality control. Assessment measures used in this study are described in detail below. Except for single-item demographics and the number of visits, all variables were constructed as latent variables.

“Baseline variables” included the demographics of child age (in years) and child gender (coded as 1 = male, 2 = female). “Parental distress” was reported for each parent (military and civilian/caretaker). Distress was assessed with three scales from the Brief Symptom Inventory (BSI), a self-report inventory with extensively published psychometric data and community norms by gender. The somatic complaints, depression, and anxiety subscales were used as indicators of parental distress. Another indicator of deployment-related distress, the “PTSD Checklist-Military (PCL-M)”, a 17-item self-report measure, assessed the severity of PTSD symptoms in the past month for the military parent.

“Child initial distress” was assessed using the Strengths and Difficulties Questionnaire (SDQ) parent report, a widely used instrument with subscales for conduct problems, emotional symptoms, hyperactivity/inattention, peer relationship problems, and prosocial behavior. (Prosocial behavior was reverse scored in these analyses.) Normative data are available for each gender and for ages 3 to 18. The subscales were used as indicators of a latent variable representing child distress (coefficient  $\alpha = 0.66$ ).

“Longitudinal assessment variables” consisted of (1) the number of session visits attended by the families during the intervention delivery period (adjusted for family size as families with more children require more visits to complete program sessions including boosters when appropriate); (2) a latent variable representing positive change in family adjustment from enrollment to intervention exit on the McMaster Family Assessment Device (FAD) completed by caretakers.<sup>38</sup> The FAD was used to assess overall family functioning and specific family processes (“problem-solving,” “communication,” “affective responsiveness,” “affective involvement,” “behavior control,” and “roles”) and was administered at program entry and exit. Scores at entry were subtracted from scores at exit to derive scores reflecting improvement in family adjustment and were used as indicators of a latent variable representing positive change in FAD (coefficient  $\alpha = 0.82$ ); and (3) a second latent variable representing reduced emotional distress among participating children in longitudinal follow-up after program completion. This variable was the difference between the emotional and behavioral distress (SDQ) assessed at baseline and then again at 4 to 6 month follow-up as reported by the caretaker parent. There was substantial interest in determining whether changes in the family functioning processes associated with family resilience and targeted by the program (problem-solving, communication, affective responsiveness, and affective involvement) would be the most efficacious in predicting

reduction in child distress. The individual components of the FAD were tested individually in a secondary analysis as predictors of change in the SDQ to determine their relative contributions.

### **Data Analyses**

The EQS Structural Equations Program estimated a two-level model using a maximum likelihood approach. We used a multilevel model because observations among members of the same family are not independent and thus violate assumptions about independent samples. We initially determined that a multilevel model was appropriate by assessing the intraclass correlations among the indicator variables. For instance, child distress intraclass correlations ranged from 0.14 to 0.23, and intraclass correlations among difference scores on child distress ranged from 0.12 to 0.22. Thus, children's distress levels were more alike within their families than across families. In this study, the family-level portion of the multilevel model was of most interest in assessing the impact of FOCUS because the program was implemented at the family level and because all children within a family had the same scores for items assessed among their parents including the parent distress scores, the military parent PCL, number of visits, and change in family adjustment (caretaker reported FAD). Of course, impact of gender of the child could only be assessed at the child level of the analysis as this was not a family-level variable.

Goodness-of-fit of the models was evaluated with the Bentler–Liang Likelihood Ratio Statistic (BLLRS), the Comparative Fit Index (CFI), and the standardized root mean square residual (SRMR).<sup>39,43</sup> The CFI, which ranges from 0 to 1, reports the improvement in fit of the hypothesized model over a model of complete independence among the measured variables. Values  $\geq 0.95$  are desirable and indicate that 95% of the covariation in the data is reproduced by the hypothesized model. The SRMR is a measure representing the size of residuals. Values less than 0.08 are desirable and indicate a close fitting model.

An initial confirmatory factor analysis (CFA) tested the factor structure of the hypothesized model and also provided correlations among all of the factors without regard to the multilevel nature of the data set. Significant correlated error residuals were allowed between similar items (e.g., distress of military parent, distress of civilian parent) to improve model fit and account for significant associations. Once the factor structure was confirmed, a similar multilevel CFA was conducted to determine correlations and factor loadings at the family level. Then, the hypothesized multilevel path model was tested in which the individual level baseline variables of child age and gender and child initial distress were used to predict reduced child distress. At the family level, child age, military parent distress, civilian/caretaker parent distress, child initial distress, and military parent PCL were used as predictors of positive change in FAD, and the number of visits. Number of visits attended also was anticipated to predict positive change in FAD. In turn, positive change in FAD was hypothesized to predict reduced child distress. Number of visits was also used initially as a direct predictor of reduced child distress. Baseline predictor variables were allowed to correlate among themselves. Nonsignificant paths and covariances were dropped gradually using the suggested model evaluation procedure of MacCallum.

### **RESULTS**

The preliminary CFA before the multilevel analysis indicated a well-fitting model (maximum likelihood  $\chi^2$  (N = 505) = 495.75, 253 df; CFI = 0.95; SRMR = 0.049). All factor loadings were statistically significant ( $p \leq 0.001$ ).

#### **TABLE I.**

Summary Statistics and Factor Loadings in the Individual-Level CFA Model and in the Family-Level CFA Model

Variable	Mean (SD) (%)	Factor Loading in Individual/Family Level
<b>Baseline</b>		
Child Age (Years) (Range 3–17)	7.44 (3.54)	NA
Child Gender (% Female)	44%	NA
<b>Military Parent Distress</b>		
BSI Somatic (0–18)	1.43 (2.93)	0.80/0.77
BSI Depression (0–20)	2.99 (3.99)	0.77/0.80
BSI Anxiety (0–20)	3.17 (3.78)	0.85/0.84
<b>Civilian Parent Distress</b>		
BSI Somatic (0–18)	1.96 (3.11)	0.76/0.77
BSI Depression (0–19)	3.82 (4.01)	0.71/0.69
BSI Anxiety (0–17)	3.71 (3.70)	0.89/0.87
<b>Child Initial Distress (1–10)</b>		
Conduct Problems	2.72 (2.25)	0.73/0.90
Emotional Symptoms	3.20 (2.49)	0.36/0.92
Hyperactivity/Inattention	4.52 (2.79)	0.64/0.89
Peer Relationship Problems	2.17 (2.00)	0.43/0.92
Prosocial Behavior (Reversed)	2.24 (2.10)	0.51/0.46
Military Parent PCL (17–82)	25.17 (11.13)	NA
<b>4-Month Follow-up</b>		
<b>Positive Change in FAD (Posttest–Pretest Difference)</b>		
Problem-solving (–0.67 to 1.67)	0.21 (0.42)	0.65/0.67
Communication (–0.89 to 1.44)	0.14 (0.39)	0.73/0.73
Affective Responsiveness (–1.17 to 1.5)	0.16 (0.46)	0.64/0.76
Affective Involvement (–0.86 to 1.57)	0.11 (0.43)	0.54/0.55
Behavior Control (–1.22 to 1.44)	0.14 (0.37)	0.52/0.55
Roles (–0.82 to 1.09)	0.17 (0.35)	0.71/0.68
Number of Visits (1–33)	15.45 (4.69)	NA
<b>Reduced Child Distress (Pretest–Posttest Difference)</b>		
Conduct Problems (–6 to 7)	1.07 (2.02)	0.67/0.88
Emotional Symptoms (–6 to 10)	1.11 (2.34)	0.42/0.84
Hyperactivity/Inattention (–6 to 9)	0.85 (2.27)	0.44/0.78
Peer Relationship Problems (–5 to 8)	0.73 (1.82)	0.42/0.80
Prosocial Behavior (Reversed) (–5 to 7)	0.80 (1.87)	0.46/0.49

<sup>fn1</sup>NA = Not applicable.

<sup>\*</sup>All factor loadings significant at  $p \leq 0.001$ .

Table I presents the factor loadings, means, and standard deviations of the measured variables for the entire group as well as factor loadings in the multilevel CFA (family level). Of note, means of parent distress (BSI) and child distress (SDQ) were generally higher than those in the general population.

**TABLE II.**

Correlations Among Single-Item and Latent Variables

	1	2	3	4	5	6	7	8	9
1. Child Age	—	0.01	0.02	-0.03	-0.08	0.02	-0.01	0.09 <sup>*</sup>	-0.05
2. Child Female	NA	—	-0.06	-0.07	-0.17 <sup>***</sup>	-0.04	-0.01	0.02	-0.08
3. Military Parent Distress	0.06	NA	—	0.28 <sup>***</sup>	0.24 <sup>***</sup>	0.78 <sup>***</sup>	0.14 <sup>**</sup>	0.17 <sup>***</sup>	0.12 <sup>*</sup>
4. Caretaker Parent Distress	-0.05	NA	0.33 <sup>***</sup>	—	0.35 <sup>***</sup>	0.18 <sup>***</sup>	0.23 <sup>***</sup>	0.14 <sup>**</sup>	0.12 <sup>*</sup>
5. Child Initial Distress	0.16	NA	0.31 <sup>***</sup>	0.59 <sup>***</sup>	—	0.19 <sup>***</sup>	0.12 <sup>*</sup>	0.08	0.53 <sup>***</sup>
6. Military PCL	0.05	NA	0.74 <sup>***</sup>	0.22 <sup>***</sup>	0.20 <sup>*</sup>	—	0.10 <sup>*</sup>	0.14 <sup>***</sup>	0.15 <sup>**</sup>
7. Positive Change in FAD	0.06	NA	0.12	0.25 <sup>***</sup>	0.27 <sup>***</sup>	0.08	—	0.17 <sup>***</sup>	0.21 <sup>***</sup>
8. Number of Visits	0.20 <sup>*</sup>	NA	0.19 <sup>***</sup>	0.13 <sup>*</sup>	0.07	0.14 <sup>*</sup>	0.17 <sup>**</sup>	—	0.09
9. Reduced Child Distress	0.22	NA	0.15	0.21 <sup>*</sup>	0.46 <sup>***</sup>	0.20 <sup>*</sup>	0.31 <sup>***</sup>	0.06	—

<sup>fn3</sup>Family-level correlations below diagonal; Individual correlations above diagonal; NA = child gender not applicable in family-level analysis.

<sup>\*</sup>  $p < 0.05$ ;

<sup>\*\*</sup>  $p < 0.01$ ;

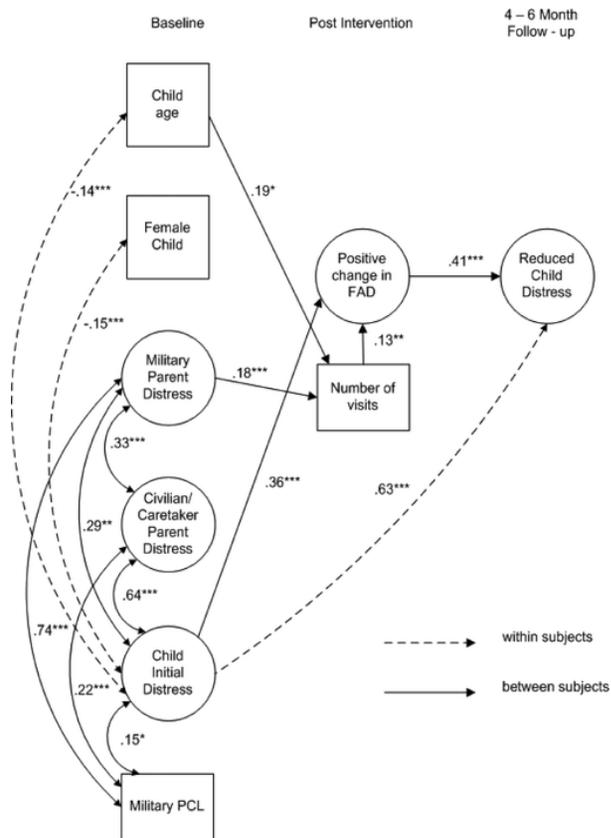
<sup>\*\*\*</sup>  $p < 0.001$ .

Table II reports the correlations among the latent variables and the single-item variables for both the preliminary CFA model and the multilevel CFA model. The 2-stage multilevel CFA had an excellent fit: BLLRS  $\chi^2 = 502.75$ , 309 df; CFI = 1.00; SRMR = 0.038. Of note, in Table II, distress among the military parent, caretaker parent, and their children was highly intercorrelated. Associations among the distress variables were higher at the family level than in the individual level. This result is particularly notable in the association between caretaker parent distress and child initial distress (0.59 at the family level, 0.35 at the individual level that does not account for dependencies within the family). Positive changes in the FAD

were associated with reductions in child distress and with the number of FOCUS program visits, although relationships were stronger at the family level. Baseline distress of the caretaker parent and distress of the child were associated with more positive change in FAD at the family level. This is partly because of lower scores at baseline in the FAD for the more distressed individuals and thus larger possible changes over time. A similar relationship held for the child's initial distress and greater reduction in stress at follow-up. They were higher at baseline and thus had more opportunity for improvement at follow-up in their change scores.

**Path Model**

The final trimmed path model is depicted in Figure 1.



Fit indexes were excellent: BLLRS  $\chi^2 = 522.50$ , 337 df; CFI = 1.00; SRMR = 0.041. Significant individual level correlations and regression paths are depicted with dotted lines such as those associated with gender, which can only be an individual variable; family-level correlations and

regression paths are depicted with solid lines. At the individual level, younger children and boys were more likely to have distress than older children or girls. At the family level, greater distress in the military parent predicted increased number of visits attended in the intervention. The number of visits attended predicted more positive change in FAD. Children with more initial distress were associated with more positive change in FAD, indicating that parents who reported stress in their children were more likely to also demonstrate improvement over time in their family functioning. Of most importance, a positive change in FAD was associated with reduced child distress, a key goal of the intervention. This portion of the model explained 17% of the variance in reduced child distress. In addition, although number of session visits did not directly predict reduced child distress, it did have a significant indirect effect on reduced child distress, mediated through a positive change in FAD ( $p \leq 0.001$ ).

The individual components of the FAD were also assessed separately to find out which aspects were most influential in predicting change in child distress. The most influential subscale was affective involvement, which had a regression coefficient of 0.34 and explained 11% of the variance in reduced child distress. Problem-solving had a regression coefficient of 0.31, and communication had a regression coefficient of 0.30. Each explained 9% of the variance in reduced child distress. Roles had a coefficient of 0.27 and explained 7% of the variance; affective responsiveness had a coefficient of 0.17 and explained 3% of the variance. Behavior control was minimal in explained reduction in child distress (regression coefficient = 0.05, 0% explained).

## **DISCUSSION**

Wartime military operations impact entire families, not just individual service members. As a military and national public health priority, the overall wellness of military families is critical to promoting psychological resilience and mitigating deployment stress risk for all family members, including the service member. Recognizing these priorities, policy directives and increased resources across the Department of Defense and Veteran's Administration have focused on the development and dissemination of prevention and treatment approaches that support military and veteran families along a continuum of care. Increased understanding of the nuanced ways that deployment and reintegration stress is transmitted across family members will assist providers in refining prevention programs designed to promote psychological health in service members and their families.

As anticipated, we found that psychological stress in military families reverberates throughout the family. For families participating in the FOCUS program, distress among the service member parent, civilian/caretaking parent, and children were all significantly related at program entry. This was also evidenced by the high intraclass correlations within families, which necessitated a multilevel approach to this study. Relative to community norms, children entering the intervention had elevated levels of emotional and behavioral symptoms, and their parents had greater anxiety and depression symptoms on standardized measures. As expected, children were more likely to be highly distressed when their caretaker parents were distressed. Notably, there were similar and significant relationships between service members' distress and that of their family members, whether spouse or child. These data underscore the relevance of addressing psychological distress across family systems. Simply treating one member of military families, often the service member, for psychological distress and related mental health problems is likely not optimal.

Consistent with earlier findings, this longitudinal evaluation provides further support that the FOCUS program reduces distress in military children and provides expanded evidence that allows us to investigate how enhancing family functioning can strengthen military families; in this case through the positive adjustment of children. Both FOCUS and its foundational interventions<sup>16</sup> were designed both to strengthen families through theoretically grounded family resilience constructs and to mitigate parental and child distress. This evaluation was undertaken to identify which

intervention or family factors are the most salient in reducing military children's distress over time. We found improved family adjustment predicted reduced distress among military children ( $r = 0.41$ , 17% of variance explained), supporting the relevance of family resilience processes as intervention targets. Notably, the aspects of family functioning associated with hypothesized family resilience processes seemed to be more salient than others in reducing military children's distress, providing initial confirmatory support for the specific family-level targets of this program.

Other factors also predicted reductions in military children's distress. Intervention dosage was associated with reductions in distress. Greater program attendance predicted improved family functioning, with the association of intervention dosage with child outcomes mediated through improved family functioning. Interestingly, more distress on the part of the service member parent predicted more attendance for the family as a whole. Perhaps, more distressed service member parents or their spouses had greater motivation to develop the resilience skills that this program provides.

We acknowledge the limitations of this study. There is the possibility of response bias in the reporting of military children's distress because the child scores are based upon the caretaker parent's report. In addition, improvements in child adjustment may be attributable in part to maturational change; however, the follow-up period was only 6 months and the children's distress was not likely to change solely because of maturity within this short time period. Further, this study is an evaluation of a service program, rather than a controlled study design. Future evaluations would benefit from an intervention control group. Although we recognize these limitations, we feel they are balanced by the importance, timeliness, and uniqueness of the sample and the longitudinal design that uses meaningful change scores within a multilevel context.

### **Study Implications**

Our findings indicate that deployment-related stress reverberates through the entire family relational system and is not limited to service members deploying to war. Notably, these evaluation findings are among the first to show that a family-centered prevention program designed to improve resilience processes can lead to improved longitudinal psychological health outcomes for military children affected by parental deployment. Given the urgent need for enhancing the continuum of effective preventive psychological health services for military and veteran families, these evaluation findings provide initial guidance to understanding the public health potential for family-centered prevention strategies and suggest important areas for future research.

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## **Management of Seizure Disorders in the Deployed Environment: A Treatment Guide for the Non-Neurologist in Theater**

Military Medicine

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### **ABSTRACT**

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Patients with seizures can present a common and challenging problem for medical providers in the deployed environment. Unfortunately, there is a paucity of controlled clinical trial data that can be used to formulate evidence-based guidelines for management. In an attempt to aid the non-neurologist deployed provider in the care of patients presenting with seizures, the authors describe two cases illustrative of common presentations. Thereafter, the authors address many facets of the management questions commonly raised by such cases and offer suggestions regarding such issues as initial pharmacologic management, the need for admission and evacuation, seizure precautions, differentiation from syncope and nonepileptic seizures, addressing patient and command concerns regarding evaluation and duty restrictions, and obtaining online management assistance.

## **INTRODUCTION**

The incidence of seizures is difficult to define since it is highly dependent on the age and other characteristics of the population under study. Approximately 10% of the population will have at least one seizure in their lifetime, and it is estimated that 0.5 to 1% of the population has epilepsy. Seizures are not uncommon in the deployed environment. Sleep deprivation, physical exhaustion, the use of workout stimulants, and the challenge of adhering to the medication regimen are but a few of the seizure-provoking conditions commonly encountered in the deployed environment. Video games and computer viewing are often carried out in a darkened tent or barracks, which may increase the risk of seizures induced by photic stimulation. In one author's experience, the most common trigger for seizures in the deployed environment is sleep deprivation (A.A. Larsen, personal communication). Many deployed service members experience more sleep deprivation than they have ever experienced previously. This degree of sleep deprivation may unmask a previously existing subclinical seizure disorder.

Herein we briefly present two cases of seizure disorders as they might present in the deployed environment. These cases generate questions that help to illustrate the scope and challenges presented in managing this complex condition in the deployed environment. Although there are insufficient studies to construct evidence-based guidelines, it is hoped that the experiences of the authors (three of whom are neurologists) will provide useful guidance that will be helpful for the deployed providers who manage this disorder.

## **CASE 1**

Fellow military service members were awakened at 2:00 a.m. by the noises from a 23-year-old male military service member who shared a living space with them. He was on the floor beside his cot and was described to be "shaking all over." The shaking stopped spontaneously after several minutes, but the service member was unconscious and could not be aroused. His computer was on and was lying beside his cot. First responders were called to evaluate the service member, and they evacuated him by ambulance to the nearest medical treatment facility (MTF). The service member regained consciousness after about 15 minutes while being transported. He had no recollection of going to bed that evening, and he could not recall events such as what he had for dinner earlier that evening. On arrival at the emergency department he was fully awake and responded appropriately. Vital signs were normal. Physical examination was normal without evidence of tongue laceration but he did have urinary incontinence. He had a normal mental status and there was no focal weakness identified. He had no significant medical history, and there were no clear epilepsy risk factors including no history of febrile seizures, no history of traumatic brain injury, no history of central nervous system (CNS) infection, no perinatal complications, and no family history of epilepsy. His only medication was ibuprofen (400 mg) for muscular pain taken on an as needed basis. Laboratory studies including electrolytes, creatinine, and glucose were normal. A noncontrast CT of the head was normal. He was admitted for observation.

## **CASE 2**

A 32-year-old service member was in the barracks preparing for a mission when he suddenly fell to the ground and began having what was described by his fellow service members as a generalized convulsion. The convulsive activity ceased spontaneously after several minutes. The service member had stable vital signs, but he did not regain consciousness. Approximately 15 minutes later, while being transported to an MTF, generalized convulsive seizure activity recurred. He was given lorazepam (2 mg) intravenously. Seizure activity ceased within 5 minutes. Vital signs remained stable but the service member remained unconscious with no response to painful stimuli. Thirty minutes later, while being brought into the emergency department, a third generalized convulsive seizure occurred. He was given two additional 2 mg doses of lorazepam intravenously and loaded with 20 mg/kg of phenytoin equivalent infused at 100 mg/min. The convulsion stopped, but it recurred 20 minutes later while the service member was being evaluated in the emergency department. The physician in charge made a decision to treat the patient with a continuous propofol infusion, since this was the agent with which the physician was most familiar. A 100 mg loading dose followed 4 mg/kg/h by continuous infusion of propofol was initiated. Mechanical ventilation was instituted. Laboratory studies including electrolytes, creatinine, and glucose were normal. A noncontrast CT of the head was normal.

### **FOLLOWING ARE QUESTIONS THAT COMMONLY ARISE REGARDING THE MANAGEMENT OF SEIZURE DISORDERS IN THE DEPLOYED ENVIRONMENT**

#### **What Types of Seizures are Likely to be Encountered in the Deployed Environment?**

There are many types of seizures. Seizure activity can be classified as partial or primary generalized. Partial seizures have onset in one part of the brain and are further subdivided into simple partial and complex partial seizures. Complex partial seizures involve an impairment in consciousness whereas patients with simple partial seizures retain consciousness and thus remain fully aware during the event. There are many subtypes of primary generalized seizures including, absence (petit mal), myoclonic, atonic (drop attacks), or tonic-clonic (grand mal). Although it is important to recognize the many seizure types mentioned above, the generalized tonic-clonic seizure is by far the most common concern in the deployed environment.

#### **Do All Patients with Possible Seizure Activity in the Deployed Environment Require Admission?**

Patients presenting with a suspected seizure in the deployed environment require admission. Admission decreases the provider's liability and removes considerable pressure for continued observation from the service member's unit. Usually the Joint Patient Movement Requirements Center (JPMRC) guidance will be that the patient be seizure-free for 24 hours before evacuation. This guidance may have to be modified for patients with status epilepticus or recurrent seizures despite available therapy.

#### **What Precautions Should be Taken for Patients Admitted with a Possible Seizure?**

Patients are at risk for recurrent seizures and should be protected from injury or harm while hospitalized. At minimum these patients should have a saline lock intravenous access placed and ready for administration of emergency antiseizure medication. Beds should be placed in a low position with wheels locked. Both side rails should be up. Activity out of bed should be supervised. Patients should ambulate with assistance. The patient should shower with someone in attendance. Patients should be monitored if they have not fully returned to their pre-seizure condition, including their baseline mental status and motor function. The patient should be placed in an area where line of sight observation is available.

### **Was the Event the Patient Experienced Truly a Seizure?**

When attempting to determine whether the event the service member experienced was truly a seizure accurate description of the event is of the utmost importance. The episode may only occur once. Further testing such as electroencephalogram (EEG) and neuroimaging may be normal even though a seizure disorder is present. A CT scanner has been available in theater for many years and EEG capability recently became available at one MTF in Afghanistan. Such assets can be used when available. It is important to interview those accompanying the patient or immediately “reach back” to those who may have witnessed the event. Medical personnel who may provide the initial care should make every effort to obtain the information that will help ascertain whether the episode experienced by the patient was truly a seizure. Table I presents a list of key questions that help determine whether the event was truly a seizure, and, if so, information that may help determine the etiology.

TABLE I.

#### **Critical Questions About the “Seizure” Event**

1. Did you see the beginning of the event? If so, what was the patient doing (sitting, standing, lying down)? Was there an associated scream or moan?
2. Were the patient's arms and/or legs shaking? Were the movements synchronous or asynchronous? Were the arms/legs stiffened up? How long did the shaking/stiffness last?
3. Was the head rotated to one side or the other?
4. Were the patient's eyelids opened or closed? If open, were the eyes looking straight ahead, rolled upward, or deviated to one side?
5. Was the patient responsive during the episode?
6. How long did it take for the patient to become responsive? When the patient became responsive was the patient coherent? Was the patient oriented to time or place?
7. Had the patient bitten their tongue, cheek, or been incontinent? If the tongue was bitten, was it the tip or the side?
8. Was one side of the body weaker after the seizure?
9. Was there any language impairment during or after the seizure?

#### **What Features May Help Differentiate Syncope and Nonepileptic Seizures from True Seizure Activity?**

There are many types of events that have “seizure-like” activity but may not be classified as true seizures. Syncopal episodes and nonepileptic seizures, which can both be seen in the deployed environment, are two conditions that often may be challenging to differentiate from seizures. Syncopal episodes may have posturing that resembles seizure activity. Although there are many causes for syncope, in the deployed setting vasovagal syncope is the most common. Vasovagal syncope is usually preceded by one or more prodromal symptoms such as “light-headedness”, “tunneling” of vision, dizziness, nausea, and diaphoresis. Often vasovagal syncope occurs during conditions such as prolonged standing, dehydration, fear, stressful situations, and pain. Twitching and jerking movements may accompany syncopal episodes, but these movements usually lack the rhythmic movements seen with seizures. Loss of bowel and bladder control is unusual in syncope. Seizures may last several minutes or longer, whereas the twitching movements that accompany syncope usually last only a few seconds. Disorientation and sleepiness often last many minutes or even hours following a generalized seizure, but rarely lasts more than 5 minutes after a syncopal event.

In addition, some patients may have nonepileptic seizures, which are not uncommon in the deployed environment. Nonepileptic seizures are sudden changes in behavior that may resemble epileptic seizures but are not accompanied by the cortical electrographic changes that characterize epileptic seizures. Although many clinical features can help differentiate a seizure disorder from nonepileptic seizures, many testing modalities that aid in making the diagnosis, such as EEG and video EEG monitoring, are not readily available in the deployed environment. Thus, even when nonepileptic seizures seem likely, evacuation to an appropriate higher level of care is usually required. Many patients with a true seizure disorder may also have nonepileptic seizures, further complicating the evaluation. In addition, patients with nonepileptic seizures require referral to behavioral health since the nonepileptic seizure may be a presenting symptom of post-traumatic stress disorder, adjustment disorder, or other behavioral health condition.

### **What Underlying Conditions May Provoke or Cause Seizures?**

A number of underlying conditions can produce seizures. In susceptible individuals seizures can be provoked by sleep deprivation or by repetitive flashing lights of particular colors or flash frequencies. Metabolic abnormalities such as hyponatremia, hypoglycemia, hypomagnesemia, and hypercalcemia can produce seizures. CNS injury because of acute trauma, previous brain injury, CNS infections, cerebrovascular events (ischemic stroke, intracerebral hemorrhage, subarachnoid, or subdural hemorrhage), brain tumors, and autoimmune disorders may cause seizures. Numerous drugs or substances may cause seizures

#### **TABLE II.**

Drugs and Substances Encountered in the Deployed Environment that may Provoke/Cause Seizures <sup>14, 15</sup>

Chloroquine

Mefloquine

Beta lactam antibiotics (usually in high doses)

Acyclovir

Quinolones

Isoniazid (INH)

Tramadol

Dietary supplements

Antidepressants

Antipsychotics

Amphetamines

Cocaine

Phencyclidine

Methylphenidate

*Additional Provocations:*

Withdrawal from alcohol, short acting benzodiazepenes or barbiturates

“Spice”  
Bath salts  
“Huffing”

Two prescription medications that have been of particular concern in the deployed environment have been tramadol and bupropion. Heavy use of or withdrawal from alcohol may increase the risk of seizures as well.

### **What is the Best Initial Treatment for Seizure Control in a Patient with Seizures?**

The initial management of seizures has not been well studied in randomized controlled trials and is thus not standardized. Management differs between institutions and even within institutions. Thus, many approaches can be considered acceptable. Management in the deployed setting may sometimes differ from that in the nondeployed setting. Despite the lack of an evidence-based comprehensive approach, we present an algorithm that the authors believe might serve as a useful framework. Once it has been determined that the event was likely a seizure, a decision must be made about the need for seizure control medications. An important consideration is the likelihood that the patient has epilepsy.

### **TABLE III.**

#### Epilepsy Risk Factors

History of:

- Traumatic brain injury
- Intracranial events (ischemic/hemorrhagic, subarachnoid, or subdural hematoma)
- Perinatal insults, ICU stays (reason for if known)
- Epilepsy or sudden death of unclear etiology in family members
- Abnormal development (late milestones, trouble getting through school)
- Epilepsy as a child (granted waiver to enter military because “outgrew them”)
- Brain abnormalities such as arteriovenous malformation, neurofibroma
- Central nervous system infection or injury

The more risk factors a patient has, the higher the risk of recurrent seizure and need to start seizure control medications.

Table III lists some of the factors one may consider when determining the likelihood of epilepsy in patients who present with a seizure. The more epilepsy risk factors the service member has, the more likely it is that the member should be treated with antiseizure medications. Patients evacuated for evaluation of a possible seizure do not need to be routinely placed on seizure control medications. Since current theaters of operations require long evacuation flights to level 4 care, antiseizure medications to reduce the likelihood of recurrent seizures during transport are sometimes requested by JPMRC.

In the nondeployed setting many patients are not placed on medication for a single seizure until further evaluation has been completed. Since placement on seizure control medications can hinder further evaluation of the patient and make a premature judgment on the need for medication, patients should not routinely be placed on seizure control medications for evacuation without consulting the theater neurologist or obtaining a neurology consult via the military online consultation service (neuron.consult@us.army.mil). It is, however, mandatory to write for seizure control medications on the patient movement request orders so that these medications are readily available for the patient should a seizure occur during transport.

### How are Recurrent Seizures Best Managed?

As previously noted there are no evidence-based comprehensive guidelines for seizure management. Approaches may differ between institutions and even among individuals within the same institution. Characteristics of seizure control medications commonly available in the deployed setting are summarized in Table IV.

**TABLE IV.**

Pros and Cons of Seizure Control Medications Likely to be Available in Deployed Settings

Drug	Onset of Action	Duration	Pros	Cons
Diazepam (Valium)	20 seconds	15–20 minutes	Readily available at all levels of care; multiple routes of administration; most providers familiar with drug	Higher incidence of ventilatory suppression; short duration of action
Lorazepam (Ativan)	2–5 minutes	4–14 hours	Long duration of action	Slower onset
Midazolam (Versed)	90 seconds	30 minutes	Perceived high effectiveness with less side effects; preferred by many for continuous infusion	Tachyphylaxis within 48 hours
Propofol (Diprivan)	1 minute	3–10 minutes	Short half-life allows smooth and rapid titration	Hypotension; propofol infusion syndrome
Fosphenytoin (Cerebyx)	15 minutes	24 hours	Perceived advantages of faster administration rate, fewer side effects	Much more costly than phenytoin; need to calculate phenytoin equivalents when dosing

If the patient has recurrent seizures, repeated doses of benzodiazepenes can be used for short-term control. A possible practical choice is lorazepam (2 mg intravenous) every 2 to 3 minutes until seizures are controlled or a total dose of 8 to 10 mg is reached. Careful observation for respiratory depression is necessary. If there are recurrent seizures, fosphenytoin is added by some to try to reduce the risk of seizure recurrence. As noted, many other approaches are acceptable 9–12 (see Table IV), and there is a paucity of literature involving evidence-based comparisons.

### How is Status Epilepticus Defined and How is it Best Managed?

There appear to be various definitions of status epilepticus. Workable definitions for the deployed environment are 5 minutes of persistent generalized seizures or 2 or more discrete seizures between which there is incomplete recovery of consciousness. Another acceptable definition is

persistent seizure activity after administration of adequate doses of first- and second-line antiseizure medications. This usually consists of benzodiazepenes and fosphenytoin in the deployed environment. Propofol has emerged as a popular alternative for control of status epilepticus. As noted previously, there is little scientific evidence regarding the best treatment regimen, and providers rely on medications and treatment algorithms with which they are familiar. The authors suggest one possible algorithm for the management of seizures and status epilepticus based on agents typically available in theater (Fig. 1).

### **What is the Suggested Workup for Seizures in the Deployed Environment?**

As previously mentioned, a thorough description of the event with particular emphasis on the questions noted in Table I is of critical importance. A general physical examination with particular emphasis on a search for injuries (including tongue laceration), signs of infection, fundoscopic changes (blurred optic disk or retinal hemorrhages), or neurologic abnormalities (especially localizing findings) should be performed. A temporary focal paralysis following the seizure (Todd's paralysis) may give clues as to the anatomical localization of the seizure. It should be noted that a transient positive Babinski's sign is not unusual after a generalized seizure and may not necessarily be indicative of other CNS pathology. When available, laboratory examinations should include complete blood count, metabolic panel (blood urea nitrogen, creatinine, electrolytes), glucose, liver function tests, and creatine phosphokinase. When available, a non-contrast CT of the head should be obtained as part of the initial evaluation. This is recommended even if there appears to be a metabolic cause. If EEG is available, that should be obtained as well.

### **Do Seizures Always Require Evacuation for Evaluation?**

Owing to the need for testing modalities that are usually not available in the deployed environment (EEG, MRI, video/EEG monitoring, special tests of blood, or CSF for infection or autoimmune disorders), almost all patients who present with a seizure will require evacuation to a higher level of care for evaluation. As noted previously, suspected nonepileptic seizures also require evacuation.

### **Are There Ever Any Special Circumstances Under Which a Patient with Suspected Seizure Would Not be Evacuated?**

If a neurologist evaluates the patient and is certain that the event was not a seizure, evacuation may not be necessary. If the service member has a known seizure disorder, is on waiver after a physical evaluation board, is taking antiepileptic drugs, the seizure was provoked by something other than noncompliance, the service member's command wishes to have the service member remain in theater, and the consulting neurologist agrees, the service member may be allowed to remain. However, it should be noted that it would be a rare exception for a service member who has had a seizure to be allowed to remain in theater. The final decision on service member evacuation remains with the service member's command.

### **Under What Category Should Patients be Evacuated?**

When patients can be promptly evacuated from theater and placed on a direct flight to a level 4 or 5 MTF, patients without recurrent seizures may be evacuated under the routine/ambulatory category. If there is concern for recurrent seizure activity, patients may require routine/litter for safety. If available medical evacuation flights will be indirect because of numerous stops, it may take many days to complete the evacuation process. In such instances it may be safer to work with JPMRC and evacuate the patient as a priority. This requires judgment based on all the data gathered regarding the event and the condition of the patient. Patients requiring frequent doses or infusion of control medications require urgent or priority

evacuation. Many of these patients will require mechanical ventilation during evacuation. Careful coordination with JPMRC and, if available, a consulting neurologist can optimize care.

### **How Does Whether a Seizure is Provoked or Unprovoked Affect Management and Prognosis?**

It is important to differentiate between a provoked and an unprovoked seizure for clinical reasons, but this difference is irrelevant to initial management in the deployed setting. Whether the seizure was provoked or not, the service member must be evacuated out of theater (except in the case of rare exceptions noted above). However, whether the seizure was provoked remains an important part of the history. Once in a garrison setting, the question of provoked versus unprovoked becomes relevant and will determine the severity and duration of subsequent restrictions. For example, a service member who had no history of seizures and no predisposing condition, but engaged in an activity while downrange that may have resulted in a seizure would be evacuated out of theater for the seizure and have a seizure workup in garrison. The service member would probably be placed on 6-month seizure restrictions with a temporary P3 profile (in the army). If the workup was unremarkable, and the service member had no further seizures at the end of 6 months, the service member might be removed from all restrictions and profiles. This decision would be strongly influenced by how strongly the neurologist felt the event was provoked. The service member's Military Occupational Specialty and branch of service also effects what restrictions may be placed on the service member. Note that there are interservice differences and the appropriate service regulations should be consulted.

### **What are Some Points for Discussion When the Patient and Command Have Questions Regarding What Workup Will Ensur and Whether the Patient is Likely to Return to Duty?**

It is likely that at a minimum the patient will get an MRI and EEG upon evacuation from theater. Once evacuated from theater it is extremely unlikely that the service member will return to theater for the remainder of the deployment. Service branches may vary in approaches to management. According to AR 40-501 (the Army Standards for Fitness) the patient must be seen by a neurologist for consultation and further evaluation. The neurologist will make recommendations regarding treatment and duty restrictions. Since there are so many factors that affect the decisions regarding the need for referral to the medical evaluation board (MEB) and duty restrictions, the neurologist is given considerable latitude for clinical decision making in AR 40-501. There are some circumstances that require an MEB; these may vary among service branches and Military Occupational Specialties.

### **What Duty Restrictions Will be Placed and for How Long?**

As noted above, ongoing restrictions will vary depending on a number of factors. In some patients there may be a question as to whether the event was truly a seizure. After evaluation the conclusion may be that a true seizure probably did not occur. In such cases no treatment or duty restrictions may be required, although this depends on the final diagnosis. If it is determined that it is likely that a seizure occurred, the circumstances surrounding the seizure help define what restrictions will be needed. For example, a single seizure provoked by sleep deprivation that resolved spontaneously may not require extensive restrictions. On the other hand, multiple unprovoked seizures may require quite stringent duty restrictions, even if the seizures have not recurred after evacuation. In most instances, service members are initially placed on duty restrictions for 6 months. The restrictions include no driving, no handling firearms or other weapons, no climbing to heights, no operation of heavy machinery, no swimming, and no sleeping on a top bunk. In addition, any other activity that could cause harm to the patient or others if seizure should recur may be precluded. The stringency of preclusion may vary. For instance, some might preclude the carrying of small infants, while

others would not. The 6 month time period is due to the fact that most seizure recurrences will occur within the first 6 months. If the service member is returning to garrison, recommendations on driving personal vehicles should be made taking into account individual state laws. However, the service member is usually restricted from driving government vehicles for 6 months. Physical training is usually allowed although swimming is, as noted previously, often precluded. Weight lifting, particularly with the use of free weights, may be precluded.

If there is only a single seizure no MEB is required. A second seizure requires an MEB. If the neurologist elects to place the service member on a trial of duty, the service member will receive a temporary P3 profile. The service member is considered nondeployable. If the service member has another seizure after 6 months, AR 40-501 states that the service member must be referred to an MEB. If the service member remains seizure-free for 1 year, the profile can be reduced to a P2 with a profile restriction "specifying no assignment to an area where medical treatment is not available." Should seizures recur at a later time, referral to an MEB is at the discretion of the physician. Once a service member has been seizure-free for 36 months, the service member may be removed from profile restrictions.

### **Where Can Deployed Providers Obtain Online Assistance Regarding Management?**

Deployed providers may often obtain valuable assistance by accessing the neurology section of the United States Military online consultation system for deployed providers at [neuron.consult@us.army.mil](mailto:neuron.consult@us.army.mil).

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## **Update: Community-Acquired Methicillin-Resistant Staphylococcus aureus Skin and Soft Tissue Infection Surveillance Among Active Duty Military Personnel at Fort Benning GA, 2008–2010**

Military Medicine

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### **ABSTRACT**

**Background:** Increasing numbers of Staphylococcus aureus infections demonstrate antibiotic resistance. Military populations experiencing crowding are at increased risk of community-acquired methicillin-resistant S. aureus (CA-MRSA) infection. High prevalence of CA-MRSA infection among Army personnel was previously documented at Fort Benning, GA from 2002 to 2007. **Purpose:** To ascertain recent CA-MRSA trends at Fort Benning regarding antibiotic susceptibility, infection rates, and treatment regimens among Army personnel. **Methods:** Incident CA-MRSA cases among active duty members/trainees from January 2008 to December 2010 were identified using active surveillance and laboratory data. **Results:** In total, 2,171 infections were identified, representing 5,794 CA-MRSA-related clinic visits. Annual rates decreased from 33 to 27 infections per 1,000 soldiers from 2008 to 2010. Approximately 78% of isolates were from training units. Approximately 4% of infections required hospitalization. Most infections (97%) were treated with antibiotics (36% received antibiotics and wound drainage). Antibiotic susceptibility patterns remained comparable to previous assessments. **Conclusion:** The observed decline in CA-MRSA rates and associated hospitalizations, coupled with stable antibiotic susceptibility patterns, is encouraging. Passive surveillance using laboratory records proved useful in identifying infection and

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could enhance detection across training sites. Given the continued high CA-MRSA prevalence among trainees, providers/public health personnel should remain vigilant to bolster prevention, detection, and treatment efforts.

## INTRODUCTION

*Staphylococcus aureus* (SA) is a well-known bacterial human colonizer and pathogen; approximately 20 to 30% of humans asymptomatically carry SA in their anterior nares. SA commonly causes skin and soft tissue infections (SSTIs), though infection can also result in life-threatening conditions, such as pneumonia, necrotizing fasciitis, and sepsis. First identified in hospital settings in the 1950s, methicillin-resistant SA (MRSA) became a recognized cause of nosocomial infection. During the late 1980s in the United States, MRSA infections of a different genotype began to appear in individuals without ties to health care institutions and were subsequently termed community-acquired or community-associated MRSA (CA-MRSA).

CA-MRSA outbreaks now occur all over the world; though they have similar epidemiologic features, the specific type of MRSA clone responsible varies geographically. In the United States, clone USA300 supplanted USA400 (predominant in the early 2000's) as the leading cause of CA-MRSA infections. USA300 is Panton–Valentine leukocidin (PVL) locus positive; though the relationship between the PVL toxin and disease severity has not been definitively determined, some evidence suggests the PVL locus is associated with increased virulence. Additionally, USA300 strains possess a mobile element (i.e., arginine catabolic mobile element) transferred from *S. epidermidis*, which is thought to result in selective advantage for surviving on human skin. Increasing multidrug (non- $\beta$ -lactam) resistance has also been described in USA300 MRSA clones. Thus, the increasing number of CA-MRSA caused SSTIs in the United States may be because of a more virulent clonal strain that is demonstrating increasing multidrug resistance.

CA-MRSA tends to differ from health care–associated MRSA (HA-MRSA) both genetically and epidemiologically, though precise definitions of CA-MRSA vary. Typically presenting as SSTIs rather than invasive and life-threatening diseases, CA-MRSA infections usually affect younger and healthier individuals, and isolates display greater susceptibility to non- $\beta$ -lactam antibiotics (including fluoroquinolones, clindamycin, and tetracycline) except erythromycin. CA-MRSA strains typically possess a smaller chromosomal cassette with the *mecA* gene as compared to nosocomial strains. Conversely, HA-MRSA strains tend to be resistant to more antibiotics, as they rarely possess genes encoding the PVL toxin. In addition, these strains are more commonly found in older people with multiple comorbid conditions and recent ties to health care facilities.

Individuals colonized with CA-MRSA are at increased risk of developing subsequent SSTIs. Estimates of CA-MRSA nasal carriage vary, but a meta-analysis of MRSA colonization surveillance resulted in a pooled prevalence estimate of 1.3% among community members. SA is typically transmitted via skin-to-skin contact with an infected person or asymptomatic carrier, though contaminated shared objects have been implicated. Chances of MRSA transmission are increased under conditions where personal hygiene is compromised, common-touch items are shared (e.g., towels, mats, razors), and where crowding occurs. MRSA outbreaks have been documented among daycare centers, athletes, military recruits, and prison inmates. It is hypothesized that compromises to the skin's protective barrier (chafing, abrasions, and insect bites) may increase transmission of MRSA among military recruits and athletes.

Increasing incidence of SSTIs and isolation of MRSA has been documented throughout the United States, with Johnson et al reporting a four-fold increase in incident MRSA infections from 2001 to 2005 (primarily presenting as CA-SSTIs). In 2001, a CA-MRSA incident tracking system was initiated at Fort Benning, GA, one of four Army basic military training (BMT) sites. This system was activated because of a perceived increase in

infection, particularly among trainees who may experience increased crowding conditions, rigorous physical training, and suboptimal personal hygiene. Using this data, Morrison-Rodriguez et al showed a high prevalence of CA-MRSA infection among active duty military personnel from 2002 to 2007. An increasing proportion of SA isolates were identified as CA-MRSA, and antibiotic susceptibility of wound isolates indicated decreasing susceptibility to clindamycin, ciprofloxacin, and levofloxacin. This article updates the Morrison-Rodriguez et al work, assessing data from 2008 to 2010. Surveillance was discontinued in 2011 because of local resource constraints, preventing assessment of more recent data.

## **METHODS**

The analysis was performed in 2012 using methods outlined by Morrison-Rodriguez et al to ensure comparability. The population consisted of military service members (SMs) from all components (active duty, reserve, and guard) assigned to Fort Benning who had a laboratory culture-confirmed MRSA infection between January 2008 and December 2010. Fort Benning's Martin Army Community Hospital (MACH) collected laboratory and medical data for all confirmed MRSA infections among SMs seeking care at MACH. CA-MRSA SSTIs were identified according to the following criteria: (1) clinically determined SSTI; (2) wound culture positive for oxacillin-resistant SA using Microscan WalkAway with the PC-33 panel; and (3) no documented history of surgery/hospitalization in the 30 days before SSTI diagnosis.

A CA-MRSA surveillance database, designed by MACH infection control personnel, was used to document demographics, clinical presentation, treatment protocol, attributable morbidity burden (i.e., days hospitalized, days of limited duty, and patient visits associated with infection), and antibiotic susceptibility results.

The Defense Enrollment Eligibility Reporting System provided aggregate population data used to determine the monthly population of SMs eligible for care within a 20-mile radius of MACH during the surveillance period. The proportion of active duty SMs stationed at Fort Benning who were trainees was determined from aggregate data provided by the Defense Manpower Data Center.

The proportion of SA isolates considered positive for MRSA among beneficiaries seen at MACH (SMs, retirees, and family members) was calculated using individual-level SA-positive laboratory culture results obtained from the Navy and Marine Corps Public Health Center. The data were also used to augment information missing from the local surveillance database from September 27 to December 31, 2009. Additionally, CA-MRSA SSTI infections among active duty SMs identified from 2010 laboratory data were compared to infections captured by MACH to assess differences in CA-MRSA SSTI case capture through active and passive surveillance.

Analysis was performed using SPSS (version 19) and SAS (version 9.1). Demographic information was summarized at the time of initial infection. A 14-day incidence rule was used to define unique infections per person. Effectiveness of prescribed antibiotics was evaluated relative to published guidelines. Antibiotics were considered effective if at least 60% of CA-MRSA SSTI isolates were susceptible.

## **RESULTS**

Fort Benning hosts the 9 week long BMT, and the 14 week one-stop unit training (OSUT), a combination of BMT and Advanced Individual Training. The average monthly population of SMs eligible for medical care within MACH's catchment area was 23,400, ranging from 19,000 to 26,000 individuals per month. Active component trainees made up roughly a quarter of the eligible SM population. The majority of identified CA-MRSA SSTI cases were male (97.8%), younger than 25 years of age (74.7%), affiliated with the Army (99.8%), and trainees (77.9%) (primarily members of OSUT units [62.5%]).

**TABLE I.**

CA-MRSA SSTI Case Summary, Active Duty Service Members, Fort Benning 2008 to 2010

Demographics at Time of Initial Infection ( <i>N</i> = 2006)	Count (%)
Age (Years)	
<20	709 (35.3)
20–24	790 (39.4)
25–29	270 (13.5)
>30	237 (11.8)
Mean Age = 22.7 ± 5.5; Range 17–50	
Gender <sup>a</sup>	
Male	1,959 (97.8)
Female	45 (2.2)
Service <sup>a</sup>	
Army	1,856 (99.8)
Marines	3 (0.2)
Unit Type <sup>a</sup>	
Trainee Units	1,441 (77.9)
OSUT <sup>b</sup>	1,156 (62.5)
BMT <sup>c</sup>	285 (15.4)
Nontrainee Units	408 (22.1)
Rangers	73 (4.0)
Airborne School	45 (2.4)
Other (Includes Permanent Party and Specialized Training Units)	290 (15.7)

<sup>a</sup>Counts do not add to the total because of missing results, i.e., gender, service, and unit assignment were missing for 2, 147, and 157 cases, respectively.

<sup>b</sup>One stop unit training lasts 14 weeks; it combines basic military training and advanced individual training.

<sup>c</sup>Basic military training lasts 9 weeks.

Although week of training was documented for trainees with CA-MRSA SSTIs in 2010, examination of this data revealed no significant associations. A total of 2,171 CA-MRSA SSTIs among 2,006 individual SMs were identified. Repeat CA-MRSA infection was observed among 147 (6.7%) SMs, ranging from 2 to 5 infections per person.

**TABLE II.**

CA-MRSA SSTI Infection Characteristics

Characteristics	Count (%)
Incident Infections	2,171
Individuals Affected	2,006
Individuals With Repeat Infection	147 (6.7)
Mean Number of Infections = 1.1 Infections Per Service Member $\pm$ 0.3; Range 1–5 Infections	
CA-MRSA Clinic Visits Per Infection <sup>a</sup>	
1	490 (24.6)
2–4	1,226 (61.4)
$\geq$ 5	280 (14.0)
Clinic Visits: Total = 5,794; Mean = 3 $\pm$ 2; Range 1–28 Visits	
Assigned to Limited Duty Profile <sup>b</sup>	790 (39.4)
Days of Limited Duty: Days = 3,928; Mean = 5.0 $\pm$ 4.5 Days; Range 1–108 Days	
Hospitalization (Postinfection) <sup>b</sup>	82 (4.1)
Days Admitted: Total = 353; Mean = 4.3 $\pm$ 1.9 Days; (Median = 4.0); Range 1–11 Days	
Wound Locations <sup>c</sup>	
1	1,694 (85.1)
2–4	297 (14.9)
Mean Number of Wound Locations = 1.2 $\pm$ 0.4; Range 1–4 Locations	
Body Site <sup>c, d</sup>	
Lower Extremity	752 (37.8)
Knee	290 (14.6)
Upper Leg	277 (13.9)
Foot	91 (4.6)
Lower Leg	81 (4.1)
Upper Extremity	628 (31.5)
Upper Arm	190 (9.5)
Axilla	188 (8.7)

### Characteristics

	Count (%)
Elbow	143 (6.6)
Hand	100 (5.0)
Genitals/Buttocks	334 (16.8)
Head/Neck	298 (13.8)
Trunk/Back	150 (7.5)

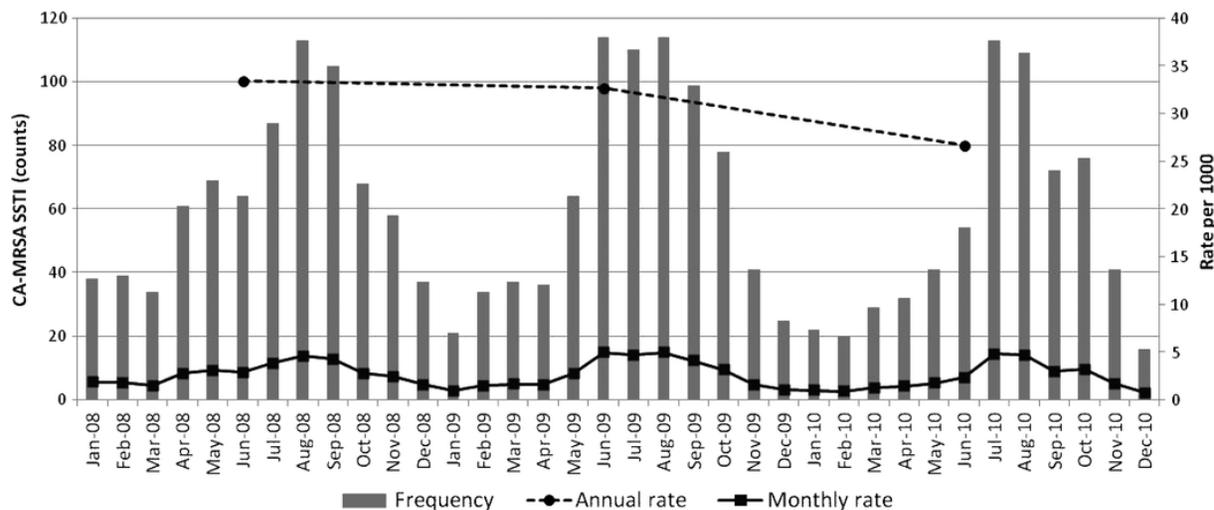
<sup>a</sup>All visits for MRSA-related care; data were available for 1,996 infections.

<sup>b</sup>Data were available for 2007 infections (missing:  $n = 164$ ).

<sup>c</sup>Not all infections had wound location information recorded (missing:  $n = 180$ ).

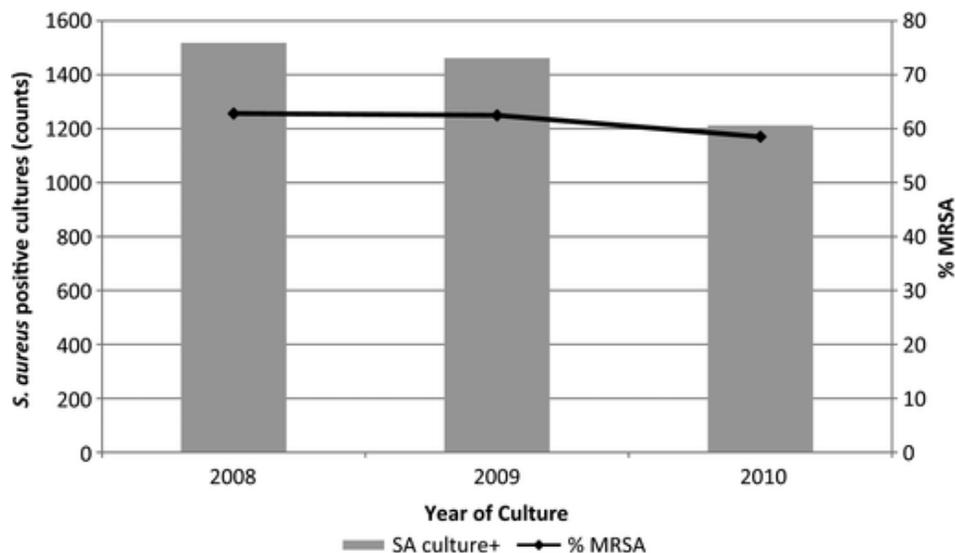
<sup>d</sup>Multiple wound locations per infection were possible.

As shown in Figure 1,



monthly CA-MRSA SSTI rates peaked at 5.0 cases per 1,000 SMs in June to August 2009, whereas annual rates peaked at 33.0 cases per 1,000 in 2008. Annual rates decreased each year, dropping to 26.6 cases per 1,000 SMs most noticeably in 2010. Seasonal variation was observed, with the highest rates occurring during warmer months (June–August).

A total of 4,192 isolates from beneficiaries seen at MACH were positively identified as SA from 2008 through 2010; of these, 2,571 (61.3%) were classified as MRSA. The proportion of SA isolates identified as MRSA decreased from 62.8% in 2008 to 58.5% in 2010.

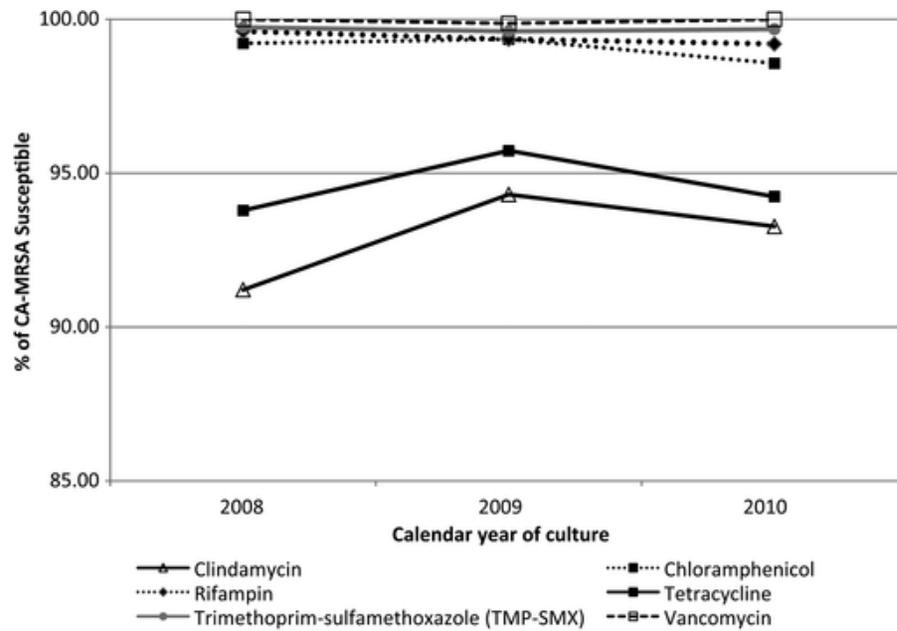


Body site was documented for 1,991 (91.7%) CA-MRSA infections; multiple locations were observed for 297 (14.9%) infections (1–4 sites per infection). As displayed in Table II, the lower extremities displayed the greatest frequency of body locations (37.8%), particularly the knee (14.6%) and upper leg (13.9%). The upper extremities accounted for 31.5% of infection locations, with the upper arm (9.5%) and axilla (8.7%) most frequently listed. A total of 5,794 CA-MRSA-associated clinic visits were documented (mean 3.0 visits  $\pm$  2.0 visits per infection, range 1–28 visits).

Disposition information was available for 2,007 (92.5%) infections and indicated that 790 (39.4%) infections resulted in limited duty days. Overall, CA-MRSA SSTIs resulted in 3,928 limited duty days (5.0 days  $\pm$  4.5 days per infection on average, range 1–108 days) and 82 hospitalizations (4.3 days  $\pm$  1.9 days per admission on average, range 1–11 days).

A total of 1,946 (97.0%) CA-MRSA SSTIs were treated with antibiotics, either alone or in combination with incision and drainage (I&D). More than half of infections were treated with antibiotics only (60.9%), 36.1% received both antibiotics and I&D, 0.3% received I&D only, and 2.6% had no documented treatment. Antibiotics most commonly prescribed included sulfonamides (TMP-SMX) (80.8%), tetracyclines (45.6%), and clindamycin (27.9%).

Overall, isolates were susceptible to five antimicrobials, which included vancomycin (100%), TMP-SMX (99.7%), rifampin (94.6%), tetracycline (94.6%), and clindamycin (92.9%); greater variability in susceptibility was observed with clindamycin and tetracycline.



Note: Only results for effective antibiotics are shown

Of the 1,946 infections for which an antibiotic was prescribed, 1,930 (99.2%) received at least one effective antibiotic.

A comparison between incident CA-MRSA infections identified by the MACH in 2010 and those identified through review of HL7 laboratory data showed that 54% (n = 464/860) of infections were captured in both surveillance systems. Active surveillance performed by MACH staff identified an additional 43 (5%) infections not found in the laboratory database and laboratory surveillance captured 353 (41%) infections not found in the local surveillance database.

## DISCUSSION

This analytic update identified decreased incident CA-MRSA infections over the 3 year study period, which is an extension of declining yearly rates documented after 2005. These findings coincide with results from a laboratory-based assessment of all Services, which concluded that MRSA incidence within the Department of Defense decreased from 2005 to 2010.<sup>24</sup>

Though incident rates of MRSA seem to be stabilizing, the continuing high burden of clinic visits (n = 5,794), lost duty days (n = 3,928), and days hospitalized (n = 353) associated with CA-MRSA SSTI occurring predominantly among trainees is concerning. These interruptions in the training cycle can have negative effects at individual and systematic levels, as recruits unable to complete training with their class may be required to repeat training, possibly leading to lost troop strength in specialized areas. Future analyses to assess direct and indirect costs in terms of repeat training, reduced manpower, and medical resource demand because of CA-MRSA SSTI among trainees should be considered.

It has been theorized that higher temperature and humidity levels may contribute to an increased risk for MRSA infection. The seasonal variation of CA-MRSA, with peak rates occurring during warmer months, correlates with the prior Fort Benning assessment and similar studies. During the summer, monthly CA-MRSA incidence rates are comparable to those observed during CA-MRSA outbreaks among recruits at other installations, roughly 4 per 1,000 SMs.<sup>20</sup> Warmer months are associated with increased skin exposure, which may place trainees at increased risk of cuts, scrapes, and abrasions, and increase skin contact between individuals during training activities.<sup>20</sup> Wound site distribution may provide insight into areas of the body at increased risk for CA-MRSA infection. The distribution of wound sites closely matches the distribution previously observed at Fort Benning, as well as the distribution noted by Crum et al,<sup>6</sup> with the majority of wounds located on bodily extremities (69%), reflecting areas with increased exposed surface area and/or locations subjected to increased friction (e.g., knees and elbows).

Although not presented in the results, 26% (521/2,007) of infections for which data was available had a documented arthropod bite. Whether this reflects CA-MRSA infection stemming from an initial arthropod bite, or CA-MRSA infection mistaken for an arthropod bite cannot be determined from the data. The role of warmer temperatures in facilitating CA-MRSA SSTI by increasing exposed surface area and/or arthropod activity cannot be determined, but enhanced insect abatement and increased use of recommended personal protection (e.g., DEET) as a feasible intervention may merit investigation, particularly in this geographic location and population.

The average number of clinic visits, days assigned to limited duty, and days hospitalized associated with each infection remained fairly stable from 2008 to 2010 compared to 2002 to 2007 (mean 3.0 versus 3.1 visits, 5.0 versus 5.3 profile days, and 4.3 versus 4.6 days of hospitalization). However, the proportion of infections requiring hospitalization decreased substantially between the two time frames, declining from roughly 10 to 4%. Further analysis of severity is needed, but this may be a reassuring indicator that infection severity has not increased.

Almost all infections were clinically managed using antibiotics. Only 36% were treated with I&D, which is the recommended treatment course for localized infections that are not severe, difficult to drain, or systemic. This represents a decline in wound drainage from the prior study (43–36%). It is reassuring that most prescriptions were appropriate, given the susceptibility profiles of tested isolates and that prescription of effective antibiotics improved between the two evaluations (82–99%). Exploring physician's rationale for prescription is essential, as only 3% of infections from 2008 to 2010 did not receive antibiotics. Aside from hospitalization information, infection severity information was not available; this type of information would enable more thorough examination of treatment regimens in comparison to standards of care.

Antibiotic resistance levels closely matched the previous analysis, with the exception of levofloxacin and ciprofloxacin. Although the 2002 to 2007 data showed that 66% and 62% of MRSA isolates were susceptible to levofloxacin and ciprofloxacin, respectively, the 2008 to 2010 data indicated that only 57% and 53% were susceptible. However, given how infrequently these antibiotics were prescribed this finding has limited clinical relevance. Susceptibility to clindamycin, chloramphenicol, rifampin, tetracycline, TMP-SMX, and vancomycin appeared stable over the study period and was generally consistent with susceptibilities reported in the literature. As CA-MRSA strains are often correlated with clindamycin susceptibility, the observed high level of clindamycin susceptibility (93%) supports the premise that CA-MRSA strains are primarily responsible for SSTI MRSA infections within this population (rather than HA-MRSA strains).

A comparison of case capture between the MACH and laboratory databases showed that approximately 95% of active duty cases were captured exclusively by centrally collected and readily available laboratory data, leading to the conclusion that laboratory data are probably the most efficient means to identify infection. Active surveillance exclusively captured the remaining 5% of infections that would go undetected by this process and provided more detailed training information that could inform prevention efforts. However, active surveillance is not always viable

when resources are limited; this comparison supports the notion that utilizing laboratory data in lieu of active surveillance may be an acceptable alternative.

Several important limitations to this study bear mentioning. First, CA-MRSA was determined based on epidemiological definitions rather than genetic typing, and relied mainly on the absence of prior hospitalization. As the lines between HA and CA-MRSA become blurred, reliance on epidemiological strain classification may be problematic. It is possible that the existence of a surveillance project could have influenced clinician's decisions to culture wounds, possibly leading to higher testing rates and identification of more CA-MRSA isolates. However, the likelihood of missed cases seems more probable, as military SMs may self-treat or seek care outside of the military health system, clinicians may decline to perform wound cultures, and MRSA infections may be misdiagnosed (e.g., insect bites). Additionally, it is possible that calculated CA-MRSA rates may be an underestimation, particularly among trainees. Since there is incentive for recruits to complete training to avoid repetition of the training cycle, trainees with less severe infections may have declined to seek medical care. The extent to which substituting laboratory data for missing data to calculate monthly rates for September 27 through December 31, 2009 affected results cannot be determined; however, graphical examination did not reveal aberrant values or trends. Additionally, incomplete personal identifier information precluded linking surveillance data with other medical data, which could have provided additional information regarding demographics, case severity, treatment patterns, and CA-MRSA recurrence. It was not possible to determine if all non-SSTIs were excluded from the laboratory database, which may partially explain the higher case capture. Furthermore, variability in surveillance practices because of gradual reductions in manpower for this project are possible, but the degree to which this may have influenced the data collected is difficult to ascertain. Lastly, differences in surveillance methodology make comparisons to national rates inappropriate.

## **CONCLUSION**

This study update documents continued high prevalence of CA-MRSA among trainees which underscores the need for adequate personal hygiene, disinfection of common surfaces, and continued vigilance among clinicians to stay abreast of CA-MRSA and antibiotic susceptibility trends to guide appropriate wound treatment. The variability in susceptibility to tetracycline and clindamycin observed in the study is noteworthy given the high frequency with which these antibiotics were prescribed. Other notable findings include stabilization in CA-MRSA rates and a decrease in the number of cases requiring hospitalization.

The surveillance initiative adds to the wealth of knowledge regarding CA-MRSA SSTI characteristics within high risk young, healthy populations. The summary also documents the end of an era in terms of active surveillance for CA-MRSA at Fort Benning and provides insight into a new period of passive surveillance. The surveillance endeavor was initiated in 2001 based on the increasing frequency of MRSA cases identified at MACH and the recognition that many cases occurred in training environments which may be amenable to the implementation of countermeasures. The inception of a locally-initiated and administered monitoring program, before the occurrence of an outbreak, reflects risk assessment and initiative that characterize key public health surveillance activities. The resultant data led to the initiation of ongoing intervention studies being conducted in collaboration with the Centers for Disease Control and Prevention and the Uniformed Services University of Health Sciences.

Further research regarding CA-MRSA carrier rates among incoming trainees and training activities associated with infection may be useful in elucidating high-risk transmission times and potential points of intervention during the training schedule. Detailed genetic analyses of MRSA isolates would allow assessment of strain type and virulence characteristics, assisting medical personnel while adding to the scientific

compendium of MRSA knowledge. Further research is needed to characterize factors contributing to sustained CA-MRSA SSTI, such as features unique to a training environment, hygiene practices, diet, crowding, and climatic factors.

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### ***Medical Protocol and Training***

## **Implications of Combat Casualty Care for Mass Casualty Events**

Journal of the American Medical Association

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Violence from explosives and firearms results in mass casualty events in which the injured have multiple penetrating and soft tissue injuries. Events such as those in Boston, Massachusetts; Newtown, Connecticut; and Aurora, Colorado, as well as those in other locations, such as Europe and the Middle East, demonstrate that civilian trauma may at times resemble that seen in a combat setting. As the civilian sector prepares for and responds to these casualty scenarios, research and trauma practices that have emerged from the wars in Afghanistan and Iraq provide a valuable foundation for responding to civilian mass casualty events. Several lessons learned by the US military were implemented during the response to the bombings in Boston in April of this year.

Military research has found that approximately 25% of persons who die as a result of explosive or gunshot wounds have potentially survivable wounds. These individuals have injuries that are not immediately or necessarily lethal and have a chance to survive if appropriate care is rendered in a timely fashion. The military has learned that implementation of evidence-based, clinical practice guidelines can reduce potentially preventable death. Certain aspects of these lessons also apply to multiple casualty scenarios in civilian settings.

The care of wounded military service personnel is based on an integrated trauma system and involves timely point-of-injury intervention, coordinated patient transport, whole blood or blood component-based resuscitation, and initial operating focused on control of hemorrhage and optimizing patient physiology. Referred to as damage control surgery, this approach involves abbreviated techniques instead of longer definitive operations. The principles of combat casualty care should be considered in 3 phases: point of injury, during transport to the hospital, and hospital-based treatment. The wars have highlighted the importance of a trauma system to coordinate these phases and improve survival. In implementing this strategy, the military developed the Joint Trauma System, which is designed to provide wounded troops an optimal chance for survival and recovery.

### **CARE AT THE POINT OF INJURY**

The majority of wartime deaths occur in the out-of-hospital setting. The point of injury component of care is termed tactical combat casualty care. During the past decade, this phase has been transformed to introduce and integrate elements of medical care with military tactics. Combat units are now trained in tactical combat casualty care, a strategy that has reduced preventable death. Kotwal et al reported that the 75th Ranger Regiment's implementation of a system based on tactical combat casualty care was associated with a historically low 3% incidence of preventable death. Moreover, none of the regiment's 32 fatalities died of preventable causes during the out-of-hospital phase of care. The critical elements of

the protocol include early control of hemorrhage using tourniquets for extremity bleeding and hemostatic dressings for bleeding not amenable to tourniquets.

#### CARE DURING TRANSPORT

Evacuation is the next step in the continuum. Findings from military research have shown improved survival associated with the use of more advanced en route care capability. Mabry et al demonstrated a 66% reduction in mortality among patients evacuated by critical care flight paramedic teams (16 deaths among 202 patients) compared with casualties transported by basic emergency medical technicians (71 deaths among 469 patients). The survival benefit was attributed to higher levels of training and experience among flight paramedics. Morrison et al extended these observations in a study of injured military personnel evacuated by the United Kingdom's physician-led platform (aircraft or airframe used to transport patients) referred to as the medical emergency response team-extended (MERT-E). In this report, there was a 33% reduction in mortality in the most severely injured who underwent evacuation with MERT-E (47 deaths among 385 patients) compared with those evacuated with conventional platforms (36 deaths among 198 patients). Many of the advanced evacuation platforms include the capacity to administer blood and blood components and to provide other lifesaving interventions prior to reaching the hospital. The personnel on these advanced platforms may be acute care nurse practitioners, flight nurses, critical care flight paramedics, or critical care trained physicians.

#### HOSPITAL-BASED CARE

The receiving trauma center provides the third phase of care. The US military's hospital-based experience with multiple casualty scenarios following single explosive events was documented in the 2009 Balad Air Base (in northern Iraq) report, which described strategies used to mitigate morbidity and mortality in 50 injured patients following 3 consecutive explosive events and quantified estimates of casualty surge capacity. Management of the most severely injured patients with complex penetrating wounds included strategies of damage control resuscitation; treatment of hemorrhagic shock with whole blood or balanced ratios of blood components such as plasma, platelets, and cryoprecipitate instead of crystalloid solutions; and damage control surgery. These approaches to combat casualty care are outlined in the Joint Trauma System clinical practice guidelines.

Damage control resuscitation is based on results of military research showing a survival benefit associated with administration of equal ratios of plasma, packed red blood cells, platelets, and more recently tranexamic acid. Damage control surgery involves performing only necessary amounts of operating to control bleeding, debride nonviable tissue, stabilize fractures, and restore extremity perfusion. Application of damage control surgery means that more definitive operations are delayed until initial resuscitation has been completed. The Balad report also documented the value of parallel operating, which involves having more than 1 surgical team simultaneously tending to a patient to reduce anesthesia and operative time. For example, a patient with extremity injuries as well as head and neck injuries may have 2 teams composed of general and orthopedic surgeons operating on these different anatomic locations at the same time. Although this strategy does not apply to all cases, it can be used for patients with multiple extremity fractures or penetrating and soft tissue injuries to several different anatomic locations.

The military has also demonstrated the effectiveness of operating on multiple patients simultaneously in a single operating room. During the surgical surges in Balad, Iraq, more than three-fourths of initial operations (involving a total of 50 patients) were performed in rooms with more than 1 patient without adverse outcomes and an overall 8% mortality. Practices like these demonstrate how space, personnel, operating room

tables and supplies, and anesthesia equipment can be used effectively to perform lifesaving operations at a pace greater than that of routine conditions.

The Balad report projected that three-quarters of patients injured enough to require admission to the hospital would need an operation and that nearly 4 procedures would be required per operation to manage penetrating injuries. Findings from the US military demonstrated that 110 procedures were performed during 40 operations on 38 patients in the first 24 hours. The report also showed that a balanced, blood component-based resuscitation was achievable in the setting of a multiple-casualty event. The report estimated that an average of just more than 3 units of packed red blood cells, plasma, and platelets would be required per hospitalized casualty. The report also characterized intensive care unit and ventilator requirements, demonstrating that 1 nurse and 1 ventilator would be anticipated for every 2 admitted casualties. The Balad report confirmed that many patients injured during explosive events required multiple operative interventions (191 procedures were performed during 75 operations, translating to 3.8 procedures per patient) in the days after the initial or index procedure (ie, a secondary wave of operating).

#### LESSONS FROM WARTIME TRAUMA CARE

These lessons from the wars in Afghanistan and Iraq are a product of the nation's investment in military trauma care and combat casualty care research. However, few military clinical practice guidelines are the result of standard, randomized clinical trials. Instead, these lessons are the result of a process of focused empiricism, or by "identifying what works and what does not, refining it over time and embracing a culture of continuous process improvement." This pragmatic approach adopted for military combat casualty care has allowed for rapid adoption of lifesaving strategies through practical methods. In this context, the evidence base supporting the military's clinical practice guidelines is driven by the results of basic science, translational large animal research, and retrospective cohort analyses. Despite the lack of randomized trials, the net outcome of the military's approach and other improvements in trauma care is the lowest case fatality rate for US service personnel recorded in the history of war.

As the United States and other nations continue to prepare for casualty scenarios from explosives or mass shooting events involving civilians, lessons from wartime trauma care and resuscitation may be helpful in planning responses. The trauma practices that have resulted from more than a decade of combat casualty care and research are transferable to the civilian world. Continuing to translate these lessons from war should provide a foundation to help reduce mortality and morbidity among civilians injured in future mass casualty events.

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## **On Access and Accountability — Two Supreme Court Rulings on Generic Drugs**

New England Journal of Medicine

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7 August 2013

In June, the U.S. Supreme Court issued two rulings regarding the marketing of generic drugs that may alter the pharmaceutical business landscape. First, in *Federal Trade Commission v. Actavis*, the Court confronted the law governing a controversial pharmaceutical marketing practice known as reverse payment agreements, or pay for delay. This practice occurs when a generic drug company identifies a vulnerable

patent held by a brand-name drug manufacturer and seeks approval from the Food and Drug Administration (FDA) for a generic version before the patent expires, provoking a lawsuit for infringement. The two companies then forge a settlement whereby the brand-name company pays the generics firm to delay commercialization of its product. Extending the monopolies of brand-name companies in this way reportedly costs consumers more than \$3.5 billion per year. Since such settlements suppress competition, the Court sent the case back to the district court to be evaluated according to the “rule of reason,” one of the standards for determining whether an action violates antitrust law.

Second, in *Mutual Pharmaceutical v. Bartlett*, the Court ruled that generics manufacturers are substantially immune from civil claims regarding injuries caused by their products — a decision that eliminates a primary incentive for evaluating safety and design defects before marketing a generic product.

The patent at issue in *Actavis* — on a gel form of previously manufactured synthetic testosterone — was challenged on the grounds that it lacked novelty. The parties settled using a reverse payment agreement, whereby the brand-name company Solvay Pharmaceuticals, acknowledging that the patent challenge was credible, paid Actavis to delay releasing its generic version, albeit not beyond the original life of the patent. Such agreements — raising issues of both patent and antitrust law — are a byproduct of the 1984 Hatch–Waxman Act, which was designed to encourage production of low-cost generic drugs while respecting the incentives that patents provide. In *Actavis*, the Federal Trade Commission (FTC) argued that pay-for-delay agreements amount to illegal conspiracies to restrain trade, in violation of antitrust laws.

When pharmaceutical companies discover a new drug, they routinely seek patent protection, which allows them exclusive marketing rights for 20 years from the filing of the application. To be eligible for patent protection (so that the company can reap monopoly profits for the duration), the discovery must be novel, nonobvious, useful, and “enabled” — that is, fully and completely described so that any person skilled in the art can make and use the invention.

Hatch–Waxman, to encourage competition among generics manufacturers, established a regulatory mechanism for expedited approval of generic drugs — the Abbreviated New Drug Application (ANDA). The ANDA process allows generics whose manufacturers can demonstrate chemical equivalence to a brand-name drug to “piggyback” on that drug’s FDA approval. Since the FDA will not approve an ANDA if it infringes on a brand-name drug’s apparently legitimate patent, the timing of the ANDA is critical. One option, of course, is for the generics company to postpone submission of its ANDA until the patent has nearly expired. But Hatch–Waxman entices generics manufacturers not to wait but to immediately pursue drugs with “weak” patents, whose validity may be vulnerable to challenge on the basis of novelty, utility, or another factor. Hatch–Waxman provides a framework for litigating those questions before the generic product is commercialized — after which its maker would be risking a lawsuit for infringement.

A brand-name drug company that is confronted with a patent challenge has little choice but to initiate aggressive litigation to protect its patent and its monopoly profits. Since weak patents are generally targeted for ANDA contests and patent litigation is notoriously costly and unpredictable, it’s not surprising that ANDA litigation is often resolved through settlement. The compromise typically entails a formula whereby the brand-name company pays the generics company (often millions of dollars per year) to delay its product’s release, allowing the brand-name company to maintain its monopoly longer. Both companies benefit financially from the compromise.

Noting that the “root of the problem lies in the perverse re-distribution of incentives created by the Hatch–Waxman Act,” the FTC argued in *Actavis* that all reverse-payment agreements should be individually scrutinized according to a standard that presumes they are anticompetitive. The FTC

urged the Court to consider such settlements suspect because they enable a brand-name manufacturer to “co-opt its rival by sharing the monopoly profits that result from an artificially prolonged period of market exclusivity.” Actavis countered that its agreement represented a legitimate settlement of an ongoing patent dispute and was consistent with patent law, since Solvay's monopoly didn't extend beyond the patent's life.

Substantially favoring the FTC's position, the Court held that reverse-payment settlements are not immune from antitrust scrutiny, but it also declined to conclude that they should be presumed unlawful. Although the Court acknowledged that its ruling may require courts to delve into the anticompetitive consequences of these complex settlements, public policy dictates against the alternative of allowing the two competing companies to divide large monopolistic profits, to the detriment of consumers.

In *Bartlett*, the Court examined generic drug manufacturers' constitutional protections against state-law tort claims. In a 2011 case, *PLIVA v. Mensing*, the Court had ruled that “failure-to-warn” claims could not be brought against generics manufacturers. In *PLIVA*, although the label for the drug in question, metoclopramide, provided insufficient warning about a particular side effect (tardive dyskinesia), the FDA requires that generic drug labels be consistent with the label of the brand-name equivalent. The Court therefore held that state-level failure-to-warn claims against generics manufacturers are preempted by federal law — and indeed that *PLIVA* could not possibly comply with both federal and state law, since it could not legally modify its drug label. In contrast, in *Wyeth v. Levine* (2009), the Court ruled that failure-to-warn claims may be brought against brand-name drug manufacturers, because they do have the legal authority to modify their labels.

The question in *Bartlett* was whether “design defect” claims against generics manufacturers are also preempted. Karen Bartlett developed toxic epidermal necrolysis while taking the generic nonsteroidal antiinflammatory agent sulindac and claimed that the drug's design was defective. In a 5-to-4 decision, the Court ruled that this type of claim was also preempted, since the alleged defect was related to the adequacy of the drug label that had failed to warn the patient about this side effect. Justices Sonia Sotomayor and Stephen Breyer both issued strong dissents. Sotomayor emphasized that companies may still be liable for misbranding if they continue to sell a drug that new information has shown to be dangerous.

The Court's ruling in *Bartlett* further extends the constitutional protection provided to generics manufacturers against state-level tort claims — protection not provided to brand-name manufacturers. The disparate rulings for brand-name and generic drugs may seem illogical but stem from the absence of specific FDA guidance. Both opinions called on Congress to address the preemption law.

For consumers, *Actavis* and *Bartlett* have mixed implications. The *Actavis* ruling favors consumers, who may see earlier access to generic equivalents and reduced drug costs. The *Bartlett* ruling, however, leaves generics companies unaccountable to consumers — but it has apparently prompted the FDA to consider revising its own labeling rule. Days after the Court's decision, the agency released a proposed revision that would “create parity” in the ability of brand-name and generic drug companies to control their labels' contents. If the proposed rule is adopted, it may increase the cost of generic drugs, since companies will be accountable for their labels' contents and so will have to invest more heavily in their own safety studies. If the *Bartlett* ruling stands, the cost of generic drugs may be reduced, since companies won't be liable for most of the harm caused by their products. Since nearly four of five prescriptions are now filled with generic drugs, the impact of these decisions on this already large and growing industry can be expected to be substantial.

Disclosure forms provided by the authors are available with the full text of this article at [NEJM.org](http://NEJM.org).

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## Taking Our Medicine — Improving Adherence in the Accountability Era

New England Journal of Medicine

Lisa Rosenbaum, M.D., and William H. Shrank, M.D.

28 August 2013

A new patient with an abnormal electrocardiogram comes to your office. He is 53, smokes, and has hypertension and hyperlipidemia. Though he comes for preoperative risk evaluation, he needs more than “medical clearance” — he needs a primary doctor. Given his risk factors and hesitance to change his lifestyle, you recommend aspirin, a statin, and an antihypertensive. When he doesn't show up for his stress test, you call him, and he says he doesn't understand what the fuss is all about — he feels fine. “Why don't you wait until something is wrong with me to give me these medications?” he asks, launching into a litany of justifications for not taking them: cost, nuisance, potential side effects, not wanting to put anything “unnatural” in his body, and lack of perceived benefit. You attempt to educate him about his risk, but he says, “No disrespect to you, Doctor, but I've just never been a pill person. But,” he adds, “if something were to happen, you would still take care of me, right?”

Of course you would. Our willingness to care for patients has never depended on their willingness to do what we say. But an estimated one third to one half of U.S. patients do not adhere to prescribed medication regimens. Because nonadherence leads to increased complications and hospitalizations, it costs the United States an estimated \$100 billion to \$290 billion annually. In a health care delivery system where physician payment will increasingly be tied to patient outcomes, nonadherence poses both new challenges and opportunities.

Recognizing that such behavior costs money and lives, researchers have begun testing interventions to improve adherence. Although the multifactorial nature of nonadherence means there will never be a one-size-fits-all solution, interventions ranging from education to elimination of selected copayments to telephone-based counseling have achieved modest improvements in clinical trials. But even if we had more robust interventions, we'd lack simple, cost-effective ways of targeting the right intervention to the right patient.

Now, however, there's a business case for investing in improving adherence. The Affordable Care Act aims to shift reimbursement from fee for service toward rewarding of improved quality, outcomes, and efficiency. Payment and delivery-system models such as patient-centered medical homes (PCMHs), accountable care organizations (ACOs), and bundled payments encourage greater care coordination by holding providers accountable for total costs and outcomes in their patient populations. Rather than maximizing billing for each patient seen, these models promote efforts to improve population health at the lowest possible cost. But will reforms designed to achieve more for less money motivate the development of innovative solutions to nonadherence — or harm the highest-risk patients?

On one level, new payment models will pressure physicians to help patients to adhere to chronic-disease treatments. But even perfectly coordinated care will fall short for a patient with heart failure who goes home and stops taking her finely tuned regimen. ACO physicians will be held accountable not only for their own adherence to guideline-driven care but for their patients' adherence as well. With their salaries indirectly tied to patients' behavior, physicians in ACOs and PCMHs will theoretically be more motivated to educate patients about medication therapy and to address barriers to its use.

August 2013

Those barriers, however, range from the practical to the deeply psychological and vary widely among patients and diseases. To address the practical barriers, such as cost or forgetfulness, physicians can prescribe generics or suggest organizational strategies such as weekly pillboxes. ACOs won't be in a position to eliminate copayments, but a recent trial involving patients who have had myocardial infarction showed that doing so improves adherence. Side effects are harder to predict and address, and there's always the risk of overemphasizing them so that they become a self-fulfilling prophecy. But for some patients, simply having a "game plan" for contacting a physician in the event of intolerance may mitigate lapses in adherence between appointments.

Though patients may be forthcoming about the more practical challenges, the psychological barriers are tougher to identify and articulate. Patients don't generally tell their physicians, "Every time I look at that pill bottle, it reminds me that I'm ill" or "I tend to discount future benefits as long as I feel well today." Such underlying psychological mechanisms probably contribute to nonadherence far more than we realize and help explain why existing interventions have brought only modest improvements.

But it's precisely the multifactorial nature of nonadherence that makes solutions at the individual and practice levels most promising. Indeed, though clinical trials are ideal for establishing the efficacy of certain interventions, when it comes to fostering adherence, local delivery-system environments may be better suited to creating and testing interventions reflecting a population's needs.

Our hope is that providers, hospitals, and health systems participating in new payment models will find economies of scale in working together to improve adherence. Groups that previously functioned independently, such as pharmacists, pharmacy benefit managers, and doctors, will share a business interest in fostering population health and have added incentives to communicate and collaborate. Already, new marketplace solutions are emerging for using data and predictive analytics more effectively to support targeted interventions. As integrated health systems spread, providers may well invest in studying lower-cost ways to help patients be healthier.

For example, a practice could easily provide its physicians with monthly data on their patients' pharmacy claims. This approach has shown promise among early adopters of new care-coordination efforts. For instance, Community Care of North Carolina, a group of 14 physician networks serving Medicaid patients, paid physicians a monthly fee for care coordination; collected data on patients' prescription-filling rates; and had clinical pharmacists reach out to patients, explain the need for the medications, and often reduce a regimen's complexity. This approach led to a 5-to-7% improvement in adherence.

As new delivery systems foster similar efforts, we'll learn about qualitative and contextual details that can help others adapt such approaches to their own environments. Electronic prescribing will result in better data sources and opportunities for real-time monitoring. We should gain insight into the best ways to provide counseling to patients, target messaging, use patients' social networks to promote healthier behavior, and deploy health information technology to promote appropriate medication use.

Of course, many intuitively sensible quality-improvement initiatives have had unintended consequences. For instance, when New York implemented public reporting of cardiac surgery outcomes in the 1980s, mortality initially decreased, but subsequent analysis revealed that high-risk patients were often turned away and that black and Hispanic patients were disproportionately denied surgery. Analysts hypothesized that surgeons perceived these minority groups as higher risk and therefore as threats to their performance ratings. If outcomes of chronic disease depend on medication adherence, what's to stop us from similarly gaming the system by denying care to high-risk patients?

One way to guard against this tendency to “cherry pick” or “lemon drop” is to alter our risk-adjustment methods to account for coexisting conditions and patients' propensity to follow physicians' recommendations. Alternatively, we could give physicians a quota of patients whose outcomes are excluded from their performance-trend analyses — a strategy resembling the outlier approach to reimbursing hospitals used by the Centers for Medicare and Medicaid Services. But what quota is big enough? How does one gauge patients' likelihood of taking medications? And how would we shield physicians who care for the highest-risk patients?

At the heart of this problem lie essential questions about human motivation and physicianhood. Whether patients take their medications is ultimately up to them, but physicians' professional responsibility entails both a willingness to help people in need and a constant effort to do better. When it comes to medication adherence, what we're doing now isn't cutting it. Though as individuals we may feel ill-equipped to transform patients into “pill people,” as a community we face an opportunity to develop better ways of caring for patients even when they're out of our sight.

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## **A Comparison of Deployed Occupational Tasks Performed by Different Types of Military Battalions and Resulting Low Back Pain**

Military Medicine

Roy, Tanja C.; Lopez, Heather P.

August 2013

### **ABSTRACT**

With deployment Soldiers must now wear body armor and additional equipment while performing occupational tasks, representing a large demand that has not been considered when studying military occupations. The purpose of this study was to: (1) describe tasks required by different occupational battalions within a Brigade Combat Team; (2) establish the incidence of low back pain (LBP) in each battalion and; (3) determine which tasks predict LBP within the different battalions. This was a prospective cohort study investigating 805 Soldiers in a Brigade Combat Team deployed to Afghanistan for 1 year. Demographic, occupational, and fitness variables were recorded. There was no difference in time spent on fitness training between the battalions. Occupational tasks performed by deployed Soldiers vary in the level of physical demand between battalions. Infantry had the highest fitness score (257); wore the heaviest equipment (70 lb.); spent the most time wearing body armor (49 hours/week), performing dismounted patrol (29 hours/week), and lifting objects (35 hours/week); spent the least amount of time working at a desk (14 hours/week); but had a similar incidence of LBP (77%) compared to other battalions. History of LBP and time spent wearing body armor were the two most consistent predictors of LBP across battalion types.

### **INTRODUCTION**

With the U.S. military engaged in conflicts in Iraq and Afghanistan over the last 10 years, Soldiers spend more time conducting combat operations than during the previous decade. Over two million service members (Army, Navy, Marines, and Air Force) have deployed in the last 10 years with 40% of service members deploying more than once. This shift from garrison activities to combat operations has resulted in a change in occupational tasks performed by Soldiers. Deployed Soldiers must now wear body armor and additional equipment even while working inside the

forward operating base perimeter, representing a significant occupational demand that was not considered when studying occupational specific tasks in the past.

The Army's basic deployable units are called Brigade Combat Teams (BCT). Within an Infantry BCT there are five different types of battalions each with different occupational task requirements: (1) Infantry Battalion (IN); (2) Field Artillery (FA); (3) Reconnaissance, Surveillance, and Target Acquisition (RSTA); (4) Brigade Special Troops Battalion (BSTB); and (5) Brigade Support Battalion (BSB). Research studies providing normative data on occupational demands in deployed U.S. Soldiers are scarce. Dean<sup>2</sup> investigated only tasks performed on patrol, but not tasks performed inside the forward operating base, in an Infantry Battalion in Afghanistan. Other types of occupational battalions have not been studied, nor have tasks performed inside the forward operating base in deployed environments been evaluated.

Epidemiological data show that changes in operational tempo over the last decade have resulted in an increase in musculoskeletal injuries.<sup>3</sup> Medical discharges because of musculoskeletal injuries have increased over sevenfold in the last 20 years with combined musculoskeletal injuries currently accounting for 78% of medical discharges from the military.<sup>4</sup> Of these musculoskeletal injuries, the low back is the most commonly injured anatomical region both in deployed and nondeployed environments.<sup>5–7</sup> In fact, low back injuries have the highest risk of permanent disability of all musculoskeletal injuries.<sup>8</sup> Low back pain (LBP) is more prevalent while deployed (21.2% in Afghanistan, 26.9% in Bosnia, and 23.2% in Iraq) compared to 17.8% (includes back and abdomen) in nondeployed military members.

No study has yet described the risk of injury resulting from physical tasks in Soldiers within different occupations in deployed environments. Studies done in nondeployed environments have found that Infantrymen, medical equipment repairers, and light-wheeled vehicle mechanics have the highest rate of musculoskeletal injury and hospitalization in garrison.<sup>11</sup> A more recent study found that Soldiers within the United States in occupations classified as "heavy demand" (occasional lifting of over 100 lb and frequent lifting over 50 lb) had an increased risk of hospitalization compared to those in occupations classified as "light" (lift a maximum of 20 lb with frequent lifting of 10 lb).<sup>12</sup> Although occupational requirements involving wear of body armor, physical training, and excessive load carriage are also known risk factors for musculoskeletal injury, such factors have not been previously considered when characterizing the physical demands level of military occupations for research.<sup>13–15</sup> In addition, no studies have investigated the difference in injury rates between occupational battalions while deployed.

The purpose of this study was therefore threefold: (1) to describe occupational tasks performed by different types of occupational battalions within a BCT deployed to Afghanistan, (2) to establish the incidence of LBP in each battalion, and (3) to establish which occupational tasks predict the occurrence of LBP in deployed Soldiers operating within the different types of occupational battalions.

## **METHODS**

This prospective cohort study was conducted in one BCT from June 2009 to August 2010. Institutional Review Board approval was obtained from Brooke Army Medical Center. All Soldiers deploying as a member of the BCT were invited to participate as a part of their predeployment Soldier Readiness Process. Current LBP was considered an exclusion criterion as these Soldiers would not be considered incident cases.

All 1,194 participants filled out a predeployment survey as a station during their predeployment Soldier Readiness Process in the month before deployment. A modified version of a previously used data collection survey was used.<sup>16–19</sup> All data were self-reports and all except history of LBP (yes/no), seen by a medical provider (yes/no), and sex (M/F) were free text. Data was collected on age; sex; Army Physical Fitness Test (APFT) score (most recent score in the 6 months before deployment); hours per week spent on cardiovascular training, core training, and strength

training; and history of LBP. The Soldiers were then deployed for 12 months. Within 1 week of returning to the United States from Afghanistan, Soldiers completed the postdeployment questionnaire as a station during their reintegration process. The 805 Soldiers provided data on the hours per day or week spent conducting various occupational tasks performed while deployed. Tasks were wearing body armor, lifting objects weighing more than 30 lb (not including or in addition to body armor), dismounted patrolling, riding in tactical vehicles, and desk work. Additional information on LBP and average weight of equipment worn was recorded. LBP was defined as pain interfering with the performance of occupational tasks.

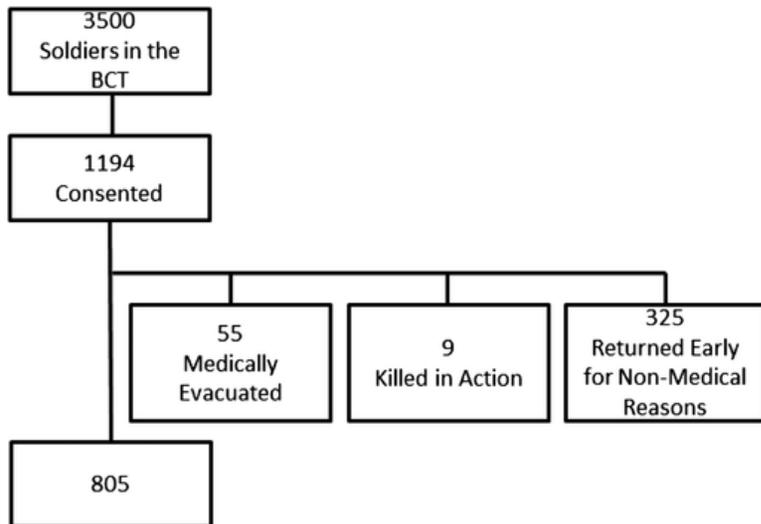
## **DATA ANALYSIS**

SPSS 20 was used for all calculations. Descriptive statistics were calculated for each battalion: BSB, BSTB, RSTA Squadron, FA, and IN. Descriptive statistics characterized time spent performing fitness training and common deployed occupational tasks, demographic information, as well as LBP. One way between subjects analysis of variance (ANOVA) was performed for each continuous occupational variable as a function of battalion type. Assumptions for this model were evaluated, followed by an omnibus F test. If the F test was significant, pairwise comparisons using Tukey's Honestly Significant Difference were performed to detect the pattern of differences. The assumption of homogeneity was violated for APFT; equipment weight; and time spent working at a desk, lifting objects greater than 30 lb, dismounted patrol, and riding in tactical vehicles. So an F test with Brown–Forsythe adjustment was conducted, then the pairwise comparisons were performed using the Games-Howell procedure.

Logistic regression was then used to identify the best predictors for the incidence of LBP (yes or no) in each battalion with more than 75 Soldiers. Logistic regression was not calculated for the FA as the sample was too small. All variables were originally entered into each logistic regression model. For cardiovascular training, core training, and strength training predeployment values were used. All variables with a regression coefficient p value of greater than 0.1 were then removed. The remaining variables were then removed and added to the logistic equation in different combinations in order to find the most parsimonious combination of variables significantly contributing to the prediction of the incidence of LBP in each battalion.

## **RESULTS**

Before deployment 1,194 eligible Soldiers, from a BCT containing approximately 3,500 Soldiers, volunteered to participate in this study. Of these, 805 filled out the postdeployment survey. Of the 389 participants lost to follow up, 9 were killed in action, 55 were medically evacuated (43 for illness and 8 for injury [2 for LBP]), and the remaining 325 did not return with the main unit for unspecified reasons that were nonmedical in nature.



**Physical Fitness** displays descriptive statistics for the demographic information, fitness scores, and equipment weight. ANOVA was performed on hours spent performing cardiovascular exercise, strength training, and core exercises before deployment as a function of battalion type. There was no significant difference between battalions in the amount of time spent performing cardiovascular exercise,  $F(4,728) = 0.532$ ,  $p = 0.712$ ,  $\eta^2 = 0.003$ ; strength training,  $F(4,738) = 0.386$ ,  $p = 0.819$ ,  $\eta^2 = 0.002$ ; or core exercises,  $F(4,737) = 1.988$ ,  $p = 0.095$ ,  $\eta^2 = 0.011$ .

ANOVA was performed for APFT score as a function of battalion type. There was a significant difference in the APFT scores between battalions,  $F(4,348.003) = 6.510$ ,  $p < 0.001$ ,  $\eta^2 = 0.037$ . Pairwise comparisons found that the IN scored significantly higher on the APFT than the BSB ( $p = 0.009$ ) and the BSTB ( $p < 0.001$ ).

**Equipment Weight** ANOVA was performed on the weight of worn equipment as a function of battalion type. There was a significant difference in the weight of equipment worn between battalions,  $F(4,320.250) = 48.653$ ,  $p < 0.001$ ,  $\eta^2 = 0.201$ . Pairwise comparisons found that the IN wore significantly heavier equipment than the BSB ( $p < 0.001$ ), BSTB ( $p < 0.001$ ), and RSTA ( $p < 0.001$ ). The RSTA wore significantly heavier equipment than the BSB ( $p < 0.001$ ). The FA wore significantly heavier equipment than the BSB ( $p < 0.001$ ) and BSTB ( $p < 0.001$ ).

**Occupational Tasks** provides a comparison between battalion types of weekly occupational tasks performed while deployed. Separate ANOVAs were performed on hours spent wearing body armor, working at a desk, lifting objects heavier than 30 lb, performing dismounted patrol, and riding in a tactical vehicle as a function of battalion type. There was a significant difference in the amount of time spent wearing body armor between battalions,  $F(4,771) = 22.385$ ,  $p < 0.001$ ,  $\eta^2 = 0.104$ . Pairwise comparisons found that the IN wore their body armor significantly more than the BSB ( $p < 0.001$ ), BSTB ( $p < 0.001$ ), and the RSTA ( $p = 0.001$ ). The FA wore body armor significantly more than the BSB ( $p < 0.001$ ) and the BSTB ( $p = 0.003$ ). There was a significant difference in the amount of time spent working at a desk between battalions,  $F(4,312.980) = 13.037$ ,  $p < 0.001$ ,  $\eta^2 = 0.078$ . Pairwise comparisons found that the IN spent significantly less time working at a desk than the BSB ( $p < 0.001$ ), and the BSTB

( $p < 0.001$ ). The RSTA spent significantly less time working at a desk than the BSTB ( $p = 0.003$ ). There was a significant difference in the amount of time spent performing lifting tasks between battalions,  $F(4,391.863) = 9.428$ ,  $p < 0.001$ ,  $\eta^2 = 0.040$ . Pairwise comparisons found that the IN spent significantly more time performing lifting tasks than the BSB ( $p < 0.001$ ), BSTB ( $p < 0.001$ ), and RSTA ( $p < 0.001$ ). There was a significant difference in the amount of time spent on dismounted patrol between battalions,  $F(4,295.275) = 53.936$ ,  $p < 0.001$ ,  $\eta^2 = 0.178$ . Pairwise comparisons found that the IN spent significantly more time on dismounted patrol than the BSB ( $p < 0.001$ ), the BSTB ( $p < 0.001$ ), and the RSTA ( $p = 0.004$ ). The RSTA spent significantly more time on dismounted patrol than the BSB ( $p < 0.001$ ) and BSTB ( $p = 0.024$ ). The FA spent significantly more time on dismounted patrol than the BSB ( $p < 0.001$ ) and BSTB ( $p = 0.004$ ). The BSTB spent significantly more time on dismounted patrol than the BSB ( $p = 0.003$ ). There was a significant difference in the amount of time spent in tactical vehicles between battalions,  $F(4,392.941) = 4.181$ ,  $p = 0.003$ ,  $\eta^2 = 0.021$ . Pairwise comparisons found that the IN spent significantly more hours in tactical vehicles than the RSTA ( $p = 0.016$ ). The BSB spent significantly more hours in tactical vehicles than the RSTA ( $p = 0.001$ ).

### Low Back Pain

**TABLE II.**

Incidence, Healthcare Utilization, and Cause of Low Back Pain by Battalion Type

	<b>Incidence of LBP (%)</b>	<b>Those with LBP Seen By a Medical Provider (%)</b>	<b>Load Caused LBP (%)</b>	<b>Lifting Caused LBP (%)</b>
BSB	71.83	8.45	35.71	28.57
BSTB	81.44	10.31	48.15	25.93
RSTA	76.47	8.82	69.39	10.20
FA	79.07	6.98	72.73	22.73
IN	77.09	7.16	74.65	7.37

provides data on LBP. The incidence of LBP was similar between the battalions and there was not a significant association between battalion type and LBP ( $\chi^2 = 3.297$ ,  $p = 0.514$ ). The two main self-reported causes of LBP were the same for all battalions, lifting and load worn (Table II). The variables that best predicted the incidence of LBP in each unit are found in Table III.

**TABLE III.**

Significant Predictors of Low Back Pain by Battalion Type

<b>Battalion</b>	<b>Variable</b>	<b>B</b>	<b>P Value</b>	<b>Odds Ratio</b>	<b>95% C.I. for OR</b>
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					<b>Lower</b>	<b>Upper</b>
BSB	HLBP	1.616	0.005	5.034	1.612	15.720
	Lifting	0.265	0.012	1.303	1.060	1.601
BSTB	HLBP	2.187	0.009	8.911	1.709	46.458
	Strength Training	-0.134	0.031	0.875	0.775	0.988
	Body Armor	0.209	0.022	1.232	1.031	1.473
RSTA	Body Armor	0.263	0.001	1.301	1.107	1.529
IN	Body Armor	0.130	0.000	1.138	1.070	1.211
	HLBP	0.788	0.011	2.200	1.199	4.035

Wearing the body armor for longer periods of time was a risk factor for LBP in three of the four battalion types. History of LBP was a risk factor for LBP in all battalions except for the RSTA. More strength training before deployment decreased the risk of LBP in Soldiers in the BSTB. Lifting was a risk factor only for the BSB. When sex was controlled for in the logistic regression, both lifting ( $p = 0.009$ ) and history of LBP ( $p = 0.011$ ) remained significant predictors of LBP for the BSB.

## **DISCUSSIONS**

### **Occupational Demands and Premorbid Fitness Levels**

This study took the novel approach of investigating physical occupational tasks and resulting LBP across the battalion types found in an Infantry BCT. Participants assigned to INs in the study cohort consistently performed more frequent and strenuous physical tasks than Soldiers assigned to other battalions (Fig. 2). Infantrymen spent the most time wearing their body armor, performing dismounted patrols, and lifting objects weighing more than 30 lb. In all cases, this study finding revealed that IN members either met or exceeded established occupational demands for the Infantry Soldier found in Army Pamphlet 611-21.20 Although Army Pamphlet 611-21 indicates that the typical Infantry Soldier frequently wears 65 lb of equipment, lift weights of 89 lb, and occasionally walks slowly for 2 hours out of 6 while carrying 26 lb, Infantrymen in the current study reported spending almost 5 hours a day on dismounted patrol if one assumes they worked 6 days a week.

Interestingly, study results revealed that despite the more physically demanding nature of their deployment experience, Infantry Soldiers did not have a higher rate of LBP than Soldiers in other battalions. This finding could be related to significantly higher APFT scores among Infantrymen indicating superior premorbid levels of physical fitness than Soldiers in other battalions. One-third of the combined APFT score comes from push-ups, one-third from sit-ups, and one-third from the two mile run speed. Rasmussen et al found no association between individual fitness components; aerobic, strength, endurance, and flexibility; but did find an association between the combined fitness score and the development of

LBP in a 2-year prospective study. Previous evidence suggests that APFT scores below 200 may be predictive of LBP.<sup>22</sup> Conversely, higher fitness levels have also been shown to be protective against musculoskeletal injury in military service members.<sup>23–26</sup> Civilian studies support these findings demonstrating that one's fitness level is predictive of the likelihood of developing LBP.<sup>27,28</sup> The current study suggests that higher levels of physical fitness likely offset risks associated with the more physically demanding task performed by Infantrymen as evidenced by equivalent rates of LBP across battalion types in the study sample.

### **Body Armor Wear**

Time spent wearing body armor was a significant predictor for a new episode of LBP in all analyzed battalions except the BSB. This supports previous findings which suggest that wearing body armor for 4 or more hours a day is correlated with higher rates of LBP, cervicalgia, and upper extremity pain in deployed Soldiers. Soldiers in the BSB wore body armor for an average of 4 hours a day while the next closest battalion averaged 4.4 hours a day. In a civilian study investigating the effect of body armor on LBP, Burton et al reported an increased risk of LBP in police officers wearing body armor 12 hours a day relative to officers who did not wear it at all. It is likely that wearing body armor for long periods of time places a prolonged compression force on the spine which could lead to injury. Biomechanical studies have shown that static loading to the spine can result in changes similar to those seen as a result of degeneration over time.<sup>30</sup> Our data suggests that approximately 4 hours a day is a threshold beyond which the risk for LBP increases.

### **History of LBP**

History of LBP was a predictor of a new episode of LBP in all groups except the RSTA. Although the reason for the exception in the RSTA group is not immediately clear, it is possible that the analysis was underpowered because of the small subgroup size. History of LBP has been linked to an increased risk of future LBP in several civilian studies. Secondary effects of lower back injuries are well established. Even after pain has resolved, lower back injuries are known to affect both biomechanical and functional performance. In a study that examined the residual effects of recent LBP in college athletes, Nadler et al found that athletes with resolved LBP had significantly slower shuttle run times than participants in an uninjured group. Seay et al reported differences in pelvis-trunk coordination between pain-free runners with and without a history of LBP such that pain-free participants who had recovered from LBP showed movement patterns similar to runners currently experiencing LBP. Therefore, even a history of LBP can result in future susceptibility to LBP and can have residual consequences on performance.

### **Repetitive Lifting Demands**

Repetitive lifting has been previously identified as a risk factor for LBP in industry. Cohen et al found that lifting objects was the most common mechanism of injury in patients medically evacuated for LBP (18%). In this study, lifting frequency predicted LBP only in the BSB. This is unusual because even though the BSB had the highest percentage of Soldiers attributing their LBP to lifting, they spent significantly less time lifting than the Infantry Soldiers. In the current study it was thought that because the BSB had a higher percentage of female Soldiers, this could result in more LBP even with less lifting because female service members have been shown to be at increased risk of LBP. However, even when sex was controlled for in the logistic regression equation, lifting remained a significant predictor of LBP. It is possible that even though the BSB was doing less lifting in terms of the amount of time spent in lifting; they may have been lifting heavier weights. Lifting heavy weights, those over National Institute for Occupational Safety and Health recommendations, have been shown to be a risk factor for injury. Thus, differences in object weight could account for the prediction of LBP by lifting in the BSB even if it did not contribute significantly to the model in other battalions.

One limitation to this study is that variables were self-reported which could have introduced the possibility for measurement error and recall bias. Soldiers were given the study survey the first week they returned home in order to minimize recall bias as much as possible. In addition, the possibility of measurement error exists because Soldiers may or may not have weighed their loads and likely did not keep exact time sheets on how many hours a day they spend on specific tasks. They provided their best estimate of the averages for these data. The armored vests start at a standard weight and at some point in time many Soldiers will weigh their equipment. In general deployed Soldiers are aware of the loads they carry for equipment and generally perform the same tasks throughout the deployment and this would increase the accuracy of measurement.

## **CONCLUSION**

Deployed Soldiers in different types of battalions engage in different levels of physical occupational tasks with the Infantry consistently spending the most time performing physical tasks. Despite their higher frequency of physical tasks, the Infantry did not have a higher incidence of low back pain than the other battalions. This may have been because of their increased fitness level. History of low back pain and time spent wearing body armor were the 2 most consistent predictors of low back pain across battalion types.

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## **Field-Based PCR for Rapid Diagnosis of Cutaneous Anthrax in the Deployed Setting Using the Joint Biological Agent Identification and Diagnostic System**

Military Medicine

Pace, Sarah; Steigelman, Daniel; Norton, Scott A.; Krivsa, Stephen

August 1023

## **ABSTRACT**

Anthrax is occasionally encountered by U.S. military physicians in the deployed setting, where limited resources make it difficult to obtain laboratory confirmation. We present a case of cutaneous anthrax diagnosed using a ruggedized polymerase chain reaction device in austere combat conditions.

## **CASE**

A 13-year-old Afghan boy presented to an allied military hospital outside Kabul, Afghanistan, for evaluation of facial edema and a black necrotic lesion on his forehead. The patient had been well until 4 days earlier, when he noted a small red papule on the left side of his forehead. The lesion rapidly evolved into a black eschar with an erythematous, vesicular-appearing edge and the facial edema extended to his jawline bilaterally. When he was brought to the hospital, he was lethargic, had decreased oral intake, and had difficulty walking and talking. He denied any trauma, or exposure to people with similar lesions. His family reported that cows, sheep, and goats live in their yard at home. Neither he nor his older brother, the only family member who accompanied him to his inpatient and outpatient visits, described any unusual soil or animal exposures that could

have led to his lesion: they assumed this was an adolescent pimple gone horribly wrong. More specific soil or animal exposure history was not pursued.

He presented to an allied tent clinic in an afebrile and hemodynamically stable state. Their medical personnel brought him to the American field hospital to pursue CT scan of head and neck for concern of severe edema of the head and neck; American physicians had not been consulted. While in the waiting area for CT, an American physician found him in a nearly obtunded state. The patient was taken to the Emergency Department; for concern of airway compromise and altered mental status rapid sequence intubation was performed. The American hospital assumed his care, admitted him to the intensive care unit, and initiated intravenous ceftriaxone and clindamycin for empiric treatment of a possible spider bite with secondary facial cellulitis. A chest radiograph was normal but CT scan of the head and neck showed diffuse, severe superficial soft-tissue swelling. Bacterial cultures taken from the eschar at initial presentation were positive for *Staphylococcus aureus* but his blood cultures were negative. Clinically, he failed to respond to empiric therapy: by hospital day (HD) 3, erythema and edema progressed from the face to the mid-chest and he became febrile. Vancomycin was started on HD3, consultations with in-hospital dermatology and pediatrics and telemedicine infectious disease led to a suspicion of anthrax. Scrapings from the edges of the eschar were analyzed by polymerase chain reaction (PCR) using the Joint Biological Agent Identification and Diagnostic System (JBAIDS; Idaho Technology, Salt Lake City, UT) on HD4 and confirmed the presence of *Bacillus anthracis*. Ciprofloxacin was started on HD4 and his condition improved significantly. He was successfully extubated on HD5 and discharged home the following day to complete a 14-day course of oral ciprofloxacin and clindamycin. On follow-up 5 days after discharge (15 days from initial onset), the facial edema and erythema had almost resolved, except for a small rim around the eschar.

## **DISCUSSION**

Following the 2001 anthrax attacks, the medical and public health communities have regarded anthrax as the subject of much concern and interest because of its potential use in bioterrorism. In addition, the American military's involvement in Southwest Asia has placed hundreds of thousands of service personnel in areas where anthrax is endemic.

Diagnosis of anthrax is generally based on clinical history and detection of characteristic gram-positive rods on gram stain or culture of the lesion, cerebral spinal fluid, or blood. Establishing a clinical diagnosis or obtaining laboratory confirmation is difficult in the deployed setting. The usual way to obtain definitive diagnosis requires 24 to 48 hours or more with specialized testing, which includes direct fluorescent antibody staining of the capsule and cell wall polysaccharide, as well as lysis of colonies by  $\gamma$ -phage. These sophisticated tests are generally limited to public health biosafety laboratories that are part of Laboratory Response Network of the Centers for Disease Control and Prevention, and unavailable in an austere medical environment. In addition, antibiotics quickly render the lesion culture negative, in which case serologic tests, examination of punch biopsy material from the edge of the lesion with silver staining, or immunohistochemical tests may aid in the diagnosis.

In addition to the above methods, several standard PCR assays that target genes on a specific plasmid of *B. anthracis* are available. These assays, however, are time consuming, labor intensive, and require multiple steps, all of which increase the chance of contamination and false readings. Newer, rapid PCR assays exploit the fact that virulence of *B. anthracis* is dependent upon 2 plasmids, pX01 and pX02, and specifically identify each of these plasmids. All steps, including PCR cycling, amplification, and probe confirmation of product can be performed in a closed reaction vessel in under 1 hour in rapid-cycle real-time PCR analysis. In addition to rapid identification of the pathogen, this form of PCR can distinguish virulent strains (pX01 and pX02 present) from nonvirulent ones (that lack either pX01 or pX02 or both). This feature may help avoid unnecessary disruption and chaos in hoax attacks, such as the increasing common occurrences of a "white powder" found in posted letters. Also,

PCR is more reliable in detecting *B. anthracis* from deteriorated blood samples that have been stored for several days. The application of the real-time PCR technology in the field has been validated by field soil and air studies, which have shown that a single spore of *B. anthracis* in 1 g soil or in 100 L air can be detected by real-time PCR.

The U.S. Army has a real-time PCR machine, the JBAIDS that is deployed for the detection of potential biowarfare and bioterrorism agents, including *B. anthracis*. The U.S. Army now uses the JBAIDS in deployments to identify potential biowarfare and bioterrorism agents. The JBAIDS is a ruggedized thermocycler, which uses room temperature stable, freeze-dried reagents. JBAIDS is approved by the Food and Drug Administration for detection of anthrax in clinical and environmental samples. JBAIDS was recently used in a small study in which Q fever (i.e., infection with *Coxiella burnetii*) was suspected and shown to have a 100% specificity (95% CI 63–100%) and 67% sensitivity (95% CI 36–97%) versus serology. Although the Q fever study was limited by a small sample size, it shows that the JBAIDS system may be a valuable asset in the deployed setting. Similarly, sensitivity testing for anthrax has yielded encouraging results. In clinical studies, the clinical specificity of the JBAIDS has been found to be at least 98% (95% CI 98–100%). JBAIDS offers the additional benefits of increased availability and rapid diagnosis in the war zone. In addition, field-based PCR does not require shipment of infectious samples to another lab, nor are the results negated by initial antibiotic coverage, as can be the case for culture. In addition, PCR is not subject to an initial period of seronegativity while a patient develops antibodies, as is the case with titers. We present this case, in which bacterial cultures (of the skin and blood) were available, yet negative, to highlight the clinical utility of the JBAIDS in a situation where standard laboratory-based PCR was not available. Further employment of this system could lead to improved diagnosis and management of anthrax, both in the deployed military setting and in the event of a bioterrorist event. Although our primary goal is to highlight the use of the JBAIDS system in the deployed setting, this case highlights key points about the diagnosis and management of anthrax, which deserve discussion. Given the relative rarity of anthrax in the United States, it is easy to imagine an American physician to overlook this diagnosis. The global nature of travel and ongoing military engagements necessitate our vigilance and consideration of anthrax in cases with any of the following clinical features: eschar, significant edema surrounding a relatively small lesion, or brisk deterioration given appropriate therapy for the presumed diagnosis. These features should trigger additional concern in patients who are living in, or have traveled to, an area where anthrax is known to be endemic and the patient may have had exposure to ruminants or contaminated soil. In addition, once the diagnosis is suspected, the laboratory should be alerted to this concern. As noted above, laboratory diagnosis can be challenging and is further complicated by the common practice of laboratories to identify *Bacillus* cultures to only the genus level, under the assumption that these positive cultures are the results of contamination with nonpathogenic *Bacillus cereus*, as opposed to disease organisms. If the laboratory is aware that anthrax is in the differential diagnosis, then the *Bacillus* cultures can be further speciated. The last unique aspect of this case that we wish to highlight is the failure of treatment with the combination of clindamycin and vancomycin, both of which have been reported to have *in vitro* activity against *B. anthracis*.

Although we believe that the JBAIDS system can play a key role in making this diagnosis, especially in the field setting, clinical suspicion is key to guiding laboratory efforts whether in culture or PCR and we must remain vigilant to avoid diagnostic delays and distractions that can lead to significant morbidity and mortality.

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## **Intra-Articular Synovial Sarcoma Treated With a Transfemoral Amputation: A Case Report and Review of the Literature**

August 2013

## **ABSTRACT**

A case of monophasic intra-articular synovial sarcoma in the right knee of a 39-year-old active duty serviceman treated with a transfemoral amputation is presented. The patient was evaluated for right knee pain and fullness. After further workup, the patient underwent computed tomography-guided biopsy, with the tissue specimen consistent with intra-articular synovial sarcoma. The patient elected for a transfemoral amputation rather than limb or joint-sparing surgery. The gross specimen measured 3.5 × 3.0 × 1.7 cm in the posteromedial knee. No metastatic lesions were seen on positron emission tomography–computed tomography. Chemotherapy and radiation therapy have not been utilized. The transfemoral amputation adds to the uniqueness of this report and is discussed with a review of the multimodality treatment toward intra-articular synovial sarcoma in prior published literature.

## **INTRODUCTION**

Synovial sarcoma is a morphologically distinct malignant neoplasm that accounts for 5 to 10% of the soft tissue sarcomas. Synovial sarcoma is characteristically found near joints with at least 50% of cases found in the lower extremities. The periarticular synovial sarcomas can secondarily spread to the joint capsules.<sup>6</sup> However, the occurrence of synovial sarcoma originating from an intra-articular location is suspected to be rare, based on the paucity of documented case reports.<sup>5,7</sup> This article describes a case of monophasic intra-articular synovial sarcoma originating from the right knee treated by a transfemoral amputation and discusses the treatment options based on a review of prior literature.

## **CASE REPORT**

This is the case of a 39-year-old active duty serviceman presenting to his primary care physician with right knee pain and fullness in May 2012. He had a significant history of trauma and surgical procedures to the right knee. In 1991, as a teenager, he tore his anterior cruciate ligament during a football game. He had multiple arthroscopic procedures followed by an anterior cruciate ligament reconstruction with a bone–patellar tendon–bone graft in 2001. In 2009, he began having posterior medial knee pain with neuropathic pain symptoms radiating down into the posterior compartment of the leg. The pain continued and in 2011 he had an electromyography and was diagnosed with tibial nerve entrapment. In December 2011, he underwent a decompressive surgery that was directed at scar tissue encompassing the tibial, saphenous, and peroneal nerves with no violation of the joint capsule. After this procedure, he was pain free for approximately 5 months. He then developed the right knee pain with fullness that led him to seek care in May 2012. His physical examination showed tenderness to palpation over the posteromedial knee just lateral to the semitendinosus tendon without a palpable mass, but with apparent fullness. The patient's range of motion of his right knee was without change from his chronic limited range of motion that was secondary to his prior surgeries.

Plain radiographs showed linear and punctate calcifications within the lateral compartment representing chondrocalcinosis. The impression was otherwise normal. A magnetic resonance imaging of the right knee with and without contrast showed an enhancing 1.3 × 1.5 × 3.3 cm mass within the posteromedial aspect of the joint, just lateral to the medial femoral condyle and medial to the posterior cruciate ligament with mass effect upon

the posterior cruciate ligament. It appeared to have continuity with the joint capsule. The lesion was hyperintense to muscle on proton density sequences (Fig. 1), and isointense to muscle on T1. In addition, there was postcontrast enhancement.

On positron emission tomography–computed tomography (PET-CT), the lesion had increased metabolic activity measuring 2.37 SUV. No metastatic lesions were seen on the PET–CT scan. The patient underwent a computed tomography (CT) image–guided core biopsy on October 10, 2012, followed by a transfemoral amputation on October 29, 2012. There were no surgical complications. After the transfemoral amputation the patient participated in intensive physical and occupational therapy, and became established into a longer term rehabilitation program. On January 14, 2013, the patient received his prosthesis with a power knee and was ambulating. The patient is undergoing routine surveillance, currently without the addition of chemotherapy and radiation therapy. The patient 6 months after surgical intervention is without evidence of recurrence or metastatic disease.

### **PARHOLOGIC FINDINGS**

The specimens obtained by CT-guided biopsy measured in aggregate 0.4 × 0.3 × 0.2 cm and consisted of light-pale, tan, fleshy red soft tissue fragments. Histologically, there was a proliferation of atypical spindle cells, vaguely arranged in interlacing bundles and fascicles, with nuclear atypia and high nuclear–cytoplasmic ratios. Rare mitotic figures were noted. In addition, there were numerous small dystrophic calcifications. The lack of an epithelial component and pure spindle cell nature of this neoplasm is consistent with the diagnosis of monophasic synovial cell sarcoma.

The gross description of the specimen obtained from the transfemoral amputation consisted of a soft mass 3.5 × 3.0 × 1.7 cm in the posteromedial knee. The mass was 5 cm from the soft tissue margin of resection and at least 7 cm from the bone margin. It had a histologic grade of 2 using the French Federation of Cancer Centers Sarcoma Group criteria, with a pathologic staging of pT1b.

### **IMMUNOHISTOCHEMICAL FINDINGS**

The immunohistochemistry staining revealed strong cytoplasmic expression of pancytokeratin (AE1/AE3), epithelial membrane antigen, vimentin, and bcl-2. The tumor cells were also positive for cytokeratin 7. MIB-1 revealed a moderate proliferation index. CD-99 showed weak, patchy, nonspecific immunoreactivity. The tumor cells were negative for S-100 and CD34.

### **DETECTION OF SYT-SSX FUSION TRANSCRIPT**

RT-PCR for t(X; 18) was positive. The SYT-SSX2 variant was detected using an assay that uses fluorescent signal detection by 5′-exonuclease technology. The above histopathology and histochemical findings were consistent with monophasic synovial sarcoma.

### **DISCUSSION**

Synovial sarcoma is a soft tissue tumor typically found near joints. However, there is a limited amount of case reports describing primary intra-articular synovial sarcoma. It is unknown what the optimal treatment course is for synovial sarcomas since it has not been prospectively studied. However, the mainstay treatment for synovial sarcoma is a wide surgical resection, removing the tumor, its pseudocapsule, and a margin of normal tissue. The role chemotherapy plays remains uncertain.<sup>9</sup> Synovial sarcoma is chemosensitive. The chemotherapy regimen of ifosfamide, with or without doxorubicin, is regarded as an initial treatment for metastatic synovial sarcoma. However, in patients with primary disease, the effect of chemotherapy on survival is unclear. Radiation therapy in both preoperative and postoperative settings can improve local control in

addition to surgical resection of a synovial sarcoma. The prognostic factors that have been used to influence treatment course for a synovial sarcoma are tumor size, histologic grade, depth of fascia layer, sex, age, monophasic subtype, microscopic residual disease after resection, poorly differentiated areas, and high mitotic index.

There is uncertainty if the outlined treatment courses and the prognostic factors for synovial sarcoma can be applied to this tumor arising in an intra-articular location. To further investigate the multimodality treatment of intra-articular synovial sarcoma a review of the literature was performed. The clinical information, histological findings, and treatment course of 19 case reports and 1 poster available from the prior literature describing intra-articular synovial sarcoma as well as the 1 patient from the author's experience are summarized in Table I.

**TABLE I.**

Summary of Clinical Findings and Treatment Courses of Known Cases of Intra-articular Synovial Sarcoma

Age (Years)	Gender	Location	Size	Histology	Surgery	Adjuvant Therapy	Follow-up	Author/Reference
39	M	Right Knee	1.8 × 0.6 × 2.0 cm (MRI), 3.5 × 3.0 × 1.7 cm (Gross Specimen)	Monophasic	Above-the-knee Amputation	No Chemotherapy or Radiation Therapy	4 months	Author
13	F	Left Knee (Initial: Posteromedial, Recurrence: Popliteal Fossa)	Initial: 6 × 3 cm (MRI) Recurrence: 2.5 cm (MRI)	Monophasic	Initial: Excision With Need for a Further Wider Excision. Recurrence: Wide Excision	Radiotherapy After Wide Excision of Recurrence		Ayoub <sup>15</sup>
33	F	Left Knee (Medial Popliteal Fossa)	3 × 2 cm (Gross Specimen/Physical Examination)	Biphasic	Excision			Dardick <sup>16</sup>
9–49		Left Knee (3), Right Knee (2), Elbow	1 cm in Greatest Dimension (2 Cases); 2.5 gm (1); Tissue Arragating to 7 × 7 × 1.5 and 6 × 5.5 × 2 cm	Biphasic (4); Monophasic Fibrous (2)				Fetsch <sup>17</sup>
25	M	Right Knee (Anterior Intercondylar Space)	5 4 × 3 cm (Gross Specimen)	Monophasic				Garcia <sup>18</sup>
27	M	Right Knee (Patellofemoral Joint)	25 × 25× 10 mm with a 7 mm Pedunculated Portion (Gross Specimen)	Biphasic	Arthrotomy/Excision		3 Years	Ishida <sup>7</sup>
16	F	Knee						Kan <sup>19</sup>
13	F	Elbow						Kan <sup>19</sup>
63	M	Knee (Suprapatellar Recess)	5 × 5 × 4 cm (MRI)	Monophasic	Excisional Biopsy			Bui-Mansfield <sup>20</sup>
16	M	Left Hip		Biphasic	Excisional Biopsy		Died at 2 Years	Bui-Mansfield <sup>20</sup>
43	M	Left Knee (Medial)	5 × 3 × 1 cm (Gross Specimen)	Biphasic	Arthrotomy/Excision, Second Wider Excision		9 Years	McKinney <sup>21</sup>
37	M	Left Knee		Biphasic	First Arthroscopy With Subtotal Synovectomy; Second Arthrotomy	Multiagent Chemotherapy	Died 4 Months After Second	McLain <sup>22</sup>

Age (Years)	Gender	Location	Size	Histology	Surgery	Adjuvant Therapy	Follow-up	Author/Reference
48	F	Left Knee (Suprapatellar Recess)	4 x 3 cm (Physical Examination)	Monophasic	Arthrotomy/Excision-Wide Only at Point of Attachment	Adjuvant Therapy Recommended-Refused	1 Year	Namba <sup>23</sup>
33	M	Right Knee			First Arthrotomy With Excision and Synovectomy; Second Total Synovectomy; Third Hip Disarticulation		Died at 3 years	Raynal <sup>24</sup>
26	M	Right Knee (Infrapatellar)	6.5 x 5.5 x 5.0 cm (Gross Specimen)	Biphasic	Extra-articular Resection and Reconstruction of the Joint	Preoperative Radiation Therapy		Editor Scully <sup>14</sup>
35	M	Knee		Biphasic	Hinged Knee Replacement		11 Months	Sistla <sup>6</sup>

Excluding a series by Fetsch, the majority of cases originated in the knee with the patient's age ranging between 13 and 63 (mean 31) and a male to female ratio of 2:1.

In review of the literature discussing intra-articular synovial sarcoma, the surgical procedures conducted varied. The majority of surgical interventions included local resection/excision via arthrotomy/arthroscopy, with 3 cases having a year or more follow-up without evidence of disease. Two other alternative surgical treatments consisted of an extra-articular resection with reconstruction of the joint and a hinged knee replacement. The hinged knee procedure consisted of an excision of the lower end of the femur to the supracondylar fossa, excision of intra-articular synovium with a safe margin, and 1 cm of the proximal tibial end. At the 11-month follow-up, the patient showed no recurrence or metastasis. In a case of a synovial sarcoma arising within a popliteal cyst published by Ayoub, the decision to undergo a wide excision over a prosthetic knee replacement was based on how the magnetic resonance imaging showed no communication with the knee joint. In the Ayoub case, there was recurrence at 16 months which was treated with wide excision. In a case report which involved local resection, the author stated that the treatment should be based on clinical findings rather than diagnosis, and proposed that radical surgery may not be necessary in every intra-articular case. The author speculated that local excision may be a cure for a small tumor that can be completely excised and involves only a portion of the synovium. It is important to stress that the surgical treatment should be in accordance with the principles of oncology with free margins and minimal damage to major neurovascular bundles and muscles.

Our case report describes a transfemoral amputation. This is the first case report published to the author's knowledge using an amputation for the surgical treatment of an intra-articular synovial sarcoma. Of note, less than 5% of lower limb amputations are performed for tumors. The patient was offered an extra-articular resection versus a transfemoral amputation. He elected for the transfemoral amputation to (1) decrease his chances of a positive margin resection complicating his recovery, (2) eliminate the chance of an extensor lag, (3) allow him to regain full weight-bearing at an earlier date, (4) possibly allow for return to active duty.

Achieving appropriate oncologic margins for an intra-articular sarcoma using an extra-articular resection around the knee joint can be extremely difficult. In addition, this case was complicated by a previous surgery to the posterior aspect of the knee. Although it did not seem the knee joint had been violated from this approach, clean margins would be difficult to ensure because of postoperative scarring from the previous surgery.

The classic extra-articular knee resection involves removal of the entire extensor mechanism. Previous studies and authors have recommended a knee fusion after the resection given the difficulty reconstructing the extensor mechanism. Reconstruction almost invariably leads to an extensor lag at the knee. The range of lag is anywhere between 0° to 70°.

Typically, there is a shorter time to walking seen in patients who undergo an amputation over a limb-sparing procedure for a tumor, with the average time being 3 to 6 months for amputees compared to 1 year for limb-salvage patients as reported in an American Cancer Society published guide addressing osteosarcoma. This was also reported in high-energy lower extremity trauma patients where the limb-salvage patients typically saw amputees walking and running earlier in the recovery process. The recovery process of an amputation was highlighted in an article by Ferrapie which reviewed 12 cases of transfemoral amputation or hip disarticulation for a primitive tumor. Ferrapie reported that inpatient rehabilitation started 14 days after amputation, lasting on average 32 days. Prosthetic fitting on average was performed 13 days after admission. All patients were able to use their prosthesis independently and had the ability to walk. The patients who were active went back to work, with 2 of the 6 surviving patients engaging in sports.

Other considerations which can delay recovery in limb-sparing procedures are the potential complications and revisions, as well as the typical need for adjuvant therapy. Complications include infections, hardware failures, and peroneal nerve palsies. In one study, the complication rate was 3 times high in the limb-salvage group compared to the amputation group of patients being treated for a lower extremity bone sarcoma. The complications above are potential reasons for reoperation, and there is a chance that limb-sparing procedures may need to be revised to an amputation. Lastly, the typical addition of adjuvant therapy in limb-sparing procedures for sarcomas can further delay healing and recovery, and are associated with their own side effects.

With regard to long-term recovery, studies addressing functional and cosmetic results between amputation and limb-salvage have been equivocal. The functional outcome and cosmetic appearance are important, though the primary objectives in surgical treatments for malignancies are the survival of the patient and prevention of local recurrences. When comparing limb-salvage with adjuvant therapy to an amputation in soft tissue sarcomas of the extremity the survival rates are similar, and in the majority of the cases limb-salvage surgery is considered the standard of care. There are many advantages and disadvantages with either amputation or a limb-salvage procedure, but for this patient the possibility of resuming activities at a level he was comfortable with earlier became the primary reason to elect for an amputation.

Chemotherapy has been discussed in the treatment plans of patients with intra-articular synovial sarcoma. The role of chemotherapy in a case report of patient without metastasis was discussed by Scully who noted that chemotherapy would have been administered to the patient if the tumor was larger than 8 cm. In the case report by Mclain on a patient with lung metastasis multiagent chemotherapy was started. Despite the chemotherapy, the patient expired 4 months after the surgical intervention. In the patient presented in our case report, chemotherapy was not given for the initial treatment. He is undergoing routine surveillance and chemotherapy will be used if the patient develops evidence of metastatic disease.

The use of radiation therapy has been reported in the prior literature on intra-articular synovial sarcoma. Scully reported on a patient receiving preoperative radiation therapy for local control of a tumor measuring 6.5 × 5.5 × 5.0 cm, followed by an extra-articular resection and reconstruction of the knee. Local radiation therapy has been used after a wide excision was performed for a recurrence of a previously excised tumor in a 13-year-old female. In the patient presented in our case report, radiation therapy was not given for the initial treatment and will be utilized if pathologic findings of local spread become apparent.

Interestingly, the patient in our case had significant prior trauma and surgery to the joint where the intra-articular synovial sarcoma developed. Two other cases reported prior surgery or trauma in the joint where the synovial sarcoma originated and discussed the possible relationship. Raynal who described a case report of a patient with intra-articular synovial sarcoma who had undergone an internal meniscectomy after trauma stated that the time between trauma and the appearance of a synovial sarcoma is either very long or very short. Raynal further states that possibly trauma reveals a preexisting occult tumor in some instance Weiss reports that most patients with synovial sarcoma do not report an “antecedent” trauma but do recall an injury. The association of an injury and synovial sarcoma could be secondary to how synovial sarcomas afflict the extremities which are commonly injured body parts.

## **CONCLUSION**

This case report highlights how an amputation can be a potential surgical treatment for intra-articular synovial sarcoma, and should be an option provided to the patient. An amputation should not be viewed as a surgical treatment failure. In this case report, the opportunity for a quicker recovery to an acceptable activity level was provided by a transfemoral amputation. The patient's significant history of knee pain and trauma before developing the neoplasm could have potentially influenced his decision for amputation over a limb-salvage procedure. Also, as an active-duty member, the patient's access to rehabilitation services could have impacted his choice. In contrast, in the civilian population there can be socioeconomic barriers encountered including the varying insurance companies' coverage on prosthetics and therapy provided. During the decision making process, educating the patient on the realistic outcomes of either limb-salvage or amputation is fundamental in positively influencing the patient's view on the success of either surgical procedure. By providing the patient with all the treatment options and their risks, benefits, and alternatives; the physician is respecting the patient's autonomy and this should be the cornerstone in planning any treatment. The limited number of case reports on intra-articular synovial sarcoma and the varied duration of follow-up preclude definitive recommendations regarding the optimal treatment and outcomes for these rare tumors.

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## **A Culture of Patient Safety in Military Medicine**

Military Medicine

Brig. Gen. Daneil O. Wyman, USAF MC CFS

August 2013

In 1999, the Institute of Medicine published a report entitled “To Err is Human: Building a Safer Health System,” which documented 44,000 to 98,000 deaths in U.S. hospitals each year attributed to preventable medical errors.<sup>1</sup> By 2009, evidence suggests that there are now approximately 200,000 deaths in U.S. hospitals each year attributed to preventable medical errors. That is more than 500 deaths per day! That is equivalent to the loss of a wide-body passenger jet every day! I cannot imagine the national outcry if we lost an airliner for even a few days in a row and yet we are essentially silent regarding these preventable health care deaths.

These errors occur in every aspect of health care. Errors occur in diagnosis or delays in diagnosis. They happen during treatment; errors during surgery or procedures, medication errors (wrong medication/wrong patient/wrong dose/wrong route), or delays in treatment. And errors occur in

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administration, logistics, and communications. So why do these preventable errors occur? I guess the simplest response is that we are all human beings and human beings make mistakes. And while this generality may be true, I do not believe that this response is adequate nor does it get us to the “root cause.” We certainly do not accept this level of preventable errors within other high-risk communities such as aviation.

Level of competence is typically not an issue regarding these errors given the comprehensive education, training, and recurrent certifications that health care professionals undertake. Although these education and training programs produce highly competent individuals, they traditionally occur in “stovepipes” (doctors train doctors, nurses train nurses, pharmacists train pharmacists, technicians train technicians), and integration as a team to provide highly effective and efficient health care rarely occurs. I consider this phenomenon to be the “root cause” fundamental to these unacceptable preventable medical errors. There are volumes of articles highlighting the principles of highly functioning teams but I believe the keys to establishing highly functioning health care teams are establishing health care standards, delineating team member roles and responsibilities, developing a mission focus, and finally, ensuring accountability.

## **HEALTH CARE STANDARDS**

There are thousands of guidelines/policies regarding the execution of health care. Many of these guidelines are evidence based and have been documented over time to significantly improve the efficiency, effectiveness, and safety of the delivery of health care. And yet, very few of these valuable guidelines have become “etched-in-stone” standards. An example is the Institute for Healthcare Improvement Central Line Bundle. Several years ago the Institute for Healthcare Improvement advocated implementation of the Central Line Bundle to decrease catheter-related bloodstream infections.<sup>2</sup> This bundle of five simple procedures (hand hygiene, maximal barrier precautions during insertion, chlorhexidine skin antiseptic, optimal catheter selection, and daily review of line necessity) has proven to significantly decrease the incidence of bloodstream infections and save time, money, and lives. But in hospitals across the United States, the Central Line Bundle is not the standard of care. In a study published in January 2011, of 250 National Healthcare Safety Network hospitals, only 49% reported having a written Central Line Bundle policy. And of those with policies that monitored compliance, only 38% of those reported full compliance. These results defy logic but unfortunately typify U.S. medicine. Guidelines and procedures that are relatively easy to execute and have been documented to decrease morbidity and mortality (and/or save time, money, and man-hours) are not the universal health care standard. This must be changed. U.S. medicine must establish universal standards of care. These standards must be codified and all health care professionals must execute to these standards.

## **ROLES AND RESPONSIBILITIES**

Health care teams should delineate roles and responsibilities as they execute to standards. As noted previously, health care professional education occurs in stovepipes. “Teaming” is typically not a focus of this process and care is thus provided by experts of segmented aspects of medicine. And preventable medical errors occur within the resulting seams of health care delivery...from misunderstandings, failed communications, poor hand-offs, and ignored mistakes. Defining the roles and responsibilities of everyone involved can minimize these seams and avert these errors. A few years ago, the Department of Defense Health Affairs and the Agency for Healthcare Research and Quality jointly developed Team Strategies and Tools to Enhance Performance and Patient Safety (TeamSTEPPS). A key principle of TeamSTEPPS is “team structure,” which includes the delineation of team composition and the identification and distribution of roles and responsibilities. Deering et al<sup>3</sup> noted an 83% decrease in medication and transfusion errors in a Combat Support Hospital following TeamSTEPPS training. Capella et al<sup>4</sup> documented significant improvements in clinical care for trauma patients following TeamSTEPPS. And numerous other studies have documented decreases in morbidity and mortality as well as improvements in efficiency and effectiveness of care delivery with training and implementation of

team-based health care. With successful team training and implementation, each and every team member develops an understanding about everyone's roles and responsibilities. Communications, situational awareness, and mutual support improve greatly and preventable medical errors are reduced.

## **MISSION**

For health care personnel, the profession of medicine is essentially a calling; voluntarily placing the service of others above self. But again, because we are trained and “grow up” in stovepipes, the focus of this service is frequently different. Physicians are driven by the search for diagnosis and appropriate treatment. Nurses concentrate on care plans, medical technicians on task accomplishment, pharmacists on correct medication dosage and drug interactions, laboratory specialists on quality control, etc. Obviously, all of these individual traits are important but it is absolutely essential for a successful team to focus on a mission; a common set of goals or objectives with a specific desired end state. In the Operating Room it is safe and efficient surgery. In the Emergency Department it is the safe and successful resuscitation of trauma victims. In the family medicine clinic it is the safe and compassionate care for a cancer patient and his/her family. The diverse members of the health care team must fuse their expertise to execute the mission of safe and effective health care.

## **ACCOUNTABILITY**

When we have established standards, defined team member roles and responsibilities and we are motivated toward a common mission, then accountability becomes the tenet for patient safety. We must be accountable to the standards, accountable to each other, and accountable to our patients and their families. According to Webster's, being accountable means being the one who must meet an obligation or suffer the consequences for failing to do so. This is not completely true in medicine as it is really our patients that suffer the consequences when we fail to meet our obligations. Even a cursory review of medical errors reveals failed accountability. Medical professionals failing to be accountable to evidenced-based protocols (i.e., Operating Room time outs/sponge counts or multiple patient identity verification or Central Line Bundles) lead to retained surgical items and medication errors and infections. Medical professionals failing to be accountable to team members and a common mission lead to wrong site or wrong patient procedures. Medical professionals failing to be accountable lead to more than 500 preventable deaths in U.S. hospitals each day!

Military medicine is at a tipping point regarding patient safety. The culture of the military is one of documented standards, defined roles and responsibilities, and full-spectrum accountability...and we are mission driven; it is “ONE TEAM, ONE FIGHT!” This culture and its foundational principles readily translate to military medicine to prevent medical errors. Partnership for Patients was recently implemented through the Department of Defense Patient Safety Program. Evidence-based guidelines were published to reduce nine preventable hospital-acquired conditions and readmissions. TeamSTEPPS training was provided to Military Treatment Facilities and each Service Surgeon has articulated their respective Mission, Vision, and Values. Each and every military medic (officer, enlisted, and civilian) must step up and be accountable...accountable to standards, accountable to each other, and most importantly, accountable to our patients and their families.

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## **When Will Acupuncture Become a First-Line Treatment for Acute Pain Management?**

Military Medicine

August 2013

Bart-Knauer, Brenda; COL Friedl, Karl E. MS USA (Ret.)  
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Acupuncture has a long history in traditional medicine, including strong evidence for effective pain management. The physiological basis of this pain relief has been examined but many important questions remain to be answered.<sup>1,2</sup> A review jointly sponsored by the Telemedicine and Advanced Technology Research Center (TATRC) and the National Center for Complementary and Alternative Medicine (NCCAM) concluded that this is a relatively mature technology and outlined additional research to refine and improve understanding and application of the treatment.<sup>3</sup> There are numerous techniques that appear to provide effective pain management for many individuals including the use of standard acupuncture points on the extremities, the scalp, and the ear. In October 2011, a NATO panel met in Bologna, Italy, and developed a consensus that the “battlefield acupuncture” technique involving five points in the ear stimulated with sterile 1 cm needles recapitulated some of the most powerful points based on Korean, Japanese, French, and other traditional acupuncture practices for pain management.<sup>4,5</sup> A new program funded through a special congressional appropriation will roll out a process for DoD-wide acupuncture training and credentialing over the next few years. This is led by the Defense and Veterans Center for Integrative Pain Management (DVCIPM) and enacts Army Pain Management Task Force recommendations to adopt acupuncture practices in military pain management.<sup>6,7</sup> These recent events represent a confluence of deliberate actions to address concern about overmedication of soldiers for acute pain and pain syndromes, an issue that has been raised in the media for several years.<sup>8</sup> The question on everyone's mind should be “what is holding us back from providing this alternative treatment today when it is so desperately needed?”

The answer is that we have started and the initial results are a resonating success. In a small demonstration project at Camp Lejeune, 37 special operations independent duty corpsman (SOIDC) and allied health professionals were trained by Colonel (Ret.) Richard Niemtzw and his team in the technique of battlefield acupuncture, based on readily accessible points located in the ear (“auricular” acupuncture). Dr Niemtzw, with the assistance of the Samueli Institute, has been training physicians throughout the Air Force and within the Department of Defense (DoD) for the past decade in this technique that involves five points on the ear: “cingulated gyrus,” “thalamus,” “omega 2,” “point zero,” and “shenmen”.<sup>9</sup> The SOIDC training is a first foray into providing this tool to nonphysician medical providers and putting it in the hands of the individuals that are usually the first line of treatment for acute pain. The training has been successful in terms of the wide acceptance and interest in the Navy medical community at Camp Lejeune. Initially skeptical users have provided reports of pain relief that had not been obtained from medication, ability to continue in training or with the mission because of the improved pain control, lack of confounding drug effects, and no reported adverse consequences. Objective data on usage and acceptance are being gathered from its use by SOIDC in Afghanistan and at Camp Lejeune.

This is where we should all stand up and salute the Marine Corps Special Operations Command (<http://www.marsoc.marines.mil/>) for their willingness to be the early adopters of good ideas. Over the years, Marine Corps representatives have stated in open forum that they are more than willing to adopt a commonsense solution that may benefit Marines, and they will count on their Army friends to follow up with a decade of research that further tests, refines, or invalidates the approach. This use of the best available solutions represents a very pragmatic “just do it” view. The fact that we did not have a complete understanding of the mechanism of action of aspirin until the 1970s did not prevent its useful application. Similarly, it may be years before we have a good understanding of the mechanisms of pain relief provided by acupuncture and other forms of peripheral nerve stimulation. Conceivably, even running exercise is a form of peripheral nerve stimulation that also moderates pain perception thresholds as an extension of the same mechanism.<sup>10</sup> If less precisely placed “sham” needling is equally effective in providing pain

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relief, this also does not reduce its value.<sup>1</sup> We can continue to discuss the theory and scientific basis for years to come but we must start evaluating its relative benefits in the real environment where it is so badly needed now.

An expected risk of moving acupuncture treatment into mainstream use is the confusion that will result from misuse. The standard of practice has no national regulating body and many exuberant users are more than willing to broaden the technique and the applications well beyond what might be considered tested and proven approaches. This represents a slippery slope for both medical application and technique. The existence of a DoD body, the DVCIPM is one management control to reduce this risk and the planned multiyear rollout of a DoD-wide training and credentialing program is an essential approach to ensuring successful entry of this new tool in pain management. Other scientific exploration will continue to test new claims of technologically enabled energy treatments; however, these are not rooted in hundreds of years of traditional practice, nor are they necessarily derived from solid science and we must proceed cautiously with derivative methods (such as different types of metals, electrostimulation, and laser stimulation).

One of the assumptions about advantages of acupuncture over drugs is that the effect is more specific to pain management without many other unintended consequences produced by the currently available pharmaceuticals.<sup>11</sup> Conceivably, a corpsman or medic could provide auricular acupuncture on the battlefield for acute pain relief and permit the individual to continue to support the mission, whereas most drug solutions will incapacitate the soldier through effects on cognitive function and situational awareness. Another assumption is that this technique can be easily mastered and there is little injury risk associated with placement of short sterile needles in external ear locations. There is always a risk of unqualified individuals practicing medicine, using acupuncture to treat pain that actually signals an undiagnosed serious illness; this should not be a greater risk than what is already present with drugs that would otherwise be provided to an injured soldier or Marine for pain management. Ultimately, we will not discover the most appropriate uses of acupuncture in military medicine until we move to real-life testing and evaluation through initiatives such as the current TATRC-supported program at Camp Lejeune.

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***PTSD***

## **Mental Health Response to Community Disasters: A Systematic Review**

Journal of the American Medical Association  
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7 August 2013

### **ABSTRACT**

**Importance** Exposure to a disaster is common, and one-third or more of individuals severely exposed may develop posttraumatic stress disorder or other disorders. A systematic approach to the delivery of timely and appropriate disaster mental health services may facilitate their integration into the emergency medical response.

**Objective** To review and summarize the evidence for how best to identify individuals in need of disaster mental health services and triage them to appropriate care.

**Evidence Review** Search of the peer-reviewed English-language literature on disaster mental health response in PsycINFO, PubMed, Cochrane Database of Systematic Reviews, Academic Search Complete, and Google Scholar (inception to September 2012) and PILOTS (inception to February 2013), using a combination of subject headings and text words (*Disasters, Natural Disasters, Mental Health, Mental Health Programs, Public Health Services, Mental Disorders, Mental Health Services, Community Mental Health Services, Emergency Services Psychiatric, Emotional Trauma, Triage, and Response*).

**Findings** Unlike physical injuries, adverse mental health outcomes of disasters may not be apparent, and therefore a systematic approach to case identification and triage to appropriate interventions is required. Symptomatic individuals in postdisaster settings may experience new-onset disaster-related psychiatric disorders, exacerbations of preexisting psychopathology, and/or psychological distress. Descriptive disaster mental health studies have found that many (11%-38%) distressed individuals presenting for evaluation at shelters and family assistance centers have stress-related and adjustment disorders; bereavement, major depression, and substance use disorders were also observed, and up to 40% of distressed individuals had preexisting disorders. Individuals with more intense reactions to disaster stress were more likely to accept referral to mental health services than those with less intense reactions. Evidence-based treatments are available for patients with active psychiatric disorders, but psychosocial interventions such as psychological first aid, psychological debriefing, crisis counseling, and psychoeducation for individuals with distress have not been sufficiently evaluated to establish their benefit or harm in disaster settings.

**Conclusion and Relevance** In postdisaster settings, a systematic framework of case identification, triage, and mental health interventions should be integrated into emergency medicine and trauma care responses.

Mental and physical consequences of major disasters have garnered increasing attention to the need for an effective community response. It is estimated that much of the US population will be exposed to a “fire, flood, earthquake, or other natural disaster” during their lives; adding technological events such as airplane crashes and intentional human acts such as terrorism to this estimate would yield even higher numbers. Mental health effects of disaster exposures are relevant to informing care for survivors of all forms of trauma, because 9 of 10 people are likely to experience trauma in their lifetimes. These mental health effects are important in their own right, as is reflected in prominent appeals for acute and long-term mental health services for survivors of several recent large-scale US disasters. In the last several years, especially since the September 11, 2001, terrorist attacks, public health expertise has been formally incorporated into disaster and emergency preparedness and response. During this period, the importance of integrating mental health into the medical and emergency aspects of disaster response was broadly recognized.

A substantial body of scientific work on the mental health effects of disasters, summarized in several major review articles, has provided a fundamental basis for the organization of disaster mental health response. These sources agree that posttraumatic stress disorder (PTSD) is the psychiatric disorder most often associated with disaster trauma exposure, which includes direct endangerment, being an eyewitness to trauma in a disaster, or having a close associate exposed to disaster trauma. PTSD may occur in up to one-third of highly exposed survivors and major depression in up to one-fourth. There is also agreement that new alcohol and drug use disorders do not usually begin following disasters, although preexisting substance abuse problems may worsen or recur. Consistently identified predictors of psychopathology after disasters in this literature are female sex, preexisting psychopathology, severity of exposure to disaster trauma, other concurrent stressors, and lack of social support.

Disaster-related psychopathology begins soon after a disaster and declines over time, becoming chronic in a substantial minority of individuals. Symptoms and unpleasant emotions not qualifying as a psychiatric disorder are referred to as psychological distress. Distress at some level is nearly universal after disasters and is far more prevalent than psychiatric disorders. The distinction between these 2 entities is critical for effective disaster response, because different interventions are needed for them.

This review provides a practical framework for delivering mental health interventions to individuals appropriate to their needs in the wake of a disaster. Much of the existing disaster mental health literature is organized into components of preparedness, response, and recovery, which provides a theoretical framework for disaster planning but is less useful for operationalizing the delivery of mental health services to affected individuals. Established approaches to emergency and medical response to mass casualty incidents include functions of search and rescue, triage and initial stabilization, and definitive medical care as main components of the response. For disaster mental health response, these functions translate into identification of mental health needs and case identification, triage and referral to appropriate services, and provision of appropriate mental health interventions, in a framework to guide disaster mental health interventions.

## **METHODS**

September 2012 to identify peer-reviewed English-language literature on mental health interventions and service delivery specific to community disasters. A medical librarian searched for citations of relevance in PsycINFO (467 citations), PubMed (234 citations), Cochrane Database of Systematic Reviews (0 citations), Academic Search Complete (EBSCOhost; 42 citations), and Google Scholar (130 citations) using a combination of subject headings and text words (*Disasters, Natural Disasters, Mental Health, Mental Health Programs, Public Health Services, Mental Disorders, Mental Health Services, Community Mental Health Services, Emergency Services Psychiatric, Emotional Trauma, Triage, and Response*) from the time of the inception of these sources. A search of PILOTS (161 citations) was conducted in February 2013. Additional literature is scattered throughout various institutional reports, books and monographs, and web-based sources not included in this review.

This search yielded 569 unique articles. Exclusion of international studies reduced the number of articles to 427 in the United States. An additional 174 articles in this collection focusing on disaster mental health effects—rather than services, as determined by the first author—were further excluded. The remaining articles were classified by type (original research, reviews, reports, commentary/opinion) based on the system of Hadorn et al, adapted by Redwood-Campbell et al to categorize disaster response studies. The articles were further categorized by focus of article (general disaster mental health response, disaster interventions referring to specific types of clinical techniques, and specific disaster services referring to disaster programs such as Project Liberty) and type of disaster (natural disasters, technological events, and intentional human-caused disasters). Last, 31 articles consisting of anecdotal reports were excluded from the final list, yielding a total of 222 unique articles on disaster and emergency mental health response, interventions, and services included in this review (eTable [Supplement]). The most frequently represented article type was commentaries (n = 88), followed by reviews (n = 49) and by reports of responses, interventions, programs, and services (n = 46). Only 39 articles were classified as original research. The type of disaster featured in the largest number of articles was terrorism, the majority of which was represented by the September 11 attacks. The articles were then organized according to the disaster response framework's components of case identification, triage, and intervention.

## **FINDINGS**

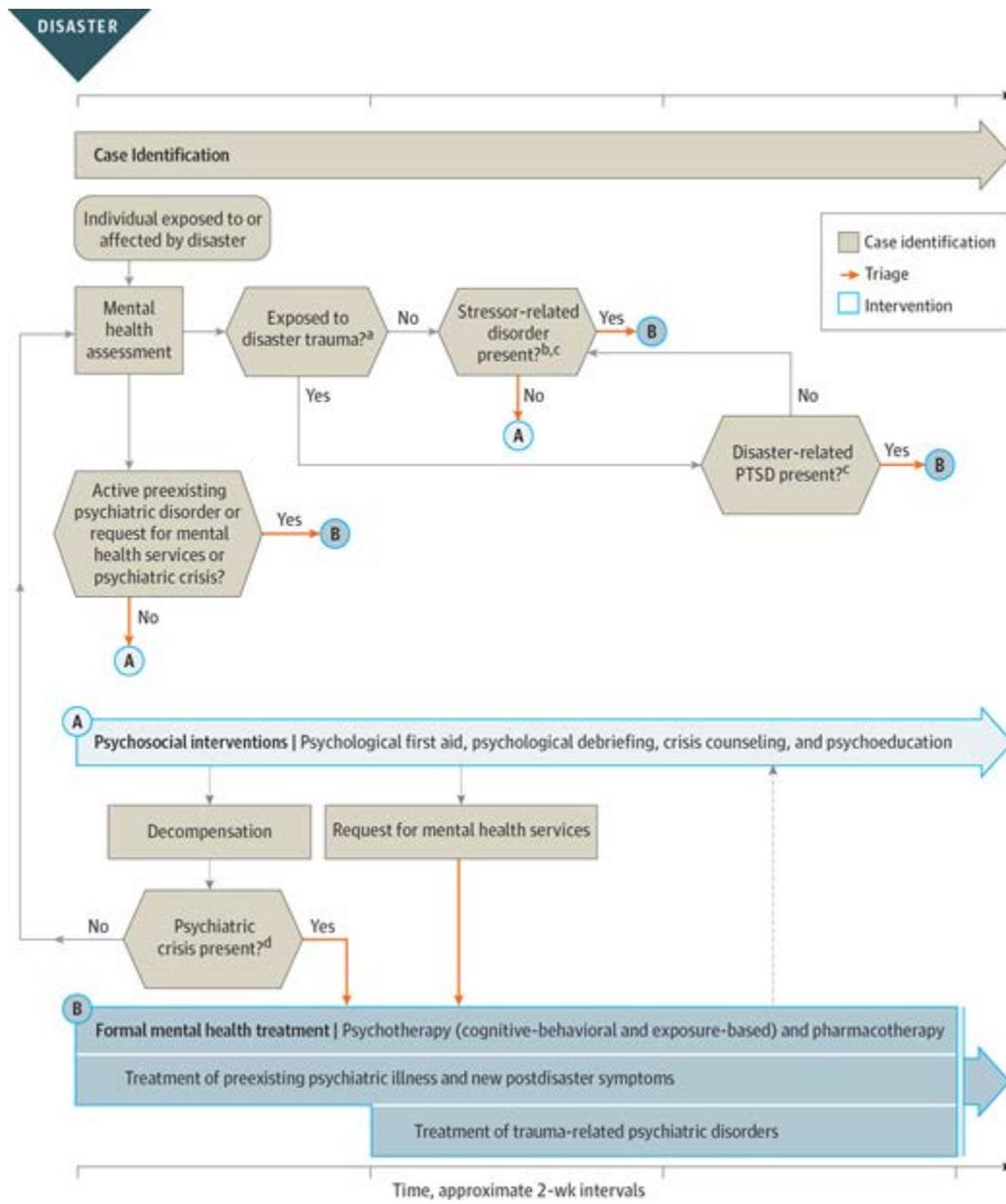
A general consensus in this literature was that mental health should be integrated into emergency and medical disaster response.

The flow diagram shown in the Figure systematically directs responders through processes of the mental health response, starting with case identification following exposure to trauma, which involves identifying psychopathology and differentiating it from normative emotional distress; proceeding to triage to the appropriate type and level of care; and concluding with delivery of appropriately targeted interventions based on accurately assessed needs. For example, an individual directly exposed to a disaster is assessed first for trauma exposure and then for PTSD and other psychiatric disorders, symptoms, and psychosocial distress. The initial assessment might take place in the disaster setting such as in a mental health clinic embedded in a large evacuee shelter or a family assistance center or in a formal psychiatric care setting such as a psychiatric emergency department or a psychiatrist's office. If PTSD or another disorder is diagnosed, the individual is referred for formal treatment and also may receive other psychosocial interventions. If no psychiatric disorder is identified, the individual is triaged to psychosocial interventions. Additionally, if an individual presents with a psychiatric crisis, has an active preexisting psychiatric disorder, or requests treatment, the individual is triaged or referred to the appropriate level of psychiatric care. Diagnostic assessment of PTSD cannot be completed until 1 month after the disaster (trauma exposure), when PTSD can first be diagnosed.

Figure.

### **Disaster Mental Health Case Identification, Triage, and Interventions**

This diagram systematically directs disaster mental health responders through 3 components of psychiatric assessment, starting with identification of psychopathology and differentiating it from normative emotional distress, proceeding to triage to the appropriate type of care, and concluding with delivery of appropriately targeted interventions based on accurately assessed needs. Activities are shown in the general sequence in which they would occur and at the approximate time they would first occur; activities would continue beyond 6 weeks into the indefinite future, as indicated by the particular situation.<sup>a</sup>Meets *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) for posttraumatic stress disorder (PTSD).<sup>b</sup>Major depression, bereavement, anxiety.<sup>c</sup>Screening may be conducted as a first step to identify individuals unlikely to develop a psychiatric disorder, but full diagnostic assessment is needed before formal psychiatric decisions are made (2 weeks are required after disaster for diagnosis of new cases of major depression and 1 month for PTSD).<sup>d</sup>Suicidal or homicidal ideation, psychosis, psychiatrically based inability to care for self or dependents.



## Identification of Mental Health Problems and Needs

Accurate assessment of mental health problems and related needs among disaster-affected groups is an essential foundation for effective disaster response. This component of disaster mental health response conceptually differs from its counterpart in disaster emergency and medical response, because unlike physical injuries incurred in mass-casualty incidents, psychological wounds are often not apparent and therefore require concerted efforts and different procedures for identification and assessment. Postdisaster assessments of mental health needs include consideration of both community-level and individual-level concerns. Community assessment involves population surveillance to develop accurate prevalence estimates of mental health conditions and related needs, which are fundamental to effective allocation of limited resources, and to inform the planning and delivery of services and interventions. In contrast, individual assessment entails personal clinical evaluation, including full diagnostic assessment for case identification to direct individuals to services appropriately targeted to their needs.

For population and individual assessments, the type of assessment varies in different postdisaster time frames, because new disorders arising after disasters develop over weeks. By definition, PTSD and major depression, the psychiatric disorders most likely to develop after disaster exposure, take 4 and 2 weeks, respectively, to develop and be diagnosed. Assessments during the first 2 to 4 weeks therefore can meaningfully address distress and psychosocial issues arising in the early postdisaster phases, as well as preexisting psychiatric disorders such as alcohol addiction and bipolar disorder, but are too early to fully capture new psychiatric disorders. Criteria for diagnosis of PTSD and major depressive disorder based on the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) (*DSM-5*) criteria are summarized in Box 1 and Box 2.

Box 1.

DSM-5 Criteria for Posttraumatic Stress Disorder (PTSD)<sup>a</sup>

Criteria

- **Exposure to trauma** (actual or threatened death, serious injury, sexual violence) in one of the following ways:
  1. Directly exposed
  2. Witnessed (in person) trauma to others (viewing electronic media, television, movies, or pictures does not qualify, unless work-related)
  3. Learned of direct trauma exposure (violent or accidental) of a close family member or close friend
  4. Repeated or extreme exposure to aversive details of trauma (eg, first responders collecting human remains; police officers repeatedly exposed to details of child abuse)
- **Intrusion** symptoms with content associated with, or beginning after, the trauma ( $\geq 1$  symptom):
  1. Recurrent, involuntary, and intrusive distressing memories of the trauma

2. Recurrent distressing dreams with dream content, affect related to the trauma, or both
  3. Dissociative reactions (feeling or acting as if the trauma is recurring, eg, flashbacks)
  4. Psychological distress with reminders of the trauma
  5. Physiological reactions to reminders of the trauma
- **Avoidance** of reminders of the trauma, persistent and beginning after the trauma ( $\geq 1$  symptom):
    1. Avoidance of or efforts to avoid distressing trauma-related memories, thoughts, or feelings
    2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing trauma-related memories, thoughts, or feelings
  - **Negative cognitions or mood** associated with, or beginning or worsening after, the trauma ( $\geq 2$  symptoms):
    1. Inability to remember important parts of the trauma (typically, dissociative amnesia not resulting from head injury, alcohol, or drugs)
    2. Negative beliefs or expectations about oneself, others, or the world (eg, "I am bad," "No one can be trusted," "The world is completely dangerous")
    3. Distorted cognitions about the trauma's cause or consequences, leading to blaming self or others
    4. Negative emotional state (fear, horror, anger, guilt, shame)
    5. Markedly diminished interest or participation in significant activities
    6. Feeling detached or estranged from others
    7. Inability to experience positive emotions (happiness, satisfaction, love)
  - **Arousal** and reactivity associated with, or beginning or worsening after, the trauma ( $\geq 2$  symptoms):
    1. Irritable behavior and angry outbursts (with little or no provocation) expressed as verbal or physical aggression
    2. Reckless or self-destructive behavior
    3. Hypervigilance
    4. Exaggerated startle response
    5. Problems with concentration

6. Sleep disturbance (eg, difficulty falling or staying asleep; restless sleep)

- **Duration** of the disturbance (criteria B, C, D, and E) is longer than 1 month
- **Clinically significant distress or impairment** in social, occupational, or other important areas of functioning result from the disturbance
- **Not attributable to physiological effects** of a substance (eg, medication, alcohol) or another medical condition
- Specifiers: (1) with dissociative symptoms (depersonalization or derealization); (2) with delayed expression (full diagnostic criteria are not met until >6 months after the trauma, although the onset and expression of some symptoms may be immediate)

Major changes to PTSD criteria in DSM-5

- Substantial changes made to PTSD criteria
- Moved from Anxiety Disorders section to new Trauma- and Stressor-Related Disorders section
- Criterion A (trauma exposure) made more specific; A2 (subjective reaction) criterion eliminated
- Symptom clusters expanded from 3 to 4 with avoidance/numbing cluster (prior symptom group C) divided into avoidance cluster (new symptom group C) and persistent negative cognitions/mood alteration cluster (new symptom group D)
- *DSM-5* criteria specifically address dissociation, aggression, distorted cognitions, and a wider range of negative emotions (with reinclusion of formerly eliminated survivor guilt)
- More developmentally sensitive for children or adolescents (lowered diagnostic thresholds and new separate criteria for children 6 years or younger)

Adapted from *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) (*DSM-5*).

Box 2.

DSM-5 Criteria for Major Depressive Disorder

Criteria

- **Depressive episode:** Five or more symptoms representing a change from previous functioning and not attributable to another medical condition present during a 2-week period ( $\geq 1$  of the symptoms is either item 1 or item 2 below):
  1. Depressed mood most of the day, nearly every day
  2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day

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3. Significant loss or gain of weight or appetite (not when dieting) nearly every day
  4. Insomnia or hypersomnia nearly every day
  5. Psychomotor agitation or retardation nearly every day
  6. Fatigue or loss of energy nearly every day
  7. Feelings of worthlessness or excessive or inappropriate guilt nearly every day
  8. Diminished ability to think or concentrate, or indecisiveness, nearly every day
  9. Recurrent thoughts of death, recurrent suicidal ideation or a specific plan for committing suicide, or suicide attempt
- **Clinically significant distress or impairment** in social, occupational, or other important areas of functioning result from the symptoms
  - **Not attributable to physiological effects** of a substance or to another medical condition
  - **Not better explained** by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders
  - **No manic or hypomanic** episode history
  - Specifiers: with anxious distress, mixed features, melancholic features, atypical features, mood-congruent psychotic features, mood-incongruent psychotic features, catatonia, peripartum onset, seasonal pattern

#### Major Changes to Major Depressive Disorder Criteria in DSM-5

- Few changes made to major depressive disorder criteria
- Bereavement exclusion criterion (major depressive episode applied to depressive symptoms lasting <2 months following the death of a loved one) eliminated, with provision of a detailed footnote to aid clinicians in making the critical distinction between symptoms characteristic of bereavement and those of major depressive disorder

Adapted from *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) (DSM-5).

Additionally, the conditional nature of PTSD dictates that the disorder by definition cannot occur in the absence of sufficient exposure to a qualifying traumatic event. Disaster-related PTSD is limited to trauma-exposed groups either located within a circumscribed trauma zone or having trauma-exposed close associates. In a study of 379 survivors of the September 11 attacks on the World Trade Center in New York, PTSD symptom criteria at any time after the disaster were met by 35% of people directly exposed to danger, 20% of those exposed only through directly witnessing trauma, and 35% of those exposed only through a close associate's direct exposure. Outside of these exposure groups, few possible sources of exposure were evident among the few individuals who were symptomatic, most of whom had preexisting psychiatric illness. However, disasters of extreme magnitude, such as the September 11 attacks, have far-reaching emotional effects extending beyond trauma-exposed

groups to others affected by disaster-related losses, hardships, perceived threat, identification with victims, or sociopolitical changes. A national survey found that 17% of the US population residing outside of New York City reported attack-related psychological symptoms 2 months after the September 11 attacks, which was associated in another study with the amount of time spent viewing television coverage of the attacks. Posttraumatic symptoms in people unexposed to the disaster trauma or otherwise not meeting PTSD criteria may represent psychological distress, symptoms of a different psychiatric disorder such as major depression, or preexisting psychopathology.

Whether for community needs assessment or for individual case finding, diagnostic assessment is resource intensive, especially if the numbers to be assessed are large. In such instances, screening can identify individuals at risk for psychiatric problems. Screening tools should be brief and uncomplicated, appropriate in content reflecting the context and disaster phase, acceptable to those being screened, and easily administered and scored. Symptom measures used to screen for PTSD and depression are listed in Table 1. Potential screening locations include workplaces, primary care settings, schools, and other venues where large numbers of affected individuals are accessible. Systematic screening of population groups can facilitate efforts to direct large numbers of symptomatic individuals into care, as illustrated by a screening program implemented after the 2005 London bombings that generated more referrals to a treatment center than did existing clinical channels. Of 596 individuals participating in the screening program, 62% screened positive for a bombing-related mental disorder. Based on a subsequent full clinical assessment, 43% of the 596 participants in the screening were referred for treatment and 32% had a psychiatric disorder, most often PTSD.

Table 1. Examples of Screening Tools for PTSD, Major Depression, and Trauma Exposure

**Table 1. Examples of Screening Tools for PTSD, Major Depression, and Trauma Exposure<sup>a</sup>**

Tool	Condition Assessed	Description	Psychometric Properties	Population Tested
PTSD Checklist (PCL)	PTSD	Self-report (17 items) corresponding to <i>DSM-IV</i> PTSD symptoms scored on 5-point Likert scale	Cronbach $\alpha = .90$ for internal consistency; optimal cutoff score of 39 for firefighters (44 in general); sensitivity, 0.85; specificity, 0.82; area under ROC curve, 0.91 vs PTSD diagnosis by structured interview (Diagnostic Interview Schedule)	September 11-exposed firefighters <sup>47</sup> ; New York City-area residents after September 11 attacks <sup>48</sup>
National Women's Study Posttraumatic Stress Disorder module (NWS-PTSD)	PTSD	Lay interview; 20 items assessing <i>DSM-IV</i> PTSD symptoms	Cronbach $\alpha = .83$ for internal consistency; $\kappa = .85$ vs Structured Clinical Interview for <i>DSM-IV</i> diagnosis; interrater $\kappa = .71$ for current and $.77$ for lifetime PTSD	New York City-area residents after September 11 attacks; field trial <sup>48</sup>
Civilian Mississippi Scale for PTSD	PTSD	Self-report (35 items) scored on 5-point Likert scale	Cronbach $\alpha = .74$ for internal consistency (.86 with reversed questions removed); $\alpha$ coefficients for 30-item scale, .38-.92	Loma Prieta earthquake (1989) <sup>49</sup> ; college students <sup>50</sup>
Impact of Event Scale-Revised (IES-R) and brief 6-item version (IES-6)	PTSD	IES-R: self-report (22 items), 5-point Likert symptom measure of subjective distress following trauma; IES-6: 6-item subset	Pooled correlation = .95 for brief 6-item (IES-6) version vs IES-R	Mixed trauma-exposed samples <sup>51</sup>
Beck Depression Inventory II (BDI-II)	Major depression	Self-report measure (21 items) of depressive symptom severity, rated on 4-point scale (range, 0-3; total score range, 0-63)	Cronbach $\alpha = .54-.74$ for internal consistency; ROC analysis: cutoff score of 18 yields best balance between sensitivity and specificity in primary care, with overall correct classification rate of 92%	Primary care patients <sup>52</sup> ; combat veterans with PTSD <sup>53</sup>
Center for Epidemiologic Studies Depression Scale (CES-D)	Major depression	Questionnaire (20 items), symptom frequency in past month scored on 3-point Likert scale	Thirty-six percent diagnosis with cutoff score of 16; 23% diagnosis with cutoff score of 22, with sensitivity = .84, specificity = .82, and area under ROC curve = .89 vs structured diagnostic interview (Diagnostic Interview Schedule)	September 11-exposed firefighters <sup>54</sup>
Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR)	Major depression	Self-report questionnaire (16 items)	Cronbach $\alpha > .81$ for internal consistency; highly correlated ( $r = .83$ ) vs structured diagnostic interview (Structured Clinical Interview for <i>DSM-IV</i> diagnosis); highly sensitive to symptom change, indicating high concurrent validity	Combat veterans <sup>55</sup> ; outpatients with major depression <sup>56</sup>
Traumatic Exposure Severity Scale (TESS)	Trauma exposure	Self-administered instrument (24 items) with 5 subscales: resource loss, damage to home and goods, personal harm, concern for significant others, and exposure to grotesque	Total Cronbach $\alpha$ for internal consistency: total, .78; subscales, .63-.73	Earthquake survivors in Turkey <sup>57</sup>

Abbreviations: *DSM-IV*, *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition); PTSD, posttraumatic stress disorder; ROC receiver operating characteristic.

<sup>a</sup> These screening tools do not provide psychiatric diagnoses and should not be used for diagnosis in assessment of individuals or for direct determination of population prevalence of psychiatric disorders. Screening tools can be used to identify individuals at risk for psychiatric disorders and to reduce assessment

burden by limiting full diagnostic evaluation to groups with identified risk, but treatment decisions require accurate diagnostic assessment for selection of appropriate interventions. Additionally, screening tools for assessment of PTSD should be used only for individuals with qualifying trauma exposures as defined in criterion A for PTSD in the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition), because most PTSD screening tools do not assess trauma exposure or necessarily anchor the symptoms to a qualifying trauma exposure.

The literature clearly emphasizes that symptom-screening instruments do not provide psychiatric diagnosis, either for assessment of individuals or for estimating the population prevalence of disorders; a positive screen result needs to be followed by full clinical assessment. Screening

instruments emphasize sensitivity rather than specificity to cast a wide net for affected individuals, but clinical evaluation is necessary to make psychiatric diagnoses based on specific combinations of qualifying symptoms, sufficient symptom duration, and detrimental effects on functioning.

### **Community Assessment**

Knowledge of the community's mental health, vulnerabilities, and resources and capacities before a disaster is important to inform the postdisaster response. Critical to valid estimation of community mental health needs after a disaster are careful selection of respondents and use of appropriate measures. Measuring PTSD in unexposed populations is fraught with potential for overestimation. Various strategies for collecting relevant data after a disaster include case reporting, conducting surveys (eg, random-digit-dial telephone surveys), holding focus groups, and consulting private and public databases (eg, to identify surges in clinic enrollments or alcoholic beverage sales). However, self-report symptom surveys can provide only rough estimates of the mental health of a community, because they are designed to identify individuals at risk for mental disorders and to maximize sensitivity over specificity. Consequently, self-report screening instruments do not provide valid prevalence estimates of psychiatric disorders from the symptoms they measure. Moreover, because most disaster survivors with psychiatric disorders do not utilize mental health treatment services, this must also be factored into planning for treatment resource allocation based on prevalence estimates of psychiatric disorders in affected populations.

### **Individual Assessment**

Individual assessments in the first few days and weeks after a disaster can identify psychosocial issues, symptoms, level of functioning, attitudes and beliefs, and current status of preexisting psychiatric disorders. The case-identification procedures in the Figure provide guidance for directing individual postdisaster mental health assessments, based on initial inquiry about qualifying trauma exposures (vs other disaster-related stressors). For example, only people with exposure to disaster trauma through either direct endangerment, directly witnessing others being injured or killed, or having a close associate who had been exposed as defined in the *DSM-5* criteria for PTSD would warrant assessment for PTSD, and major depression and anxiety are also of potential concern for them. Those who sustained major losses in the disaster warrant assessment for bereavement or major depression.

Clinical evaluation is achieved through a personal interview by a clinician to determine the most appropriate intervention based on diagnostic and psychosocial assessment. Especially in the early postdisaster phases, this evaluation may be conducted in nontraditional locations such as in shelters or evacuation centers; after referral to treatment, it will likely occur in a more traditional setting such as in the clinician's office. The chaos associated with acute disaster situations and time pressures may limit the content of the history but should not sacrifice identification of constellations of symptoms and related criteria that constitute psychiatric illness and that represent the focus for treatment, as well as other relevant information. At a minimum, abbreviated diagnostic evaluation should cover details of the individual's disaster experience, full diagnostic assessment for PTSD and other disorders, a mental status examination, and history of preexisting disorders and other trauma exposures and stressors. Psychiatric assessments providing these essential elements were successfully conducted with 421 sheltered Hurricane Katrina evacuees in the first 2 weeks after the disaster and with 848 people in a community-based psychiatrist response program at a family assistance center during the first 2 months after the September 11 attacks. Potential sources of mental status changes that may need to be considered in disaster settings are head injury, toxic exposures, medical illness, delirium, dehydration, drug withdrawal or intoxication, and interruption of previously established medication regimens.

## **Triage and Referral to Services**

Following adequate assessment, the next major component of the disaster mental health response, as in general emergency disaster response, is triage to appropriate care (Figure). Individuals identified as having active psychiatric disorders will require referral to formal mental health services. This is particularly relevant as days to weeks pass after the disaster, when new disaster-related cases of PTSD and major depression emerge and can be diagnosed.

Additionally, acute psychiatric crisis (suicidal or homicidal ideation, psychosis, psychiatrically based inability to care for oneself or one's dependents) and recurrence or worsening of preexisting psychiatric illness require referral to appropriate care (triage processes for these are also shown in the Figure). Preexisting psychiatric disorders can sometimes represent a substantial proportion or even most of the emerging psychopathology. For example, among sheltered Hurricane Katrina evacuees assessed in a mental health clinic, 40% were treated for preexisting mental illness and 24% for a new postdisaster disorder. Among directly exposed Oklahoma City bombing survivors with a postbombing diagnosis, 63% had a preexisting psychiatric disorder.

In the Project Liberty crisis counseling program in New York City after the September 11 attacks, use of an enhanced services referral tool (the 12-item expanded Short Post-Traumatic Stress Disorder Rating Interview [SPRINT-E]) resulted in referrals to enhanced services for 543 of 800 participating individuals in the program, 71% of whom accepted the referral. An additional 9 individuals were identified as being at risk for suicide and triaged to immediate psychiatric intervention. The strongest predictor of referral acceptance was the number of intense reactions (defined on a 1-5 point rating scale as a score of 4 [quite a bit] or 5 [very much]).

## **Disaster Mental Health Interventions**

Disaster mental health interventions include formal psychiatric treatment for psychiatric disorders and an array of wellness- and resilience-based psychosocial interventions for emotional distress and social problems (Table 2 and Figure). The most effective interventions are those chosen appropriately for the type of need determined in the clinical assessment. Although most people affected by disasters do not develop psychiatric disorders, almost everyone with exposure to severe disaster trauma will experience distress for at least a brief period. For example, although less than one-half of survivors directly exposed to the Oklahoma City bombing developed a psychiatric disorder after the bombing, 96% reported having at least 1 posttraumatic symptom. Thus, early interventions are indicated for the majority of survivors to reduce distress, provide emotional support, educate, and normalize emotional responses, even before new psychiatric disorders have time to develop and be diagnosable. Among the most commonly described interventions in the disaster mental health literature reviewed are psychological first aid, psychological debriefing (eg, critical incident stress debriefing), and crisis counseling (eTable [Supplement] and Box 3).

Table 2. Mental Health Interventions in General Trauma Care and in Disaster Response Situations, for Selected Conditions Relevant to Disaster Exposure

Table 2. Mental Health Interventions in General Trauma Care and in Disaster Response Situations, for Selected Conditions Relevant to Disaster Exposure

Condition and Intervention Type	General Trauma Care		Disaster Response	
	Specific Intervention	Evidence Level <sup>a</sup>	Specific Intervention	Evidence Level <sup>a</sup>
<b>PTSD</b>				
Psychotherapy				
	Cognitive-behavioral	A <sup>65-68</sup>	Cognitive-behavioral	A <sup>69-71</sup>
	Exposure-based	A <sup>67,68</sup>	Exposure-based	A, <sup>72</sup> B <sup>73</sup>
	Other <sup>b</sup>	A <sup>68,74</sup>	Other <sup>b</sup>	C <sup>75</sup>
Pharmacotherapy				
	Antidepressants, especially serotonin-selective	A <sup>67,76</sup>	Antidepressants	C <sup>63,64</sup>
	Adjunctive medications <sup>c</sup>	A <sup>67,76</sup>	Adjunctive medications <sup>c</sup>	C <sup>63,64</sup>
<b>Major depression</b>				
Psychotherapy				
	Cognitive-behavioral	A <sup>77-80</sup>	Cognitive-behavioral	B <sup>77-80</sup>
	Other <sup>d</sup>	A <sup>77-81</sup>	Other	
Pharmacotherapy				
	Antidepressants	A <sup>67,80,81</sup>	Antidepressants	C <sup>63,64</sup>
	Adjunctive medications <sup>e</sup>	A <sup>80</sup>	...	
	Neurostimulation <sup>f</sup>	A <sup>80,82</sup>	...	
<b>Traumatic grief</b>				
Psychotherapy	...	B <sup>83</sup>	...	D <sup>84</sup>
Pharmacotherapy	...	A <sup>83,85</sup>	...	
<b>Psychological distress</b>				
Psychosocial interventions	Debriefing	B (possible harm) <sup>86,87</sup>	Debriefing	D <sup>26,88</sup>
	Psychoeducation	B (ineffective, possible harm) <sup>89</sup>	Psychoeducation	D <sup>26,88</sup>
	Supportive psychosocial care	B <sup>89</sup>	Psychological first aid	D <sup>88</sup>
			Crisis counseling	D <sup>88</sup>
Pharmacotherapy	...	B <sup>90,91</sup>	...	C <sup>63,64</sup>

Abbreviations: PTSD, posttraumatic stress disorder. Ellipses (...) indicate no specific intervention for that intervention type.

<sup>a</sup> Level of evidence graded A through D based on description by Shekelle et al<sup>92</sup>: A, based on category I evidence (from randomized controlled trials); B, based on category II evidence (from nonrandomized or quasi-experimental studies or extrapolated from category I evidence); C, based on category III evidence (from nonexperimental descriptive studies, such as comparative, correlation, or case-controlled studies; or extrapolated from category I/II evidence); D, based on category IV evidence (from expert committee reports or opinions or clinical experience of respected authorities or extrapolated from category I/II/III evidence).

<sup>b</sup> Includes eye movement desensitization and reprocessing therapy, narrative therapy, interpersonal psychotherapy, psychodynamic psychotherapy, brief eclectic psychotherapy, and hypnotherapy.

<sup>c</sup> Includes antiadrenergic agents (prazosin, propranolol, clonidine, guanfacine), anticonvulsants, benzodiazepines, other serotonergic agents (cyproheptadine, buspirone), and atypical antipsychotics.

<sup>d</sup> Includes psychoanalytic psychotherapy, psychodynamic psychotherapy, interpersonal therapy, behavior therapy, brief dynamic therapy, emotion-focused therapy, and family-focused therapy.

<sup>e</sup> Includes lithium, thyroid hormones, and atypical antipsychotics.

<sup>f</sup> Includes electroconvulsive therapy, magnetic seizure therapy, transcranial magnetic stimulation, transcranial direct current stimulation, vagus nerve stimulation, direct cortical stimulation, and deep brain stimulation.

### Box 3.

#### Commonly Applied Early Psychosocial Interventions

##### Psychological First Aid

- **Definition:** A set of practical early interventions and principles administered by clinicians or nonclinicians to address emotional distress
- **Goals:** Stabilize psychological and behavioral functioning, facilitate psychological and behavioral adaptation, promote access to further care if indicated
- **Elements:** Establish contact, address basic needs, protect from further harm, listen and gather information related to mental health needs and psychosocial concerns, provide reassurance and education, respond to distress and psychological symptoms, assist with coping and problem solving, and connect with support systems and formal services.

##### Psychological Debriefing

- **Definition:** An intervention consisting of 1 or more individual or group sessions provided hours or days after a traumatic event
- **Goals:** Normalize survivors' reactions, process their trauma experiences, address psychological distress, enhance resilience
- **Elements:** Assist survivors in sharing their experiences and ventilating their emotional reactions, provide education about common reactions, encourage further intervention if appropriate

##### Crisis Counseling

- **Definition:** Poorly defined, brief strengths-based mental health intervention delivered by trained, experienced crisis workers and paraprofessionals
- **Goals:** Support survivors, enhance coping, connect with other services
- **Elements:** Conduct outreach in nontraditional community settings, provide public education, offer supportive individual and group counseling, conduct assessment and referral, link to resources and other services if needed

“Psychological first aid” is a popular term used to describe a set of practical early interventions and principles administered by clinicians or nonclinicians to address emotional distress. Psychological first aid is akin to physical first aid, with parallel goals: to stabilize psychological and behavioral functioning by meeting basic physical needs and then addressing psychological needs; to mitigate psychological distress and dysfunction; to facilitate return to adaptive psychological and behavioral functioning; and to promote access to further care. Psychological first aid should be embedded in public health, mental health, medical, and emergency response systems. It can be delivered in diverse settings including homes as well as shelters, medical-triage areas, disaster-assistance centers, family-reception and assistance centers, workplaces, schools, and other community settings. The elements of psychological first aid are establishing contact through a calm, comforting, and compassionate presence; meeting basic physical needs and protecting individuals from further harm; listening and information-gathering; fostering articulation of

survivors' needs and concerns; meeting basic psychological needs; delivering accurate and timely information about disaster operations and available resources; providing social support and coping assistance; and facilitating connections to social-support networks and referrals for ongoing care. Several available psychological first aid toolkits provide a common set of basic principles and techniques. Psychological first aid was developed from expert consensus but has not been empirically tested.

“Psychological debriefing” consists of 1 or more individual or group sessions provided hours or days after a traumatic event. Its main elements are emotional ventilation, trauma processing, and psychoeducation. This intervention garnered considerable popularity internationally, without empirical evidence of its effectiveness. A review of 11 randomized controlled trials of single-session debriefing for individuals subsequently found the intervention to be ineffective for PTSD prevention or treatment. Two longer-term follow-up studies covered in this review documented significantly worse posttraumatic symptom outcomes in individuals who received debriefing—by as much as a factor of 3, but only in those at most risk for PTSD. Psychological debriefing was not intended to prevent or treat PTSD or as a treatment or stand-alone intervention; rather, it was designed to provide opportunities for processing the trauma, facilitating normal recovery, providing education, and linking with resources. Those at risk for PTSD or other psychopathology may worsen with debriefing, and these individuals should be identified and referred for psychiatric services instead.

“Crisis counseling” is a poorly defined, brief mental health intervention delivered by trained, experienced crisis workers and paraprofessionals in acute disaster settings, especially in the context of the federally funded Crisis Counseling Assistance and Training Program. This strengths-based program reaches out to provide support to individuals in nontraditional community settings such as shelters, faith-based organizations, and homes. Crisis counseling shares many fundamental elements with psychological first aid. It can be delivered to individuals or groups to help survivors understand their reactions, enhance coping, consider options, and connect with other services. Norris and Rosen have cautioned that although crisis counseling can be broadly helpful for postdisaster distress, it is not sufficient for the needs of some individuals who will require formal treatment for psychiatric illness emerging after disasters.

The early psychosocial interventions described above are not considered formal treatment for psychiatric disorders, although they may sometimes be appropriate interventions in addition to treatment or before treatment can be initiated. Treatment of psychiatric disorders and other psychological conditions is provided by mental health professionals. This treatment typically occurs in traditional office or clinic settings for patients referred for these services, particularly as time evolves and psychiatric problems have had time to develop and be identified. In early postdisaster phases, however, formal psychiatric treatment may be provided in the disaster setting, ideally integrated into the disaster medical response. For example, a mental health clinic was embedded in a medical unit in a large hurricane evacuation shelter that housed 2500 evacuees in Dallas, Texas, for 2 weeks, allowing integrated psychiatric, psychological, and medical care. This arrangement provided psychiatric care to 421 individuals in 503 separate contacts by 152 psychiatric professionals including 72 psychiatrists; another approximately 500 individuals received some undocumented form of mental health contact. Severe and persistent mental illness represented 28% of the psychiatric problems treated. The 40% rates of preexisting psychopathology presenting for treatment eclipsed the rates of 11% with acute stress disorder and 24% with any posttraumatic stress-related problems identified. After the September 11 World Trade Center attacks, 268 psychiatrist volunteers who were colocated with other disaster responders at a family assistance center evaluated 848 distressed individuals, most of whom (14%-38%) were assessed as having stress-related and adjustment disorders; however, bereavement, major depression, and substance use disorders were also observed in 1% to 12%. Although psychiatric diagnoses could not be confirmed in the crisis setting, most of the assessed individuals were perceived to have a psychiatric diagnosis, and a substantial proportion received psychotropic medication. A follow-up evaluation as part of this project concluded that

psychiatrists have unique and specific roles in the early postdisaster setting. Placement of mental health services in disaster recovery areas may help address the surge of mental health needs among evacuee populations in the face of already overcrowded emergency departments and overburdened mental health care systems.

Pharmacotherapy and psychotherapy are the standard treatments for psychiatric disorders related to trauma in general and to disasters specifically. Usual clinical practice for management of trauma-related disorders and symptoms is generally appropriate. A timeline for addressing mental health problems arising after disasters is provided in the Figure. In early postdisaster phases, sedating medications may be provided transiently for sleep and anxiety symptoms, and medication refills may be provided to prevent interruption of ongoing treatment for preexisting psychiatric disorders. After passage of sufficient time for diagnosis of incident trauma-related disorders, psychopharmacotherapy may be initiated for disorders including PTSD and major depression in clinical settings. Psychotherapy also may be provided for disaster-related psychiatric disorders. The most commonly recommended psychotherapies in the trauma treatment literature include trauma-focused cognitive-behavioral therapies and exposure-based therapies. Cognitive-behavioral therapies help patients learn to identify and correct unrealistic negative thoughts and perceptions that contribute to unpleasant emotions and maladaptive behaviors, including those related to trauma. Exposure-based therapies introduce individuals to memories and reminders of their traumatic experiences to help them modify their emotional reactions.

A substantial literature is devoted to describing and testing the effectiveness of interventions including psychotherapies and pharmacotherapy for PTSD, but the strongest evidence (eg, randomized controlled trials) for these modalities has emerged from studies of populations with other types of trauma, such as that resulting from motor-vehicle crashes in nondisaster settings. Table 2 describes empirical evidence for mental health interventions in general trauma care and in disaster response situations for conditions relevant to disaster exposure. Considerable evidence has been gained for cognitive-behavioral and exposure-based therapies in disaster-affected populations. However, little or no empirical evidence of benefit for many mental health interventions commonly used in disaster settings is available.

## **DISCUSSION**

The primary purpose of this review is to organize the disaster mental health literature into an operational framework for the delivery of mental health services to individuals affected by disasters. The 3 components of case identification, triage, and intervention are consistent with established approaches to emergency and medical response to mass casualty incidents and may therefore facilitate integration of mental health services into the medical disaster response. Principles of triage to appropriate interventions for psychiatric illness and other psychosocial issues are established. A number of trauma-focused psychiatric treatments have been developed and tested in other populations (including randomized controlled trials) and successfully applied to disaster-exposed groups. Thus, this literature includes the ingredients to inform policies and planning for disaster mental health, but it has not previously been organized into a framework to logically guide the response from case identification to triage to intervention.

Despite the availability of these ingredients for disaster mental health response, few articles in this literature search underscored the need to start with assessments that include psychiatric diagnosis; instead, most articles proceed with recommending various strategies and interventions without emphasizing this fundamental foundation. Most of the literature has focused on providing interventions for distress with a wellness-based focus, neglecting to include care plans for people with psychiatric disorders. Provision of services without assessment of psychiatric illness creates potential for failure to treat psychiatric disorders as well as potential for doing harm, such as was found with the extensive history of use of debriefing indiscriminant to psychopathology. Traditionally, federally funded programs such as the Crisis Counseling Assistance and Training

Program have provided primarily low-intensity services aimed at psychological distress and have not sufficiently addressed psychiatric disorders arising after disasters. Communities facing disasters in the future will be challenged to provide assessment-directed referral and formal treatment for individuals who need more than the federally funded crisis counseling services. Survivors requiring formal treatment usually represent a minority of those affected, but their suffering compels the most sincere consideration of those responsible for disaster response. Conversely, treatments for psychiatric illness are not necessarily appropriate for psychological distress, and because the majority of disaster survivors do not develop a psychiatric illness, targeting psychiatric treatment services for psychiatric disorders and directing other less intensive interventions for distress is cost effective, conserves scarce resources in disaster settings, and avoids the potential harm of unneeded treatments. This point highlights the importance of conducting well-designed disaster mental health needs assessments, because, for example, failure to differentiate PTSD from distress in unexposed populations who have been affected by disasters with massive scope and magnitude such as the September 11 attacks has the potential to overestimate need for psychiatric services and related costs by magnitudes as high as 10.

The limitations of this review reflect the current state of the research and the literature on disaster mental health response. Recent reviews of the observational research that comprises much of the general disaster emergency and medical response literature have characterized this literature as having a limited evidence base and lacking methodological rigor. Scientific investigation of disaster and emergency response is inherently difficult to conduct in the characteristically chaotic and pressured settings of community catastrophes. This review addresses the mental health response for the community as a whole and does not specifically address the needs or interventions for rescue personnel (such as emergency medical services, police, fire, or other first responders) or personnel involved with care of patients in disasters (such as emergency and surgical staff), who may have intense disaster-related exposures of a different character. This review of mental health response to disaster trauma exposure was further informed by numerous rigorously conducted studies of interventions in populations exposed to other types of trauma and a large body of less rigorous disaster-oriented articles.

In conclusion, the extant literature has identified the importance of integrating these interventions and services in public health and clinical systems of care. Compelling issues that must be addressed in improving disaster mental health response capacities focus on matching interventions and services to specified mental health outcomes (eg, psychiatric illness vs disaster-related distress) for exposed and unexposed groups, encouraging the use and integration of appropriate assessment and referral, and evaluating the effectiveness of the interventions and services offered. The model and flow diagram in this article provide a framework for this work and place proper emphasis on the role of accurate assessment in all disaster response proceeding through triage and treatment.

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## **Management of Acute Stress, PTSD, and Bereavement WHO Recommendations**

Journal of the American Medical Association  
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7 August 2013

In 2010, the World Health Organization (WHO) launched the Mental Health Gap Action Program (mhGAP) Intervention Guide for nonspecialized health settings (ie, for general health staff in first- and second-level health facilities, including primary care and district hospital settings) to address

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the wide treatment gap for mental disorders in low- and middle-income countries. Several priority mental disorders, including depression and substance use, have been addressed in previous mhGAP modules and related guidelines.

To inform development of a new module on conditions specifically related to stress, WHO developed new guidelines to be released this week for the following symptoms occurring in the first month after trauma exposure: acute traumatic stress symptoms, insomnia, enuresis, dissociative symptoms, and hyperventilation (Table). In addition, guidelines were developed for posttraumatic stress disorder (PTSD) and bereavement. These conditions were chosen for their relevance in nonspecialized health settings. This Viewpoint describes work underpinning the expansion of the mhGAP Intervention Guide to include a module on assessment and management of conditions specifically related to stress—using terminology for conditions consistent with proposals for the *International Classification of Diseases*, 11th revision.

Table. New World Health Organization mhGAP Recommendations

Table. New World Health Organization mhGAP Recommendations<sup>a</sup>

Mental Health Condition	Recommendation	Strength of Recommendation <sup>a</sup>	
Acute stress (first month after exposure to a potentially traumatic event)	Acute traumatic stress symptoms	Cognitive behavioral therapy with a trauma focus should be considered in adults	Standard
		Benzodiazepines should not be offered to adults	Strong
		Antidepressants should not be offered to adults	Standard
		Benzodiazepines and antidepressants should not be offered to children and adolescents	Strong
Secondary acute insomnia		Relaxation techniques and advice about sleep hygiene should be considered for adults	Standard
		Benzodiazepines should not be offered to adults	Standard
		Benzodiazepines should not be offered to children and adolescents	Strong
Secondary nonorganic enuresis		Education about the negative effects of punitive responses should be given to caregivers of children	Strong
		Parenting skills training and the use of simple behavioral interventions should be considered. Where resources permit, alarms should be considered	Standard
Hyperventilation		Rebreathing into a paper bag should not be considered for children	Standard
Posttraumatic stress disorder		Individual or group cognitive behavioral therapy with a trauma focus, eye movement desensitization and reprocessing, or stress management should be considered for adults	Standard
		Individual or group cognitive behavioral therapy with a trauma focus or eye movement desensitization and reprocessing should be considered for children and adolescents	Standard
		SSRIs and tricyclic antidepressants should not be offered as the first line of treatment in adults. SSRIs and tricyclic antidepressants should be considered if (a) stress management, cognitive behavioral therapy with a trauma focus, and/or eye movement desensitization and reprocessing have failed or are not available or (b) if there is concurrent moderate-severe depression	Standard
		Antidepressants should not be used in children and adolescents	Strong
Bereavement		Structured psychological interventions should not be offered universally to bereaved children, adolescents, and adults who do not meet criteria for a mental disorder	Strong
		Benzodiazepines should not be offered to bereaved children, adolescents, and adults who do not meet criteria for a mental disorder	Strong

Abbreviation: SSRI, selective serotonin reuptake inhibitors.

all circumstances. Standard indicates that there may be circumstances in which the recommendation does not apply.

<sup>a</sup> Strong indicates that the recommendation should be followed in all or almost

means nothing should be done. In these cases, potential courses of action such as referring to existing guidelines were included. For example, for acute stress symptoms a previous WHO GDG had recommended psychological first aid, rather than psychological debriefing.<sup>3</sup>

Prior to the development of these mhGAP recommendations, there were no evidence-based guidelines for managing conditions specifically related to stress in nonspecialized settings in low- and

middle-income countries. The recommendations form the basis of a new module to be added to the mhGAP Intervention Guide.<sup>9</sup>

Future research should collect data on a broader range of outcomes, including functionality, adverse effects, and long-term outcomes. Meanwhile, practitioners are offered these evidence-based guidelines to strengthen care for people exposed to extreme stress.

Guidelines were developed following WHO's rigorous guideline development methodology. A guideline development group (GDG) was responsible for making recommendations based on systematic appraisal of evidence. Details on the conditions, interventions, and the development of evidence profiles for each question (ie, evidence retrieval, synthesis, and interpretation) can be found in the guidelines.

Acute traumatic stress symptoms include reexperiencing, avoidance, and hyperarousal associated with significant functional impairment that present in the first month after trauma exposure. These symptoms may be similar to those of PTSD, but occur before PTSD is often assessed. For these symptoms, the guidelines recommend against the use of benzodiazepines and antidepressants in adults, adolescents, and children. The

guidelines recommend cognitive behavioral therapy with a trauma focus (CBT-T) for adults. Similarly for insomnia, the guidelines recommend against the use of benzodiazepines for adults, adolescents, and children and recommend relaxation techniques and sleep hygiene for adults. For bedwetting in children and adolescents the following is recommended: parenting skills training, simple behavioral interventions, and education of caregivers about the negative effects of punitive responses. No recommendations could be made based on available evidence with regard to psychological interventions for acute traumatic stress symptoms and insomnia in children and adolescents or for dissociative symptoms and hyperventilation in children, adolescents, and adults during the first month after exposure to the event. However, the guidelines recommend against the common practice of rebreathing in a paper bag for hyperventilation in children.

For adults, adolescents, and children with PTSD, recommended treatments include individual or group CBT-T, eye movement desensitization reprocessing (EMDR) and, in adults, stress management (eg, stress inoculation training and relaxation training). Stress management was determined to be less effective than CBT-T and EMDR but was rated high on feasibility, which is important for scaling up interventions in low-resource settings. Consistent with the UK's National Institute for Health and Care Excellence (NICE) recommendations, but in contrast to American Psychiatric Association guidelines, antidepressants were not recommended as a first-line treatment for adults because of the small effect size of these drugs for the treatment of PTSD. The guidelines recommend antidepressants for adults with PTSD when psychological treatments are not available or have not been effective or when people have concurrent moderate to severe depression. The guidelines recommend against the use of antidepressants for PTSD in children and adolescents.

For bereaved adults, adolescents, and children without a mental disorder, the guidelines recommend against use of benzodiazepines and the routine use of structured psychological interventions. The latter recommendation is in contrast to the routinely offered grief counseling after bereavement.

Several key issues were discussed by the GDG. First, the recommendations should be applicable in low- and middle-income countries and nonspecialized health settings, but most evidence comes from specialized settings in high-income countries. Research on task sharing in low- and middle-income countries has shown that with training and supervision, nonspecialized health care staff can effectively implement advanced psychological interventions. Nevertheless, there is uncertainty about the likelihood of health care workers achieving similar treatment effects in routine health care in the absence of strict fidelity and supervision protocols that are common in research settings. The GDG particularly emphasized the importance of sufficient health care worker time and appropriate supervision for CBT-T and EMDR and recognized this requires human resources. Second, for many interventions low-quality evidence was found, especially for children and adolescents. Third, outcome measurement has been too often limited to symptoms, whereas measurement of functionality, adverse effects, and long-term outcomes has been relatively rare, especially for nonpharmacological interventions. Last, the GDG was wary of suggesting that the absence of evidence means nothing should be done. In these cases, potential courses of action such as referring to existing guidelines were included. For example, for acute stress symptoms a previous WHO GDG had recommended psychological first aid, rather than psychological debriefing.

Prior to the development of these mhGAP recommendations, there were no evidence-based guidelines for managing conditions specifically related to stress in nonspecialized settings in low- and middle-income countries. The recommendations form the basis of a new module to be added to the mhGAP Intervention Guide.

Future research should collect data on a broader range of outcomes, including functionality, adverse effects, and long-term outcomes. Meanwhile, practitioners are offered these evidence-based guidelines to strengthen care for people exposed to extreme stress.

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## The Role and Importance of the ‘D’ in PTSD

RAND Corporation  
Michael P. Fisher and Terry L. Schell  
21 August 2013

### Key Issues

- After considering the matter, the APA opted not to change the name of posttraumatic stress disorder (PTSD) despite a request by senior U.S. Army leadership.
- The Army’s reasoning was that the term “disorder” is stigmatizing, and that removing or replacing it—for example, with the term “injury”—would encourage more U.S. military service members suffering from symptoms to access care.
- Some individuals within military communities are already using the term “posttraumatic stress” (PTS) informally, although the impact of this use—on mental health stigma or otherwise—is unclear.
- Few studies specifically demonstrate stigmatization among U.S. military service members with PTSD, and no known studies have shown that PTSD-related social stigmas reduce the utilization of treatment.
- Psychiatric diagnoses are used within institutions such as the U.S. military in ways that may adversely affect how a diagnosed individual is treated—for example, when determining eligibility for security clearances or fitness for deployment.
- Without changing the broader institutional factors that result in discrimination against those with the PTSD label, modifying that label seems unlikely to result in a significant increase in individuals willing to be diagnosed or treated.

In December 2012, the American Psychiatric Association (APA) board of trustees voted on changes to the new edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM). Among the decisions was one to retain the word “disorder” in the term “posttraumatic stress disorder” (PTSD). U.S. Army leadership initially requested the change in terminology, stating that the word “disorder” is stigmatizing and that removing it would encourage more individuals suffering from symptoms to access care. Although the APA has issued its ruling, the term “posttraumatic stress” (PTS) is being used informally by some individuals within military communities. It is unclear whether informal use of the term will continue, or whether military leaders will continue to advocate future changes to the DSM. Our intent is to further the discussion regarding the removal or revision of the term “disorder.” We explore the rationales for not changing the diagnostic terminology, and to the extent possible, anticipate what the effects of widespread informal use of new terminology might be.

Post-traumatic stress disorder (PTSD) among U.S. military service members has emerged as an important policy issue. Prevalence estimates of PTSD among those returning from service in Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn

range from 5 to 20 percent, although the most representative studies find the prevalence of PTSD to be 10 to 14 percent among all of those previously deployed (Ramchand, Schell, et al., 2010).

In response to high rates of PTSD among deployed U.S. military service members, a myriad of programs and initiatives to address PTSD and other psychological health issues have been developed by practitioners, health services professionals, and researchers. The Department of Defense (DoD) alone sponsors or funds more than 200 programs that address psychological health or traumatic brain injury (TBI) across the prevention, identification, and treatment continuum (Weinick, Beckjord, et al., 2011).

Nearly half of these programs have some component that specifically addresses PTSD among military service members. DoD also provides care for PTSD through its military treatment facilities and its health care program, TRICARE. The Department of Veterans Affairs (VA), likewise, maintains a network of Veterans Affairs medical centers and community-based outpatient clinics, of which 96 percent and 75 percent, respectively, provide specialized PTSD services (Watkins and Pincus, 2011). With the APA deliberating on the content of its fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM), senior U.S. Army leadership seized its chance to seek changes to the labeling of PTSD (Sagalyn, 2011a; Sagalyn, 2011b; Jaffe, 2012). The initial request was sent by then-Army Vice Chief of Staff General Peter Chiarelli to the APA's president at that time, Dr. John Oldham. It called for dropping the term "disorder" from the diagnostic label. The request represented what appears to be a more widespread concern within military communities—as well as for some who advocate on behalf of or provide treatment to traumatized or victimized individuals—that the term "disorder" is stigmatizing and that removing it would encourage more individuals suffering from symptoms to access care (PTS Injury endorsements web page, 2012; Sagalyn, 2011a; Sagalyn, 2011b; Jaffe, 2012).

In December 2011, the APA stated that it was open to discussion and would consider modifications to the DSM-5 terminology with this concern in mind (Sagalyn, 2011b; Jaffe, 2012). Specifically, the president of the APA indicated the possibility of adding a diagnostic subcategory of PTSD such as "combat posttraumatic injury," or changing the name of the diagnosis to "posttraumatic stress injury." In May 2012, the APA convened a panel discussion that focused on the topic. In late 2012, however, the APA's board of trustees eventually decided not to alter the term, omitting it from the proposed changes to DSM-5. Yet, while the APA's board of trustees deliberated changing the diagnostic terminology, military leaders and others increasingly used their own language to refer to PTSD. The term "posttraumatic stress" (PTS) is now being used by some individuals to refer to a range of posttraumatic stress responses, both those that meet the clinical threshold for PTSD and those that do not.

Although the APA's board of trustees decided not to alter diagnostic terminology, informal use of the term "posttraumatic stress" may continue, and the possibility of a future change remains, as military leaders may continue to press their case. In this paper, we review the historical, sociological, and clinical literature on the diagnosis of psychiatric disorders with a focus on PTSD. We restrict our attention in large part to peer-reviewed journal articles and books. In our effort to explore the effects of a change in terminology, we first provide an overview of the DSM and the functions it serves, followed by a brief history of PTSD. We then highlight the intended functions of the PTSD diagnosis, which include interpreting, categorizing, and measuring the condition, as well as facilitating treatment, treatment financing, and disability compensation. We also address other, possibly unintended, consequences of the PTSD diagnosis across a wide range of organizations and institutions and in the broader culture. These include legitimization of the condition, stigmatization of those with the condition, and discrimination against those with the condition. We conclude by summarizing the key points discussed in this paper and by offering our perspective, informed by the literature, on the possible implications of removing or replacing the term "disorder" in PTSD.

An Overview of the DSM and Psychiatric Classification

August 2013

The APA-published DSM details the diagnostic criteria for the full range of recognized mental disorders. The first edition was published in 1952, and several new editions and revisions have since been released, including the fifth edition published in 2013. In the current published edition, a mental disorder is defined as “a syndrome characterized by clinically significant disturbance in an individual’s cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental processes underlying mental functioning” and is “usually associated with significant distress or disability in social, occupational, or other important activities” (APA, 2013). An “expectable or culturally approved response to a common stressor or loss, such as the death of a loved one” would not be considered a mental disorder, nor would “socially deviant behavior (e.g., political, religious, or sexual) and conflicts that are primarily between the individual and society . . . unless the deviance or conflict results from a dysfunction in the individual, as described above” (APA, 2013).

A number of criteria are applied to a condition to ensure that it is appropriate for classification as a disorder in the DSM. These include a condition’s clinical utility, reliability, descriptive validity, and psychometric performance characteristics (APA, 2013; APA, 2000; see also Robins and Guze, 1970). While these systematic principles are applied when considering whether to include a condition in the DSM, the process is not considered infallible, nor is the manual meant to represent the full range of possible conditions for which an individual may be treated (APA, 2013). Instead, the material contained within the DSM is considered to be a consensus of the evolving knowledge in the field. Disorders are used in the DSM to signify psychiatric diagnoses, generally. However, not all diagnostic categories within the DSM explicitly contain the term “disorder” in their titles. For example, “major depressive disorder” contains the term, while disorders such as schizophrenia do not.

Psychiatric diagnoses defined by the DSM are intended to serve several functions pertaining to treatment, research, and education. These include guiding clinical practice (e.g., classifying individuals into groups that might usefully direct their treatment), facilitating research and improving communication among clinicians and researchers, improving the collection of clinical information and communication of public health statistics, and providing a tool for teaching psychopathology (APA, 2013). As noted in the DSM-5’s “cautionary statement for forensic use,” the classification system is designed to meet the needs of the mental health treatment, research, and educational communities, and therefore the classifications may not be useful for other purposes. Notably, they do not correspond to legal categories related to culpability or dangerousness, nor are they designed to provide information about the capabilities of individuals performing specific tasks, including work-related tasks.

The World Health Organization (WHO) has developed international classification standards to categorize and code various types of disease, disorder, or injury. These standards include the International Classification of Disease (ICD), 2 the International Classification of Functioning, Disability and Health (ICF), and the International Classification of External Causes of Injury (ICECI). WHO has also developed “derived classifications,” which are based on information in the ICD and ICF that has been augmented, rearranged, or aggregated (WHO, 2012a). Derived classifications include the ICD-10 for Mental and Behavioral Disorders Clinical Descriptions and Diagnostic Guidelines and the ICD-10 for Mental and Behavioral Disorders Diagnostic Criteria for Research (Centers for Medicare and Medicaid Services, 2012). WHO’s classification standards were developed in conjunction, and are closely aligned, with the DSM’s categories for classifying mental disorders (APA, 2013). These standards serve as the official coding system for psychiatric disorders and diseases in the United States and several other countries. Diagnostic codes label disorders and diseases alphanumerically and are used for a wide range of epidemiological, health management, and clinical purposes. These include monitoring the incidence and prevalence of disease, analyzing the health situations of populations, classifying disease on health and vital records, and, in many instances, determining financial reimbursement for treatment (WHO, 2012b; WHO, 2010).

WHO’s classification manuals also offer definitions of terms such as “disorder” and “injury.” WHO echoes the APA in defining a mental disorder as “the existence of a clinically recognizable set of symptoms or behavior associated in most cases with distress and with interference with personal

functions,” while specifying that “social deviance or conflict alone, without personal dysfunction, should not be included in mental disorder as defined here” (WHO, 1992). WHO defines an injury as “a (suspected) bodily lesion resulting from acute overexposure to energy (this can be mechanical, thermal, electrical, chemical or radiant) interacting with the body in amounts or rates that exceed the threshold of physiological tolerance” (WHO, 2004). According to the sum of the definitions of “mental disorder” offered by the APA and WHO and the definition of “injury” offered by WHO, disorders and injuries may involve a behavioral, psychological, or biological reaction, but the term “injury” is reserved for those instances when an external physical force is the direct cause of the reaction.

### A Brief History of PTSD

Many societies have recognized, through the use of various labels, that some individuals show a range of problems after exposure to traumatic events—including, but not limited to, trauma encountered during war. Terms used in the United States prior to “PTSD” include “soldier’s heart” during the Civil War era, “railway spine” during the late 19th century, “shell shock” and “war neuroses” during the World War I era, and “combat fatigue” during the World War II era. A set of problematic symptoms, labeled “gross stress reaction,” was recognized in the first edition of the DSM published in 1952 but was absent from the second, the DSM-II, published in 1968. As American service members returned from Vietnam, they exhibited problems stemming from exposure to traumatic events, which were recognized informally as “post-Vietnam syndrome” (Scott, 1990, 2004; Young, 1995; Dean, 1997; Shepard, 2001; Finley, 2011). In 1980, the APA incorporated the PTSD diagnosis into the DSM-III to classify responses to traumatic events that met a defined set of criteria (APA, 1980).

Formal recognition of PTSD resulted in part from years of advocacy and collaboration among psychiatrists and several groups representing victimized or traumatized individuals, including groups representing Vietnam veterans (Scott, 1990; Scott, 2004). In 1977, as plans were under way to revise and release the DSM-III, a group of mental health professionals who studied the psychological impacts of war trauma collaborated with veterans’ advocates to form the Vietnam Veterans Working Group. The group mobilized the support of psychiatrists researching the psychological impacts of war and other types of trauma (Bloom, 2000), and proposed adding the diagnostic categories that would soon be labeled PTSD to the APA’s Committee on Reactive Disorders, the collective body tasked with reporting to the DSM-III task force on issues of posttraumatic stress.

When the diagnostic entry was first proposed, the working group labeled it “catastrophic stress disorder” and suggested that a subcategory termed “post-combat stress reaction” accompany the diagnosis (Shatan, Smith, and Haley, 1976; see also Scott, 1990; Scott, 2004). The Committee on Reactive Disorders supported the recommendation with two change diagnostic label was to be “posttraumatic stress disorder.” Second, the combat-specific subcategory would not be present, since there was little evidence that trauma from combat produces a significantly different set of clinical symptoms or impairments than severe noncombat trauma, such as rape or assault.<sup>3</sup> Therefore, the newly formed PTSD diagnosis made no distinction between trauma experienced in combat and trauma experienced in other situations, such as personal assaults or natural disasters.

PTSD was added to the DSM-III in part to recognize the suffering of traumatized individuals, including Vietnam veterans, and to provide a channel for obtaining treatment (Scott, 1990, 2004; Young, 1995; Finley, 2011). At the same time that the APA was codifying the PTSD diagnosis, Congress was also recognizing the mental health needs of Vietnam veterans. In 1979, President Jimmy Carter signed Public Law 96-22, which established Vet Centers to provide “readjustment” counseling to Vietnam veterans (Young, 1995; Shepard, 2001; Scott, 2004). Although not created to address PTSD explicitly, these community-based Vet Centers offered counseling for a range of mental health issues, including the set

of symptoms that was being labeled as PTSD in the DSM-III. The PTSD diagnosis also expanded treatment options for diagnosed individuals beyond Vet Centers, facilitating greater access to mental health treatment in other VA facilities and in private health systems.

The formal recognition of PTSD was also an attempt to distinguish the phenomenon from existing mental disorders (e.g., depression) that share several symptoms, but which typically have a different etiology and time-course, and to recognize this set of symptoms as a condition to be treated, rather than as cowardice or malingering (Scott, 1990; Scott, 2004; see also Jutel, 2009; Mezey and Robbins, 2001). As with all other DSM disorders, PTSD is used to differentiate normal functioning from a type of impaired functioning that might benefit from treatment that may be available. For instance, while many of the symptoms of PTSD may be considered normal or healthy during, or shortly after, a traumatic event, the PTSD diagnosis specifies that the symptoms must be present beyond one month a traumatic event. More specifically, PTSD is defined by the persistence of these symptoms after the source of traumatic stress is gone and by the failure of the impairing symptoms to spontaneously resolve themselves. Since its incorporation in the DSMIII, the PTSD diagnosis was changed slightly in the subsequent editions of the manual, the DSM-IV and DSM-IV-TR. Notably, the original PTSD diagnosis did not require that individuals respond to a traumatic event with fear, helplessness, or horror; this criterion was added to the DSM-IV.

When the APA published the DSM-IV in 1994, it included a new diagnostic category termed Acute Stress Disorder (ASD) to categorize individuals suffering from problems stemming from exposure to a traumatic event for more than two days but less than four weeks after the event (APA, 1994). A primary function of defining ASD was to facilitate the early identification of individuals who would be unlikely to recover spontaneously after traumatic events (Cahill and Pontoski, 2005). It was hoped that this classification would lead to earlier treatment for those who suffered significant impairment and were at high risk developing PTSD (Cahill and Pontoski, 2005). The criteria for ASD are similar to those for PTSD but feature one fundamental difference: ASD is diagnosed within the first month following a traumatic event.

The DSM-5, released in May 2013, includes several changes to the PTSD and ASD diagnostic criteria.

- The changes to the PTSD criteria include removal of the requirement that an individual respond to the traumatic event with fear, helplessness, or horror; more explicit requirements about how an individual must have experienced a traumatic event; the separation of the avoidance and numbing “cluster,” or set of similar symptoms, into two clusters (avoidance and negative alterations in cognitions and mood); the addition of two symptoms (persistent and distorted blame of self or others and persistent negative emotional state) to the negative alterations in cognitions and mood cluster; the addition of one symptom (reckless or destructive behavior) to the alterations in arousal and reactivity cluster; the revision of various symptoms to clarify symptom expression; and the addition of preschool and dissociative “subtypes,” or homogeneous subclassifications of the disorder which may have different etiologies (APA, 2013).
- The changes to the ASD criteria include removal of the requirement that an individual respond to the traumatic event with fear, helplessness, or horror; and the collapsing of several symptoms into a single cluster, which encompasses five types of symptoms: intrusion, negative mood, dissociation, avoidance, and arousal (APA, 2012). The newly expanded cluster describes a more varied acute stress response that does not require the presence of dissociative symptoms, as did the previous edition of the DSM.

The Intended Functions of the PTSD Diagnosis

The diagnosis of a mental health condition such as PTSD serves several purposes intended by the mental health treatment, research, and educational communities. These include interpreting, categorizing, and measuring the condition as well as facilitating treatment, treatment

financing, and disability compensation for the condition. We discuss each of these topics below. In later sections, we explore other, possibly unintended, consequences of classifying disorders in an effort to identify the full range of \ implications of the PTSD diagnosis.

#### Interpreting, Categorizing, and Measuring the Condition

The disorder classification system of the DSM provides a common language for use by the mental health treatment, research, and educational communities and has been widely adopted as the defining nomenclature in the field. This common language facilitates communication between clinicians and researchers, clinicians who collaborate to care for patients, clinicians and the organizations that pay for treatment, and clinicians and their patients (APA, 2013). The DSM categories also prompt the development of standardized tools such as diagnostic questionnaires and psychometric devices. Further, diagnostic categories, which are a product of research evidence supporting their inclusion in the DSM, spur the further development and distinct boundaries of a research base and allow for stable comparisons of sets of symptoms or behaviors over time and across populations. These interrelated activities have not occurred historically in examining problems stemming from exposure to traumatic events (Young, 1995; Dean, 1997).

#### Facilitating Treatment, Treatment Financing, and Disability Compensation

Another function of diagnosis is to facilitate treatment of the diagnosed condition so as to minimize impairment and suffering (Mezey and Robbins, 2001; Dumit, 2006; Jutel, 2009; Jutel, 2011). Identifying a set of symptoms or behaviors as a disorder effectively communicates that it is unhealthy (i.e., distressing, functionally impairing, or associated with a significant increase in suffering) and that individuals who exhibit those symptoms or behaviors may benefit from evaluation and treatment. A diagnosis often communicates to clinicians, insurance companies, and health systems that individuals with those symptoms may be eligible to have their financial obligations for treatment covered (contingent upon other factors such as whether the treatment is medically necessary) (Dumit, 2006; Jutel, 2009). Moreover, a diagnosis communicates to patients that a sometimes diverse and seemingly unrelated set of symptoms (e.g., emotional numbing and exaggerated startle response) may be linked and that treatment may be available to minimize those unpleasant symptoms or mitigate their impact.

Prior to the inclusion of PTSD in the DSM-III, war veterans encountered substantial difficulty obtaining treatment for problems stemming from exposure to traumatic events. Gross stress reaction, listed in the first edition of the DSM, did not capture delayed or chronic conditions (Scott, 2004), and, as stated above, the diagnosis was not included in the DSM-II. Not surprisingly, mental health clinicians in the VA during the 1970s noted a “lack of fit” between veterans’ symptoms and the diagnoses in the DSM-II, and in this respect, the DSM-II functioned as a substantial barrier to mental health treatment for Vietnam-era veterans (Scott, 2004; see also Shepard, 2001).

Formally identifying a set of symptoms or behaviors as a disorder also plays a critical role in facilitating appropriate, high-quality treatment. A diagnosis both justifies and facilitates research into new treatments. As these treatments are developed and determined to be effective, they can be applied to other individuals with the same disorder. Eventually, this research base allows for practice guidelines that ensure the wider dissemination of effective treatments. For example, defining PTSD as a disorder that can exist across both combat and non-combat trauma has facilitated the application of therapies that were originally developed for rape victims to combat veterans (Foa, 1991).

Finally, classifying PTSD as a disorder has facilitated the receipt of benefits designed to offset the financial impact of disabilities associated with the disorder. Across both the VA and Social Security Administration, disability benefits are often available with an appropriate diagnosis in conjunction with a demonstration of specific impairments related to the diagnosed disorder. For example, a PTSD diagnosis permits certain

veterans to receive disability compensation from the VA. Section 38 4.130 of the Code of Federal Regulations designates codes for mental disorders, including PTSD, and outlines the formula for rating disability resulting from a mental disorder. The formula assigns scores of 0, 10, 30, 50, 70, or 100. A rating of 0 signifies that a mental disorder has been diagnosed but that symptoms do not interfere with social or occupational functioning. A rating of 100 signifies that an individual suffers from total social or occupational impairment (U.S. Government Printing Office, 2010).<sup>4</sup> Depending on the rating, an individual may be eligible for cash benefits and greater access to VA health services.

### The Broader Impacts of the PTSD Diagnosis

The diagnostic categories that have been crafted to meet the needs of the psychiatric profession are also used within a wide range of other organizations or institutions for their own purposes. Use of these diagnoses within organizations or institutions outside the psychiatric community may have implications for how society perceives or responds to disorders such as PTSD. In particular, such broad and varied use of a diagnosis may lead to legitimization of the condition, stigmatization of those with the condition, and discrimination against those with the condition. We address each of these topics below to explore the full range of implications of the PTSD diagnosis.

#### Legitimization of the Condition

A diagnostic classification generated by the medical profession can affect how society views those with the condition as well as how those with the condition view themselves. A diagnosis may result in increased recognition and acceptance of the underlying phenomenon by diagnosed or symptomatic individuals, as well as by society in general (Jutel, 2009). It may also render pain and suffering more visible and give sufferers the tools to explain what makes them different from “healthy” individuals (Parsons, 1951; Jutel, 2009). With this, sufferers are able to make socially “legitimate” illness claims and attain recognition of their suffering (Dumit, 2006; Jutel, 2009). Legitimization of a condition can lead to a wide range of social benefits—including, but not limited to, increased access to medical treatment. Legitimization may enable sufferers to avoid blame for their ailments (Jutel, 2009) and exempt them from their everyday roles in society (Freidson, 1970; Jutel, 2009). For example, it may alter others’ expectations of the diagnosed individual at work or in family life. For these reasons, the nonmedical characteristics of a diagnosis—for example, the label itself and the perceptions that it engenders—may be of substantial concern to those diagnosed. When a condition is not formally recognized with a diagnostic classification, sufferers of that condition may engage in the process of scientific discovery or diagnostic formation (e.g., Crossley, 2006; Brown and Zavestoski, 2004; Brown, 1995) in an attempt to gain recognition for their suffering in a way that is acceptable and useful to them. To a certain extent, this is what occurred in the case of PTSD’s incorporation in the DSM-III; as previously noted, Vietnam veterans, as well as individuals representing other traumatized groups, played a role in the process of diagnostic formation (Scott, 1990; Scott, 2004).

The 2012 proposal to change the PTSD diagnostic label was voiced by senior U.S. Army leadership, and a number of individuals both within the military and outside it appeared to be in favor of such a change (e.g., PTS Injury, 2012). However, there is no known empirical evidence demonstrating that the proposed name change is perceived as beneficial among service members, would result in a more socially acceptable category, or would increase the number of those seeking treatment. Although the creation of the PTSD diagnosis in 1980 is perceived by many to have legitimized the set of symptoms experienced by individuals with PTSD, there is no evidence that the specific name change proposed would generate a or broadened effect. Nor, to our knowledge, is there a unified collective statement or set of statements on the part of service members, veterans, or groups that advocate for them regarding the proposed change; formal positions appear to be limited and varied (e.g., PTS Injury, 2012; Vietnam Veterans of America, 2012).

To better inform discussion of the issue, the American Legion hosted a meeting in June 2012 addressing the implications of the proposed name change, with a report outlining the findings and recommendations released later in the year (American Legion, 2012). A coherent “voice” may eventually emerge among service members, veterans, or the groups that advocate for them. But at this point, if the APA is interested in revisiting the issue—or the military, service members, and veterans are interested in creating a label that frames the PTSD diagnosis in a way that is more socially legitimizing and increases treatment utilization—they should take steps to ensure that discussions about the proposal are informed by more systematic input from representative samples of those military service members, veterans, and other traumatized or victimized individuals who would be directly affected by the change.

### Stigmatization of Those with the Condition

While diagnosis is designed to reduce suffering, it can instead serve as a basis for blame and create a stigmatized social category (Jutel, 2011; Jutel and Nettleton, 2011). A stigma is the negative evaluation resulting from a social label (e.g., diagnosis) or attribute (Goffman, 1963; Jones, 1984; Link, Phelan, et al., 1999). To be stigmatized is to be devalued, dehumanized, or seen as flawed due to one’s attributes or group membership (Goffman, 1963; Crocker, Major, et al., 1998). It is plausible that concerns about, or fear of, PTSD-related social stigmatization inhibit treatment seeking or treatment-adherence for PTSD (U.S. Department of Health and Human Services, 1999). In fact, there is a great deal of evidence to support the existence of mental illness stigmatization in general. However, there is little empirical evidence documenting the nature of PTSD-related stigmatization specifically or demonstrating negative effects of PTSD-related stigmatization on treatment utilization.

Research shows that, in general, people dislike or desire social distance from (i.e., stigmatize), those with mental illness. For example, negative representations of the mentally ill have been shown to be quite common in the media (Signorielli, 1989; Wahl, 1995). Some individuals consider mental illness to be a socially undesirable label, on par with drug addiction or exconvict status (Albrecht, Walker, et al. 1982). Those suffering from a mental illness are regularly seen as dangerous or too incompetent to handle their own affairs (Link, Phelan, et al., 1999; Pescosolido, Monahan, et al., 1999).

Few studies (Pietrzak, Southwick, et al., 2009) specifically demonstrate stigmatization among U.S. military service members with PTSD. Moreover, it is difficult to assess the extent to which research demonstrating the existence of mental illness stigmatization generally can be applied to PTSD-related stigmatization specifically (or to stigmatization associated with major depressive disorder, which is highly comorbid with PTSD). The reason is that not much is known about how people interpret the term “mental illness.” Some researchers assert that the term “mentally ill” is commonly applied to those with nonpsychotic illnesses (Phelan, Link, et al., 2000), while others argue that the term is more synonymous with the labels “insane” or “psychotic” (Thoits, 1985), which do not describe individuals with PTSD. Others have suggested that mental health treatment, regardless of the underlying diagnosis, may result in negative views of the individuals receiving it (Link, Phelan, et al., 1999). Based on this literature, it is unclear whether the available claims about the stigmas of mental illness can be extended to PTSD-related stigmas.

Similarly, there are no known studies showing that PTSD related social stigmatization reduces the utilization of treatment. Some research exists on the relationship between treatment utilization and stigmatization associated with major depressive disorder, an illness that shares some symptoms with PTSD, but the effects documented in the research are not consistent. For example, stigmatization concerns have been shown to have a negative effect on treatment utilization by depressed individuals living in rural areas, but the effect is not present for depressed individuals living in urban areas (Hoyt, Conger, et al., 1987; Rost, Smith, et al., 1993). In addition, stigmatization concerns have been found to be associated with treatment discontinuation among depressed older adults but not among depressed younger adults (Sirey, Bruce, et al., 2001). While these

studies indicate that fear of stigmatization may serve as a barrier to treatment for depression, the effects that have been found to date apply only to certain populations or settings. Hence, it is possible that the characteristics of various military populations and the contexts in which they seek treatment affect whether and how PTSD-related social stigmatization affects the utilization of treatment.

Inconsistencies in the evidence of stigmatization as a barrier to care may be due to a complex relationship between and treatment seeking. For instance, one might argue that concerns about being stigmatized could motivate a sufferer to seek treatment. Thoits (1985) implies that in some situations an individual may be highly motivated to eliminate symptoms of a psychiatric disorder to avoid stigmatization. In such situations, the stigmatization might encourage individuals to seek treatment as a means of eliminating the symptoms and behaviors associated with the diagnosis. The treatment-motivating effect of stigmatization can be seen with other types of medical diagnoses such as sexually transmitted diseases, which are often more stigmatizing than mental illnesses (see Westbrook, Legge, et al., 1993

Given the inconclusive nature of the existing evidence further research may be needed to more accurately predict the effect of PTSD-related stigmatization on treatment utilization. In particular, we may need a better understanding of the root cause of PTSD-related stigmatization. If it is related to the specific pattern of symptoms or behavior typical of PTSD, then fear of stigmatization may motivate individuals to seek treatment as a means of eliminating the symptoms or behaviors. If it is related to the diagnostic label—be it the term “disorder” or the existence of a psychiatric diagnostic label more generally—then fear of stigmatization may cause individuals to eschew treatment providers in order to avoid the diagnosis. If it is related to the mental health treatment, then fear of stigmatization would reduce treatment utilization regardless of the name given to the disorder. In the absence of research addressing these competing hypotheses, it is not known whether the existing label results in a stigma that reduces treatment utilization.

#### Discrimination Against Those with the Condition

While psychiatric diagnoses are designed to meet the needs of the mental health treatment, research, and educational communities, they are often used within other organizations or institutions for purposes beyond their designed intent. Discrimination is one such practice (Jutel, 2011; Jutel and Nettleton, 2011). For example, a PTSD diagnosis may be used against an individual in court to suggest that he or she should not be given custody of a child, despite the fact that the diagnosis itself does not require any assessment of parenting skills or competencies. Similarly, the diagnosis may be used by an employer to select workers or to determine work assignments and promotions even though the diagnosis does not require any assessment of task competencies or reliability. While some social, occupational, or other type of impairment is a necessary diagnostic criterion of PTSD, the disorder manifests differently in each individual; the mere presence of a diagnosis provides no reliable information about how broad or narrow the impairment may be. It is worth noting that, as with other forms of institutional discrimination (Merton, 1970; Feagin and Feagin, 1978), PTSD-related discrimination within organizations or institutions may exist regardless of the attitudes or intentions of individuals within those institutions and so, too, regardless of social stigmatization. Discriminatory practices and procedures may become ingrained in the fabric of an organization or institution. Therefore, PTSD-related discrimination may persist even if individuals with PTSD were generally admired or seen as heroic. The U.S. military—and in some cases, the government more broadly—uses information about psychiatric diagnoses, such as PTSD, or mental health treatment for purposes that may adversely affect how a diagnosed individual is treated. For instance, the DSM definition of PTSD is routinely used to aid government efforts to assess potential security risks or trustworthiness, despite the fact that the diagnosis does not require any assessment of those characteristics. Individuals are required to report mental health treatment and diagnoses as part of the process for determining eligibility for security clearances, 5 and because security clearances are a requirement for many military

occupations and some post military careers, service members may forgo treatment to avoid any potential harm to their military or post military careers.

The U.S. military also uses information about psychiatric diagnoses and mental health treatment as part of its evaluation of personnel, in particular to determine whether service members are fit for deployment. Information about diagnoses and treatment is made available to commanders to aid in their management of personnel and units. However, the inferences that commanders draw from this information may not correspond to the assessment that led to the diagnosis or may be based on an inaccurate understanding of the disorder. For instance, the DSM criteria for PTSD do not require any assessment of an individual's ability to carry out his or her military occupation, nor do the criteria address how the individual would respond to deployment. The PTSD diagnosis does entail some functional impairment, but for some individuals, the impairment may be limited to no occupational situations, such as intimate relationships. Indeed, it has long been recognized that many PTSD symptoms are both normal and functional when the individual is engaged in a demanding or stressful activity (Cannon, 1932; Hoge, 2010). Some researchers have speculated that soldiers with PTSD perform better than average during combat (Hoge, 2010).

Service members who are deemed not deployable and placed on restricted or modified duties can face significant, negative career impacts. These individuals are separated from their units during deployment and, as a consequence, might not receive the substantial financial benefits provided to those who deploy. They might not be eligible for the types of responsibilities or experiences that lead to promotion. Moreover, their absence could inconvenience or irritate others in their units, which could damage personal relationships or negatively affect their personnel evaluations. Although PTSD diagnosis or treatment does not automatically disqualify a service member for deployment, the information is routinely shared outside the mental health treatment team for use in evaluating personnel. Hence, a PTSD diagnosis could have a negative impact on an individual's career trajectory, even if the individual is deemed qualified to deploy.

While these forms of discrimination are prohibited by law in civilian environments, military service members are not protected by these same laws. The Americans with Disabilities Act and the Rehabilitation Act, for example, require public and private businesses to make certain accommodations for those with disabilities; however, the Disabilities Act does not apply to DoD, and the Rehabilitation Act applies only to DoD civilians and not to uniformed military service members. The Health Insurance Portability and Accountability Act, which protects the privacy of individually identifiable physical and mental health information, contains military exemptions. These exemptions permit the release of health information to commanders for certain purposes, such as determining whether a given service member is fit to perform his or her military duties.

Data support the claim that fear of discrimination is a significant barrier to the seeking of treatment by U.S. military service members. In its 2008 Invisible Wounds of War study, RAND surveyed military service members about factors that might prevent them from seeking mental health treatment if it were needed (Schell and Marshall, 2008). Barriers related to discrimination in the workplace were among the most highly cited: 44 percent of respondents thought they might not get help because it would harm their careers. In contrast, social stigmatization concerns were not as highly endorsed; only 12 percent of respondents suggested they would not get treatment because their friends or family would respect them less.

#### The Proposed Change to the PTSD Label

In late 2011, U.S. Army leadership requested that the APA drop the term "disorder" from the PTSD diagnostic label in its new edition of the DSM, the DSM-5. The proponents' rationale for using this new term was that it is less stigmatizing and would encourage more U.S. military service

members suffering from symptoms to access care. The APA considered adding a diagnostic subcategory of PTSD, such as “combat posttraumatic injury.” It also discussed changing the name of the diagnosis to “posttraumatic stress injury” and there is some indication that the latter option may have been preferred at the time of the initial request (Jaffe, 2012; Oldham, 2012). The option of simply removing the word “disorder” was not considered by the APA. Ultimately, the APA decided to retain the word “disorder,” (the “D”) in PTSD. It is unclear whether the debate over the diagnostic terminology will continue in the months or years following the publication of the DSM-5.

Despite the APA’s decision to retain the “D” in “PTSD,” the proposal raised questions about whether the term “injury” is preferable to “disorder.” Proponents of the change have argued that “injury” is the preferred term because it would lead to an increase in treatment utilization by reducing the stigma associated with the diagnostic label. However, there is no known empirical evidence indicating that a psychiatric “injury” generates less stigmatization than a psychiatric “disorder.” In fact, it may be the case that the public views psychiatric “injury” as more permanent, more severe, or more disabling than psychiatric “disorder.” Without the requisite empirical evidence, it likely would have been premature for the APA to replace the term “disorder” with “injury” in order to reduce stigmatization.

Adopting the term “injury” also could have implications beyond the effect on the likelihood of stigmatization. There is no known empirical evidence pertaining to the use of the term “injury” in “PTSD,” thus making it unclear exactly what these implications may be. However, it is conceivable that a new label could be misleading to patients and clinicians in several ways. First, the term “injury,” as it is commonly used and as it is defined by WHO, refers to physical (rather than psychological or emotional) harm or impairment inflicted upon an individual. Thus, the term “posttraumatic stress injury” may suggest that the disorder happens to the individual, when in fact the disorder is the individual’s response to a traumatic event. It is unclear how individuals suffering from PTSD might perceive their ability to seek or continue treatment if they view themselves as victims of an injury.

Second, it is unclear how populations that are not physically engaged in frontline combat (e.g., pilots of remotely piloted aircraft, care providers, and chaplains) might perceive the term “injury” and how that perception might affect their willingness to seek treatment if they experience PTSD symptoms. It is possible that the term “injury” would lead to the mistaken impression that an individual would need to have been in a position to be physically harmed in order to obtain the diagnosis and be eligible for treatment.

Third, it is unclear whether the term “injury,” which usually signifies an instance of being injured, is an appropriate term to describe a phenomenon defined by one’s current level of functionally impairing symptoms rather than a discrete event in the past. Individuals with delayed-onset symptoms may be misled by an “injury” diagnosis because their symptoms do not coincide temporally with an incident they recognize as an injury. Alternatively, those whose PTSD symptoms persist continuously from the time of a traumatic event may mistakenly perceive that the basis for the disorder lies in the past rather than in a current cognitive and emotional state. In fact, symptoms may be adaptive at one time (e.g., in the face of trauma) and functionally impairing at another time (e.g., upon return from deployment). In short, labeling PTSD as an injury may give the erroneous impression that the disorder is determined entirely by discrete events in the past, thereby understating the role of one’s current cognitions, emotions, and environment in maintaining the disorder. Such a misperception might, in theory, make the disorder appear less treatable.

Moreover, we note that (a) no empirical evidence exists to support a link between adopting the term “injury” and a reduction in stigmatization, and (b) the discriminatory practices linked to the PTSD label could be easily transferred to the new label. Hence, we believe that altering the label or acronym—making more wholesale changes to how the disorder is defined, how diagnosed individuals are treated, or how the military uses

information about diagnosis and treatment—is unlikely to generate dramatic changes in treatment-seeking or treatment utilization. Further, there exists a body of work on the barriers to psychiatric treatment (see Parcesepe and Cabassa, 2012; Vogt, 2011), and implementing strategies informed by this evidence may be more productive than changing the PTSD label.

It is also worth noting that while the U.S. military has requested that the APA change the diagnostic label from “disorder” to “injury,” the military does not currently treat PTSD as it does other combat injuries. PTSD is not sufficient to earn a Purple Heart, an honorable decoration awarded to service members who have been wounded or killed in action. Only service members who have suffered enemy-inflicted physical injuries (e.g., those caused by enemy fire or explosive devices) are entitled to receive the award. If the APA decides to change the term “disorder” to “injury” but the U.S. military continues to omit PTSD from the category of combat injuries that qualify for a Purple Heart, the new label’s intended effect of reducing stigmatization may be undermined. There is some precedent for awarding decorations such as the Purple Heart to service members with PTSD: Canada’s military awards the Sacrifice Medal, an equivalent to the Purple Heart, to those with mental disorders (or operational stress injuries) attributed to hostile action (National Defence and the Canadian Forces, 2012).

#### The Informal Use of “PTS”

Military leaders and others have informally used the term “posttraumatic stress” or “PTS” to refer to PTSD as well as stress responses that do not meet the clinical criteria for a mental disorder. For example, the U.S. Army has begun using the term in place of “PTSD” on certain documents and websites and in some statements and presentations by senior leaders. The rationale echoes the impetus behind the desired diagnostic label change—the term “PTS” is thought by some to be less stigmatizing than “PTSD” and expected to encourage more U.S. military service members suffering from symptoms to access care. Given the APA’s recent decision not to change the PTSD diagnostic terminology, it is unclear whether and to what extent use of the term “PTS” will continue, and what the full range of its effects may be.

The term “PTS” may be misleading to service members or the general public if used in common lexicon in lieu of or alongside formal diagnostic terminology. This may be especially true if “PTS” is used to refer to chronic and clinically significant reactions. Although “PTS” may be appropriately applied to posttraumatic stress responses that do not meet the clinical criteria for PTSD—for example, transient reactions lasting a matter of hours or days—referring to disordered reactions as “stress” obfuscates one of the defining features of PTSD. The disorder is characterized not by the presence of stress itself but rather by the failure to spontaneously recover from stress in a normal manner. The pattern of symptoms associated with PTSD may be perfectly normal and healthy during exposure to a stressful situation. PTSD is a disorder only to the extent that it persists long after the actual stress is removed. Labeling a problematic set of symptoms with “PTS” fails to convey this distinction between a normal stress response and a problematic one (which persists and is functionally impairing).

Even if “PTS” is used to refer to transient or subclinical stress responses, the term could still be misleading to members of the military or the general public. For example, service members experiencing PTSD symptoms could, in theory, assume that these symptoms are characteristic of a less severe “PTS” and therefore not feel that treatment is warranted or would be beneficial. In other words, labeling subclinical stress responses could normalize these responses and convey the message that they should not or will not become problematic. This may be especially true if messages about a normal and transient “PTS” within military communities were to become highly prevalent and overshadow messages emphasizing the importance of or channels for seeking mental health treatment. Moreover, the U.S. military already utilizes its own specific terminology, “combat and operational stress reaction,” (COSR) to refer to combat-specific reactions that do not meet the clinical criteria for PTSD or other mental disorders (Brusher, 2011). In addition, some COSR and/ or “PTS” cases could meet the clinical criteria for ASD. It is not known

whether the existence of these multiple and potentially overlapping labels—that is, PTS, COSR, and ASD—may further complicate service member or general public understandings of combat-related stress. Nor is it known whether the coexistence of these labels could affect the likelihood that service members suffering from symptoms would seek treatment.

Further, the use of an additional term such as “PTS” to label PTSD or PTSD-like symptoms may create challenges for the military disability system and the Veterans Health Administration, as well as service members and veterans accessing benefits through these systems. The widespread use of this label may make it more difficult to claim disability benefits for those service members who could be accurately labeled with a disability eligible code from the DSM or ICD-10 taxonomy, but are instead labeled with “PTS.” Currently, the term “PTS” does not confer eligibility for disability benefits or medical retirement. Therefore, individuals labeled with “PTS” who also meet the criteria for a psychiatric disorder such as PTSD may require multiple labels to access the appropriate range of benefits, services, or accommodations.

The use of nonstandard terminology may also result in confusion among mental health care providers or lapses in care. For example, as individuals transition from the military health system to the VHA or civilian environments, providers in these settings may not be aware of the term “PTS,” its specific meaning or clinical implications, and the standards for its care. Although many of these problems could be avoided if “PTS” were used only to refer to transient or subclinical responses, current use of the term does not appear to be limited to these instances. Moreover, the benefit of such usage is unclear, particularly given its possible overlap with the current COSR and ASD labels.

Proponents of the term “PTS” assert that this label is useful because it would lead to an increase in treatment utilization by reducing the stigma associated with the term “disorder.” However, as with the term “injury,” no known empirical evidence documents stigmatization specifically related to the term “disorder,” particularly among individuals with PTSD. Nor does evidence demonstrate negative effects of PTSD-related stigmatization on treatment utilization. To the extent that such a stigmatization could exist (and not be documented), this stigma could be easily transferred to the “PTS” label. So, too, could the discriminatory practices linked to the PTSD label. Further complicating the effects of any changes in PTSD terminology is the widespread adoption of the acronym by the U.S. military and the general public. The acronym is used as a stand-alone word without reference to the underlying terms denoted by each letter. It is not known how many people associate the term “disorder” with the PTSD label, nor whether replacing the term PTSD with “PTS” would induce a noticeable change in the way society perceives the underlying problems.

It is worth noting that the Canadian military, like the U.S. military, uses its own terminology to refer to certain mental health issues. The term “operational stress injury” describes any of a number of ongoing clinically significant psychological difficulties resulting from military service (Veterans Affairs Canada, 2012a). The term was created in response to concerns about mental illness stigma similar to those found among U.S. military service members, and includes PTSD as well as other mental health ailments, such as anxiety and depression. The term “operational stress injury” refers to clinical disorders as well as other, less-severe conditions that still interfere with daily functioning (Veterans Affairs Canada, 2012).

### Concluding Thoughts

Problems stemming from exposure to traumatic events have been characterized by numerous labels and subject to varying degrees of recognition over time. It was not until 1980 that PTSD was incorporated into the DSM, in part as a result of advocacy by and collaboration among psychiatrists and individuals representing traumatized groups. The creation of a PTSD diagnostic category was seen by many veterans’ advocacy groups as a

major victory. The diagnosis encourages treatment utilization, research into treatments, and the development of practice guidelines to improve the effectiveness of treatment. It also legitimizes suffering and enables service members suffering from PTSD to receive VA disability compensation.

To ensure that these gains are maintained and that the diagnostic category remains useful, any changes to the PTSD label or endorsement of using new terminology should be supported by evidence that reflects the perspectives of the mental health treatment and research communities as well as the perspectives of military service members, veterans, and other traumatized individuals who would be directly affected by the change in terminology.

Currently, there is no evidence that PTSD-related social stigmatization has a strong or consistent association with treatment seeking. It is possible that making the symptoms less stigmatizing would reduce, rather than increase, treatment utilization. In addition, there is no formal evidence that the term “injury” generates less stigmatization than the term “disorder” does, and it is possible the term “injury” may come with its own set of unintended, negative consequences. Moreover, informal use of the term “PTS,” particularly when applied to clinically significant stress responses, may obfuscate the distinction between normal stress responses and problematic ones, and may therefore engender its own set of negative consequences.

More generally, the manner in which institutions use the diagnosis, rather than the specific label, is an important determinant of how service members view the disorder and how likely they are to seek treatment. Using information about psychiatric diagnoses or mental health treatment in ways that may adversely affect how the diagnosed individual is treated is likely to undermine efforts to reduce stigmatization and increase treatment utilization, regardless of the label used to describe the disorder. If information about the diagnosis and treatment of “PTSI” is made available to commanders for use in conducting personnel evaluations or managing military units, as it has been for PTSD, then the new label will also be seen as a direct threat to one’s military career. Use of the term “PTS” may persist, and the APA may eventually change course and alter the name of the disorder, but without changes to broader institutional factors, a name change at any level is unlikely to generate a significant increase in individuals willing to be diagnosed or treated.

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## **Treatment of Comorbid Substance Dependence and Posttraumatic Stress Disorder**

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Approximately 11 million US adults have posttraumatic stress disorder (PTSD), and approximately one-third of these individuals also have alcohol dependence, a substance use disorder. Compared with individuals with either disorder alone, people with co-occurring PTSD and substance use disorder have worse physical and mental health, poorer treatment outcomes, and a more long-term course of illness. Furthermore, both disorders have been shown to maintain and exacerbate each other. It is therefore not surprising that clinicians consider patients with these 2 conditions to be particularly difficult to treat.

In this issue of *JAMA*, Foa and colleagues report the main findings from a randomized clinical trial (RCT) comparing the efficacy of naltrexone, prolonged exposure therapy for PTSD, and their combination, in the treatment of comorbid PTSD and alcohol dependence. Prolonged exposure therapy is an evidence-based approach whereby a patient undergoes a series of formal sessions in which he or she is exposed to memories and reminders of past trauma, and then is encouraged to discuss his or her thoughts and feelings about these events. In this trial, participants (n = 165) were randomly assigned to 1 of 4 groups: (1) naltrexone, (2) naltrexone plus prolonged exposure therapy, (3) pill placebo plus prolonged exposure therapy, or (4) pill placebo. In addition, all participants received supportive counseling. This trial represents an important contribution to the literature pertaining to the treatment of this common comorbidity; however, to appreciate its full significance, the results of the study should be considered within the context of the considerable public health and clinical challenges imposed by comorbid PTSD and alcohol dependence.

Caring for patients with comorbid PTSD and substance use disorder is challenging due to the lack of evidence for effective treatment. Based on early case reports, practitioners were advised against treating PTSD when comorbid with a substance use disorder until a substantial period of abstinence or stabilization had occurred because of fear that the distress invoked by such treatment might lead to serious adverse consequences. Consequently, the majority of PTSD treatment trials excluded individuals with substance use disorders. Therefore, the probability of a patient receiving PTSD treatment if he or she also had a co-occurring substance use disorder was exceedingly low. Consistent with the theory that patients with PTSD use substances to self-medicate their symptoms, patients frequently report that their PTSD symptoms are exacerbated in the absence of substance use, thus making it difficult to maintain abstinence or reduced use. As a consequence, patients in this population group have not received the care they need.

The study by Foa and colleagues is the first RCT to examine the combined use of a psychotherapy and a pharmacotherapy for the treatment of comorbid PTSD and substance use disorder. The predominance of research to date has focused on the efficacy of either trauma-focused or non-trauma-focused psychotherapies; a small number of studies have examined pharmacotherapies, but none have examined them in combination.

Consistent with previous research examining the use of naltrexone in the treatment of comorbid alcohol dependence and PTSD, Foa and colleagues report a significant main effect for naltrexone during the treatment phase of the study in relation to alcohol outcomes. Specifically, patients randomized to receive naltrexone (either alone or in combination with prolonged exposure therapy) had lower percentages of days drinking and reduced cravings posttreatment compared with patients randomized to receive placebo (with a mean difference of 7.93% in days drinking and 3.14 points on the Penn Alcohol Craving Scale). As in previous research, degree of improvement in PTSD symptoms did not differ significantly between patients randomized to receive naltrexone or pill placebo. Collectively these studies provide evidence that naltrexone may be efficacious in the treatment of alcohol dependence among individuals with PTSD, without exacerbating PTSD symptoms.

Although there were no differential effects in PTSD outcomes at the end of treatment between those randomized to receive prolonged exposure therapy and those who were not, prolonged exposure therapy was found to be protective with regard to relapse during the 6-month follow-up period. Patients randomized to receive prolonged exposure therapy did not have a significant increase in the percentage of days drinking during the follow-up period, whereas patients randomized to receive no prolonged exposure therapy had an increase of 15.9% in days drinking. Furthermore, although the primary analysis of PTSD outcomes showed no difference in outcomes between groups at the end of treatment, an exploratory analysis of PTSD symptoms at the 6-month follow-up revealed a gradient of effect whereby low-level PTSD symptoms (score of  $\leq 10$  on the PTSD Symptom Severity Interview) were most prevalent among those randomized to receive naltrexone and prolonged exposure therapy, followed by those who received prolonged exposure therapy alone, and naltrexone alone. These findings are consistent with those of 2 recent trials that found support for the efficacy of prolonged exposure therapy in patients with PTSD and substance use disorder.

Contrary to the expectations of Foa and colleagues, none of the interactions for naltrexone and prolonged exposure therapy were significant, indicating that the combined use of these treatments conveyed no added benefit to the use of either treatment alone. However, these results should not be regarded as conclusive. Evidence regarding the combined use of pharmacotherapies and psychotherapies for PTSD is lacking, and findings from the broader treatment literature indicate that the relationship between these treatment types may be complex.

Another novel aspect of the study by Foa and colleagues is that it examined the concurrent treatment of alcohol dependence and PTSD (in which both disorders were treated simultaneously by 2 different practitioners), as opposed to the integrated treatment of this comorbidity (in which both disorders are treated simultaneously by the same practitioner). An integrated approach has been advocated for the treatment of PTSD and substance use disorder based on the interdependence of the disorders; however, a concurrent approach may be more feasible for the majority of services in which clinicians do not have the specialized training required to treat both disorders. Further research is needed comparing the relative efficacy of integrated vs parallel approaches to treatment.

Even though the findings of Foa and colleagues add to the knowledge surrounding the treatment of alcohol dependence and PTSD, as with all studies, the findings should be considered in light of some limitations. Most particularly, the sample size was relatively small given that it was a 4-group RCT. Recruitment to clinical trials can be difficult, and as demonstrated by the length of time taken to conduct the study by Foa and colleagues, research undertaken with this population is particularly challenging. This is not surprising given the nature of the research, in which participants are asked to confront some of the most terrifying events that have ever happened to them, and simultaneously try to abstain from using alcohol and other drugs, which are often the only means by which they have felt that they could cope with the consequences of those events. Nonetheless, the small group sizes and low rate of retention in the study by Foa and colleagues limited the analyses that could be conducted. Only 56% of the original cohort completed the posttreatment and follow-up interviews. It is unclear whether retention in the study was related to any baseline characteristics (eg, severity of alcohol use or PTSD), which may have introduced bias in the results.

Despite these limitations, the study by Foa and colleagues is a timely contribution to the literature regarding the treatment of comorbid alcohol dependence and PTSD. The study provides evidence regarding the treatment of this commonly occurring comorbidity and provides hope that the gap in treatment provision for this population may begin to narrow.

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## **Recovery After Violence and Human Rights Abuses**

Journal of the American Medical Association  
Thomas B. Cole, MD, MPH; Annette Flanagan, RN, MA  
7 August 2013

Quality of life after trauma is shaped by the capacity for physical and psychological healing and recovery, which may be facilitated by evidence-based treatment of physical and psychological injuries and their sequelae. This and previous JAMA theme issues on violence and human rights have included several evaluations of interventions to promote recovery after exposure to trauma.

In a case-based review in this issue, Crosby discusses the clinical management of a patient with chronic weakness, pain, and posttraumatic stress disorder (PTSD) as a consequence of the trauma she experienced as a refugee from the civil war in Somalia. This management includes a multidisciplinary approach designed to be culturally acceptable to the patient. Also in this issue, 2 related Viewpoints summarize new evidence-based guidelines from the World Health Organization (WHO) to help with clinical management of patients exposed to trauma and violence. Van Ommeren and colleagues discuss new WHO recommendations, many based on substantial evidence, for management of acute stress symptoms after trauma exposure, especially in low- and middle-income countries with limited resources. For example, these guidelines recommend cognitive behavioral therapy with a trauma focus for trauma-exposed adults with acute stress symptoms and PTSD and recommend against the use of benzodiazepines for acute stress and against the use of antidepressants as first-line treatment for PTSD unless there is concurrent moderate to severe depression. Feder and coauthors summarize other WHO recommendations, primarily based on low to moderate levels of evidence, to assist clinicians with decisions about and management of women exposed to intimate partner violence. The guidelines recommend cognitive behavioral therapy or eye movement desensitization and reprocessing interventions, delivered by health care professionals with a good understanding of violence against women, for those with PTSD who are no longer experiencing violence.

Based on a systematic review of the literature, North and Pfefferbaum present an evidence-based framework for assessing and delivering mental health services to individuals experiencing psychological distress following a disaster. The framework provides guidance that differentiates types of assessment, referrals, and interventions for individuals following a disaster based on whether they were exposed to trauma, have or do not have a preexisting mental health disorder, and the timing and type of mental health symptoms observed. In a related Viewpoint, Elster and coauthors present lessons learned from combat casualty care that may help management of civilians exposed to mass violence and mass casualty events. In another Viewpoint, Manley and Maas discuss the need for an international collaborative approach to research, data collection, and improved classification of traumatic brain injury (TBI) to better guide assessment and clinical management of TBI survivors. These articles highlight a common problem with the recommendations for clinical management of patients who experience various forms of trauma to help facilitate their recovery: while research in these areas continues to improve, evidence for many interventions is still evolving and for some conditions is lower in quality compared with evidence for interventions for other disorders, such as heart disease and cancer. However, recent evidence from clinical trials has begun to provide strong support in favor of some interventions and against others.

The need for stronger levels of evidence, such as those from clinical trials, continues, but these studies are challenging to conduct and fund in settings in which many people are affected by interpersonal, mass, or incidental violence or trauma. Thus, the report of the clinical trial by Foa et al in this issue is a welcome contribution. In this trial, the investigators address the clinical challenge of treating patients with concurrent PTSD and alcohol dependence who may self-medicate with alcohol and other drugs in an effort to relieve their stress. Clinicians have been reticent to engage patients with PTSD complicated by alcohol or other substance use disorders in exposure therapy—an evidence-based treatment for PTSD that is designed to provoke intense emotional responses and recovery—because of concern that the stress of therapy might result in relapse and failure to manage the substance use disorder. However, the results of the clinical trial by Foa et al demonstrate that exposure therapy given with naltrexone does not result in an exacerbation of alcohol disorder.

Previous JAMA theme issues have also addressed recovery from violence and human rights abuses and the needs for better evidence to support recovery-aimed interventions. For example, randomized trials have reported reductions in PTSD symptom severity for former child soldiers treated with narrative exposure therapy, partners or spouses with PTSD participating in cognitive behavioral couple therapy, and patients receiving an

integrated treatment for PTSD and substance dependence, but not for trauma-exposed veterans receiving adjunctive risperidone. Trials of interventions for groups of patients have reported reductions in PTSD symptom severity for conflict-exposed children in school settings and reductions in depressive symptoms for adolescents treated in refugee camps. Other studies published in previous JAMA theme issues on violence and human rights have assessed potential barriers to recovery associated with war crime tribunals, beliefs about justice, and the ability to develop methods of coping. Taken collectively, these studies provide substantial support for psychotherapy and other treatments to aid recovery after trauma.

In the life of an individual, an incident or even a series of incidents of violence or human rights abuse is not the end of the story. With the help of an empathetic clinician who can provide evidence-based therapy, a survivor of violence or abuse may be able to turn the page in his or her life story and be better able to cope with symptoms, manage or eliminate impairment or disability, recover from the trauma, and ultimately, become more than just a “survivor.”

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## **A Yoga Program for the Symptoms of Post-Traumatic Stress Disorder in Veterans**

Military Medicine

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### **ABSTRACT**

The purpose of this pilot study was to evaluate the feasibility and effectiveness of a yoga program as an adjunctive therapy for improving post-traumatic stress disorder (PTSD) symptoms in Veterans with military-related PTSD. Veterans ( $n = 12$ ) participated in a 6 week yoga intervention held twice a week. There was significant improvement in PTSD hyperarousal symptoms and overall sleep quality as well as daytime dysfunction related to sleep. There were no significant improvements in the total PTSD, anger, or quality of life outcome scores. These results suggest that this yoga program may be an effective adjunctive therapy for improving hyperarousal symptoms of PTSD including sleep quality. This study demonstrates that the yoga program is acceptable, feasible, and that there is good adherence in a Veteran population.

### **INTRODUCTION**

War-related post-traumatic stress disorder (PTSD) exacts an incalculable toll on survivors, their interpersonal and occupational networks as well as the Veterans Affairs (VA) Health Care and Benefits systems and society as a whole. The prevalence of PTSD among Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans from all branches of service from 2007 to 2008 was 13.8%,<sup>1</sup> and PTSD has been identified by the House Committee on Veterans Affairs as one of the signature wounds of Veterans returning from these wars. In 2005, 14 years after the Gulf War, Veterans reported PTSD rates of 15.2%.<sup>2</sup> Results of the National Vietnam Veterans' Readjustment Study (NVVRS) showed a lifetime PTSD prevalence of 30.9 % among male and 26.9% among female Vietnam theater Veterans.<sup>3</sup> According to the Department of Veterans Affairs Strategic Plan, rates of PTSD are steadily rising within the Veteran population.

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Two evidence-based psychotherapy treatments that are supported as first-line treatments for PTSD by the Veterans Health Administration are prolonged exposure therapy (PE) and cognitive processing therapy (CPT). Although both of these therapies have been shown to reduce overall PTSD symptoms in Veterans, improvements in the hyperarousal symptom cluster of PTSD have not been consistently observed. In addition, although CPT and PE are effective in many cases, some Veterans do not improve with these treatments or remain somewhat symptomatic. In one study of CPT, 31.7% of Veterans were classified as unchanged and 10.6% deteriorated based on PTSD checklist (PLC) scores. For PE, 26% of OEF/OIF Veterans completing the treatment still had PLC scores above the suggested cut-off value for PTSD. Therefore, there is a need to investigate additional treatments that may be used as adjunctive therapy as well as interventions that address the treatment of hyperarousal symptoms of PTSD.

Problems with sleep and anger are components of the hyperarousal symptom cluster of PTSD and hyperarousal symptoms may actually determine subsequent PTSD symptom severity. Sleep problems are more frequently experienced in Veterans with PTSD than those without PTSD. In Veterans with lifetime PTSD, lower quality of sleep was directly correlated to hypervigilance scores which are part of the hyperarousal symptom cluster.<sup>16</sup> Furthermore, it is possible that sleep problems may predict PTSD symptoms. Anger, a primary component of combat-related PTSD, appears to be a function of PTSD itself since studies have shown that aggression and anger were not correlated with combat exposure or the presence of concurrent psychiatric disorders.

Sleep and anger problems are often experienced as severe and acutely distressing. In Veterans, the hyperarousal symptom cluster had the strongest impact on overall functioning compared to the reexperiencing and numbing/avoidance clusters. Poor overall functioning, in turn, can result in decreased quality of life and as many as 59% of subjects with PTSD from 11 treatment trials had severe quality of life impairment. Vietnam Veterans with PTSD have been shown to have a significant risk of diminished well-being and Gulf War Veterans with PTSD have also reported lower levels of functioning and quality of life compared to those without PTSD. Clinically significant PTSD improvement in Vietnam Veterans as a result of PTSD treatment has been associated with improvement in quality of life domains and both improvements occurred at the same time in the course of treatment. Therefore, treating PTSD is expected to improve quality of life.

Yoga is a system of mind-body techniques for improving physical and mental health and includes physical postures, breathing, focused concentration, and meditation. Yoga has been shown to improve quality of life in military personnel deployed to Iraq and in Veterans with back pain. Many studies have been done showing that yoga can improve sleep and reduce anger in a variety of populations. However, none of these studies have been done in Veterans with PTSD. The effect of yoga on Veterans with PTSD has only been reported in one qualitative study to date. Eleven combat Veterans reported reduced rage, anxiety, and emotional reactivity and increased self-awareness and self-efficacy after participation in a yoga nidra intervention (iREST). This intervention is based on principles from yoga and other forms of therapy but it does not involve performing a series of yoga postures and PTSD symptoms were not directly measured.

A few studies have been performed on the effects of yogic interventions for PTSD in non-Veterans. Two pilot studies are briefly described in a review article on PTSD.<sup>34</sup> In the first study with 8 participants, 8 sessions of yoga significantly improved PTSD-related reexperiencing, avoidance, and total scores on the Clinician-Administered PTSD Scale, but not hyperarousal. In the second study, 4 women with PTSD had decreased in the frequency of intrusions and hyperarousal symptoms after 1 session of hatha yoga exercises compared to 4 women receiving dialectical behavioral therapy. Improvements in PTSD symptoms in survivors of the 2004 South-East Asia tsunami were also measured using an intervention involving yogic breathing alone, but not yoga postures.

Although currently there is a lack of empirical data on yoga for Veterans with PTSD, various forms of meditation have been shown to be helpful. Transcendental meditation, mindfulness meditation, and mantra meditation have all been shown to reduce PTSD symptoms in Veterans. Both yoga and meditation are mind-body modalities that decrease parasympathetic activity and are likely to work via similar mechanisms to reduce PTSD symptoms. A recent theory suggests that stress can be reduced by yoga-based practices that shift regulatory systems such as the hypothalamic–pituitary–adrenal axis, and neuroendocrine, cardiac, metabolic and immune systems toward optimal homeostasis.<sup>40</sup> Meditation is often practiced as a component of yoga and the focused attention aspect of meditation, including the use of mantra, is incorporated into some yoga traditions. Given these common characteristics, yoga is also likely to have a beneficial effect for PTSD.

To our knowledge, this is the first study using a yoga intervention that includes performing yoga postures for reducing PTSD symptoms in Veterans. The purpose of this preliminary pilot study was to evaluate the feasibility of providing a yoga intervention in an outpatient VA PTSD population and the acceptability of this therapy to this population of Veterans as well as to examine the effects on PTSD symptoms, sleep problems, anger, and quality of life. This investigation is consistent with a major initiative identified in the Department of Veterans Affairs strategic plan to explore innovative treatment approaches, including testing complementary medicine techniques, for treating mental health conditions.

## METHODS

### Participants

All procedures followed were in accordance with the ethical standards of the G.V. (Sonny) Montgomery VA Medical Center Institutional Review Board and the Southeast Louisiana Veterans Health Care System Institutional Review Board. Participant characteristics are listed in Table I.

**TABLE I.**

#### Participant Characteristics

	<b>Value</b>
Age in Years, Mean (SD), (Range 58–64)	62.2 (2.2)
Sex ( <i>n</i> )	
Male	10
Female	2
Military Status ( <i>n</i> )	
Veteran	11
Reserve Member	1
Military Branch ( <i>n</i> )	
Army	7
Navy	4
Marine Corps	1

	<b>Value</b>
Period of Military Service ( <i>n</i> )	
During Vietnam Only	9
During and After Vietnam	1
Post-Vietnam	2
Race ( <i>n</i> )	
Black/African American	6
White	5
American Indian/Alaskan Native	1
Highest Level of Education ( <i>n</i> )	
College Graduate	3
Some College	6
High School Education	3
Living Situation ( <i>n</i> )	
Married and Living With Partners	5
In a Relationship But Not Living With Partners (2 Divorced/Separated; 1 Widowed)	3
Not in a Relationship and Living Alone (1 Divorced/Separated; 1 Widowed)	2
Divorced/Separated, Not in a Relationship and not Living Alone	2
Employment Status ( <i>N</i> )	
Unemployed	10
Steady Employment	1
Temporary Employment	1
Receiving Disability for PTSD ( <i>N</i> )	9

Participants were previously diagnosed with PTSD by a thorough clinical interview conducted by a mental health professional specializing in assessment and treatment of military-related PTSD as part of the routine evaluation procedure in a PTSD Clinical Team at a Veterans Affairs Health Care System in the Southeast region of the United States. Exclusion criteria included current or lifetime bipolar or psychotic disorder; current substance dependence; pregnancy; or a significant medical condition that would interfere with participation in the yoga intervention. Participants were recruited for the study by referral from PTSD Clinical Team clinicians. There were 25 referrals and 15 participants were enrolled in the study. The others were not enrolled because 3 could not accommodate the schedule of the yoga sessions and 7 did not respond in time. Three subjects withdrew during the 6 week yoga intervention and were not included in the data analysis. Reasons for withdrawal included experiencing pain unrelated to the intervention, side effects of new medication, and a daycare scheduling conflict. No adverse effects were reported.

### **Yoga Intervention**

The yoga intervention for this study was developed and taught by 3 certified yoga teachers and was based on the yoga tradition of the Krishnamacharya Healing and Yoga Foundation (KHYF). This yoga style emphasizes a therapeutic approach that links the breath to movement and uses a specific meditative focus. The yoga intervention was designed to provide practitioners the experience of focus, peace, and calmness and to help them develop self-awareness and the ability to be more present in the moment. According to this yoga tradition, by learning these skills participants may gain a sense of control of their thoughts and emotions; feel safer in their daily environments; and experience an overall decrease in stress.

The yoga intervention was held for 1 hour twice a week for 6 weeks (12 sessions total). Each session was structured to include about 3 minutes for self-awareness by “checking in” with the body, mind and breath; 40 minutes of postures with breath awareness; and 5 to 10 minutes of full body relaxation with a focus on extending the exhale and a guided visualization. The simple and gentle yoga postures emphasized flexibility with flowing movements while coordinating the breath with the movement to facilitate the movement and to help maintain focus. Throughout the series, the yoga postures remained fairly consistent. Commonly used postures included a dynamic side angle stretch (a gentle version of *parsvottanasana*) followed by *chakravakasana* (sunbird); *virabhadrasana* (warrior pose) followed by *uttanasana* (standing forward bend); and alternate leg *urdhva prasarita padasana* (upward stretched legs) followed by *apanasana* (knees to chest pose).

The coordinated breath with the postures gradually progressed over the sessions; moving from normal breathing, to extending the exhale, to inserting a pause between the inhale and exhale. Participants were taught Ujjayi breath to learn how to comfortably control the breath, to feel the spaces between the breath, and to achieve an inner focus. Ujjayi breath is slow deep breath involving a slight constriction of the back of the throat so the breath becomes audible. Sound, in the form of humming, was also included to assist in breath extension and to allow participants to feel a gentle vibration to increase the relaxation response. The guided relaxations at the end of each session included themes such as increased sense of well-being, self-nourishment, creating space around the heart, focusing on a peaceful place, and mentally connecting with sources of joy.

All 3 teachers completed a 4-year KHYF Yoga Therapy Training Program. They were present at the beginning and ending sessions. The rest of the sessions were attended by 2 teachers: one observing and the other teaching. Attendance was recorded and written records were kept of feedback given by the instructors and participants at the end of each session.

## **Measures**

PTSD symptoms were measured using the PTSD checklist—military version (PCL-M).<sup>11</sup> The PCL contains 17 items corresponding to the Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.; DSM-IV-TR) criteria for PTSD. Past month symptom severity is indicated using a 5-point scale. Higher scores indicate greater PTSD symptoms. The PCL has been shown to have excellent internal consistency (Cronbach's  $\alpha = 0.94$ ).<sup>41</sup> It has good test–retest reliability,<sup>11</sup> sensitivity, and specificity<sup>41</sup> and has significant convergent validity with established PTSD instruments.

The Pittsburgh Sleep Quality Index (PSQI) was used to measure quality of sleep. The PSQI is a 19 item questionnaire that measures 7 components of sleep: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication,

and daytime dysfunction. Each component score has a range of 0 to 3. The global score is a sum of the component scores and can range from 0 to 21. A score greater than 5 indicates poor sleep quality. The PSQI has good internal consistency (Cronbach's  $\alpha = 0.83$ )<sup>43</sup> and moderate to high convergent validity with other sleep quality scales.

The State-Trait Anger Expression Inventory-2 (STAXI-2) was used to measure anger. This is a 57 item consisting of a 4-point scale that consists of 6 scales and an Anger Expression Index. The 6 scales are as follows: State Anger measures the intensity of anger at a particular time; Trait Anger assesses how often angry feelings are experienced over time; Anger Expression—Out measures expressing anger in aggressive behavior; Anger Expression—In measures how often angry feelings are experienced but suppressed; Anger Control—Out assesses how often the outward expression of anger is controlled; Anger Control—In measures the suppression of angry feelings by calming down. The Anger Expression Index is based on the responses of the Anger Expression and Anger Control scales and provides an overall index of anger expression. The STAXI-2 has been shown to have good concurrent validity.

Quality of life was measured using the Outcome Questionnaire 45.2 (OQ-45.2).<sup>46</sup> The OQ-45.2 is a 45-item scale that measures functioning in 3 domains: Symptom Distress (particularly depression and anxiety), Interpersonal Functioning, and Social Role. Each item is rated using a 5-point Likert scale ranging from 0 to 4. The possible range of scores is from 0 to 180 with higher scores indicating greater psychosocial impairment. The OQ-45.2 has been shown to have good internal consistency (Cronbach's  $\alpha = 0.93$ ) and test-retest reliability ( $r = 0.84$ ) as well as high to moderately high concurrent validity with a variety of standardized scales intended to measure similar variables.

A program evaluation was also given at the end of the last session to provide an opportunity for participants to give written comments about the yoga program. The evaluation also asked participants how much they enjoyed the sessions, how helpful they found the sessions for improving their quality of life, and how likely they were to recommend the program to other Veterans.

### **Data Analysis**

Baseline and post data were assessed for normal distribution using the Shapiro–Wilk test. Differences in the pre- to post-measurements of normally distributed data were analyzed using a 2-tailed paired t-test. Differences in pre- to post-measurements of data that were not normally distributed were analyzed using the Wilcoxon signed rank test. P-values less than 0.05 were considered statistically significant. Responses for one missing question on the PCL-M and one missing question on the PSQI were imputed with the Expectation/Maximization (EM) algorithm. All data were analyzed using SYSTAT (v.12.02).

### **DISCUSSION**

The results of this preliminary study suggest that this yoga program may be an effective adjunctive therapy for improving hyperarousal symptoms of PTSD, including some elements of sleep quality. Total PTSD scores were not significantly improved, however. This yoga program was feasible and had good adherence in a Veteran population. Although most of the Veterans in this study were from the Vietnam era, the fact that the program was well attended and enthusiastically accepted suggests that a yoga intervention may also be appealing to other PTSD Veteran populations, including Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND) Veterans. Offering supplemental or

complementary treatment options as an alternative to traditional psychotherapy may improve treatment engagement with OEF/OIF/OND Veterans since there is a need in this population to improve retention in mental health treatment.

It is noted that improvements were not detected on the OQ-45.2 quality of life measure. However, on the evaluations most Veteran's subjectively rated the yoga classes as being "very" or "extremely" helpful in improving quality of life. Similar observations have been reported in studies with acute stress disorder where participants gave high ratings on evaluations for the "usefulness" of either a writing exercise or a self-help booklet but neither PTSD symptoms nor depression or anxiety were improved compared to control groups using standardized measures. This discrepancy suggests that, although there was a perception of improved quality of life in our study, this perceived improvement may have been too small for measurement or in domains not detected by the quality of life scale.

Although the mechanisms by which yoga may improve PTSD symptoms have not been fully studied or elucidated, a recent theory has been proposed involving the role of  $\gamma$ -aminobutyric acid (GABA). Low serum levels of GABA in subjects involved in road traffic accidents predicted the development of acute PTSD 6 weeks later. At 1 year follow-up, subjects with chronic or delayed onset PTSD had significantly lower post-trauma GABA levels than those who did not develop PTSD. Other evidence for the role of GABA in PTSD is suggested by improvement in PTSD symptoms by treatment with a selective GABA reuptake inhibitor that enhances GABA neurotransmission.<sup>5</sup> Finally, a neuroimaging study demonstrated decreased binding to the GABAA receptor in Veterans with PTSD compared to Veterans without PTSD. Brain GABA levels have been shown to increase as a result of a single yoga session compared to a reading session<sup>56</sup> and brain GABA levels were correlated with improved mood and decreased anxiety in participants of a 12-week yoga intervention as compared to a walking control intervention. Though these studies suggest that GABA may be one of the neurotransmitters that plays a role in the improvement in PTSD symptoms as a result of a yoga intervention, this remains a theory until the appropriate studies are performed.

Limitations of this study include the small sample size and lack of a control group. To address the VA mandate to "explore new approaches to diagnosing and treating mental health ... including complementary and alternative medical treatments,"<sup>4</sup> our aim was to perform a small pilot study to determine if a yoga intervention was acceptable and feasible. The lack of measurable change in overall PTSD and sleep quality scores, and in the anger and quality of life outcomes may have been due to the study being underpowered regarding sample size. Our initial power calculation showed that a sample size of 13 people was needed for the PTSD primary outcome measure to have a 0.80 power to find an effect size of  $d = 0.7$  at an  $\alpha$  level of 0.05. Although we recruited 15 people, only 12 completed the intervention which likely left the study underpowered. In addition, it is possible that the duration of the yoga program was not long enough to result in measurable improvements in total PTSD scores, quality of life (which was perceived as having improved), and some of the sleep subscales. A study with a larger sample size, a longer yoga program, and a control arm matched for time, attention, and expectancy is required to give more definitive results. Finally, this study investigated the yoga program as a whole. Yoga consists of postures, breathing, relaxation, and meditation. Therefore, future studies would be useful to determine which of these components are the most important for the treatment effect and whether there is an additive or synergistic effect when they are combined.

The amount of home practice performed as part of a yoga or meditation intervention has been shown to positively correlate with outcomes. Yoga home practice as part of a mindfulness intervention was significantly correlated with increased psychological well-being, and decreased stress and anxiety. This study had no home practice assigned although the Veterans requested and received a DVD at the end of the study with a sample

session so that they could continue the practice. Assigning a home practice and including compliance measurements in future studies would be helpful to determine if home practice would be associated with greater improvement in PTSD symptoms.

A recent survey on the use of yoga in specialized VA PTSD treatment programs showed that yoga programs have been implemented in 28.8% of VA specialized PTSD treatment programs.<sup>59</sup> The most commonly reported barriers to providing yoga programs were lack of trained staff (84.9%) and lack of funding (53.5%). Lack of research supporting efficacy was also reported by 26.7% of the respondents. If additional studies show yoga to be beneficial for improving PTSD symptoms in Veterans, then there would be evidence to support examining ways to increase access to yoga for PTSD Veterans.

This preliminary study provides evidence that a yoga intervention may improve the hyperarousal symptoms of PTSD. Given that some Veterans do not improve or remain somewhat symptomatic even with the current evidence-based psychotherapy treatments, a simple and inexpensive yoga intervention that is widely accepted among Veterans may be a valuable adjunctive therapy for PTSD treatment.

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### ***Sexual Assault***

## **An Evidence-Based Response to Intimate Partner Violence**

Journal of the American Medical Association

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In June 2013, the World Health Organization (WHO) published *Responding to Intimate Partner Violence and Sexual Violence Against Women*, providing evidence-based recommendations to guide clinicians. This guidance is important because a clinician may be the first professional contact for persons exposed to intimate partner violence (IPV). The guidelines are based on systematic reviews of a range of topics, including identification and approaches to providing care for women and their children after disclosure of IPV and sexual violence. Although there is overlap in the guidance for both conditions, in terms of first-line response and subsequent follow-up care, there are also specific recommendations related to sexual violence (ie, postexposure prophylaxis for infection and emergency contraception). Even though men also experience IPV, the guidelines focus on women because women experience substantially more IPV than men and the morbidity and mortality are more severe. In this Viewpoint, we summarize and discuss the IPV recommendations (Table).

Table. Summary of Selected Intimate Partner Violence Recommendations From the World Health Organization

Table. Summary of Selected Intimate Partner Violence Recommendations From the World Health Organization

Category	Recommendation	Quality of Evidence	Strength of Recommendation
Woman-centered care	Women who disclose any form of violence by an intimate partner (or other family member) should be offered immediate support by clinicians, at a minimum. If clinicians are unable to provide this first-line support, they should ensure that someone else (within their health care setting or another that is easily accessible) is immediately available to do so	Indirect	Strong
Identification of survivors	Universal screening not recommended	Low-moderate	Conditional
	Ask about exposure to IPV when assessing conditions that may be caused or complicated by abuse	Indirect	Strong
Care for survivors	Written information about IPV should be available in all health care settings	No relevant evidence	Conditional
	Women with a preexisting diagnosed or IPV-related mental disorders should receive mental health care delivered by health care professionals with a good understanding of violence against women	Indirect	Strong
	Cognitive behavioral therapy or eye movement desensitization and reprocessing interventions, delivered by health care professionals with a good understanding of violence against women, should be offered to women with posttraumatic stress disorder who are no longer experiencing violence	Low-moderate	Strong
	Women who have spent at least 1 night in a shelter, refuge, or safe house should be offered a structured program of advocacy, support, and/or empowerment	Low	Conditional
	Pregnant women should be offered brief- to medium-duration empowerment counseling (by counselors with specific training about IPV) and IPV advocacy/support, including a safety component	Low	Conditional
Training of clinicians	For children exposed to IPV at home, a psychotherapeutic intervention should be offered	Moderate	Conditional
	Training at prequalification level in first-line support for women who have experienced IPV should be given to clinicians (in particular physicians, nurses, and midwives)	Very low	Strong
Health care policy	Clinicians offering care to women should receive in-service training integrated with training on managing sexual assault	Low-moderate	Strong
	Care for women experiencing IPV should be integrated into existing health services rather than as a stand-alone service	Very low	Strong
Mandatory reporting	Mandatory reporting to the police by the clinicians is not recommended; clinicians should offer to report the incident to the appropriate authorities (including the police) if the woman wants this and is aware of her rights	Very low	Strong

Abbreviation: IPV, intimate partner violence.

*Woman-Centered Care.* Any clinician may need to respond to a patient who discloses IPV, defined as behavior by an intimate partner that causes physical, sexual, or psychological harm, including acts of physical aggression, sexual coercion, psychological abuse, and control. In such situations, health care professionals should, as a minimum, be prepared to provide first-line support. This includes emphasizing confidentiality and recognizing its limits (eg, where there is mandatory reporting of children exposed to IPV), ensuring privacy, being nonjudgmental and supportive and validating that it is not acceptable for anyone to experience violence, and assisting the woman in increasing the safety of herself and her children. In these situations, clinicians may not be able to provide detailed information about available services; however, they need to help the patient access information about resources and facilitate social support or be able to refer the patient to someone who can. It is essential that the response to disclosure of IPV does not result in harm. As highlighted in a meta-analysis of qualitative studies on the experiences and expectations of survivors, attitudes and behaviors to be avoided by the clinicians include judging, pitying, blaming, and trivializing. Women reported positive experiences when they were not pressured to disclose information, leave the relationship, or pursue charges, and were allowed to “progress at their own therapeutic pace.”

*Identification of Survivors of IPV.* WHO guidelines recommend against IPV screening or routine inquiry about exposure to IPV. However, they recommend that clinicians ask about IPV exposure when assessing conditions that may be caused or complicated by IPV (eg, unexplained injuries or symptoms of depression), or when other risks or clinical indications are present. This recommendation differs from the 2013 US Preventive Services Task Force recommendation “that clinicians screen women of childbearing age for IPV....” The WHO recommendation is based on growing evidence that while IPV screening increases the identification of women with IPV, it has not been shown to reduce IPV or to improve

women's health outcomes. In addition, a recent Cochrane review on screening women for IPV in health care settings concluded that there is insufficient evidence to justify screening.

*Care for Survivors of IPV.* Although not all clinicians require in-depth knowledge about interventions that may be helpful to women experiencing IPV, it is important to understand the high prevalence of mental health conditions (ie, depression or posttraumatic stress disorder) associated with such exposure and to appreciate that evidence-based interventions exist for these conditions. The WHO guidelines recommend cognitive behavioral therapy (CBT) interventions for women who are experiencing posttraumatic stress disorder and are no longer exposed to IPV, but note that there is insufficient evidence to recommend CBT when violence is continuing. The guidelines highlight the need for clinicians delivering these interventions to have a good understanding of violence against women, including the risks of disclosure and the appropriateness of interventions after disclosure, which requires specific training, because there is potential for harm. There is some evidence for specific advocacy, support, and empowerment services, but this recommendation is limited to women who have spent at least 1 night in a shelter or to women in the course of prenatal care, because the evidence for improved outcomes outside these contexts is uncertain. In addition, the guidelines recommend psychotherapeutic interventions for children exposed to IPV, based on evidence of effectiveness from trials conducted in North America, although there is a caveat about applicability to low- and middle-income countries, as there is with other recommendations on interventions after disclosure.

*Training of Clinicians.* The key recommendation regarding training is the inclusion of first-line response competence in curricula for all clinicians before and after qualification. There is evidence of the effectiveness of training, particularly when linked with referral pathways to support programs for women experiencing IPV.

*Health Care Policy.* The main recommendation for policy makers is the integration of care for survivors of IPV into health services, rather than as stand-alone services. However, the guidelines acknowledged that one-stop centers that combine health care, social work, counseling, and legal advice have some advantages and may be appropriate in some regions. Although this was a strong recommendation, the quality of evidence was very low, largely based on descriptive and qualitative studies.

*Mandatory Reporting.* Although reporting of IPV disclosures to criminal justice authorities by clinicians is mandatory in some countries and some US states, the guidelines recommend against this policy regarding competent adults. The guideline development group decided that the possible benefits of mandatory reporting did not outweigh impingement of the woman's autonomy and decision making. This was another strong recommendation based on very low-quality evidence.

Each recommendation has a summary of the relevant evidence followed by a narrative (from evidence to recommendations), which also highlights when the guideline development group did not unanimously support a recommendation. An example is the rationale for not recommending mandatory reporting. These narratives provide some insight into how the guideline development group interpreted the evidence and the group's considerations when formulating recommendations (ie, resource constraints in low- and middle-income countries).

Violence against women is a complex psychosocial and international problem. Clinicians should be part of a larger, multisystem, and coordinated solution that takes into account individual-, community-, and system-level responses, as well as a lifespan approach to violence risk assessment and prevention for those who experience IPV, as well as for perpetrators. Research evidence should inform clinical actions, regardless of the disease, condition, or exposure. Although the quality of available supporting evidence is low to moderate, the new WHO guidelines provide

evidence-based recommendations to assist clinicians to respond in a caring, respectful, and safe manner to women exposed to violence and may contribute to a better health care response to IPV internationally.

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### ***Substance Abuse***

## **Abusive Prescribing of Controlled Substances — A Pharmacy View**

New England Journal of Medicine

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21 August, 2013

Public health advocates are increasingly focused on illness and deaths caused by inappropriate use of controlled substances — in particular, opioid analgesics. Opioid prescriptions have increased dramatically, by more than 300% between 1999 and 2010. This increase has led to substantial iatrogenic disease. Most strikingly, the number of deaths due to overdose in the United States increased from 4000 in 1999 to 16,600 in 2010. Indeed, overdose is now the second-leading cause of accidental death in this country, where more than 2.4 million people were considered opioid abusers in 2010.

The causes of increases in prescriptions and the prevalence of abuse are manifold. In the mid-1990s, advocates for treatment of chronic pain began arguing that pain was largely undertreated and appropriately exhorted clinicians to be more liberal in their treatment. In addition, a number of new formulations of opioid agents became available, with purported advantages in analgesia.

But perhaps just as important, inappropriate prescribing has grown. The worst form of such prescribing occurs in so-called pill mills, wherein fully licensed physicians with valid Drug Enforcement Administration (DEA) numbers write prescriptions that provide large quantities of powerful analgesics to individual patients. Such bogus pain clinics cater to younger patients, operate on a cash basis, and draw clients from a broad geographic area. States and the DEA have attempted to curb pill-mill activities — the best example being Florida's closure of 254 "pain clinics" — but the efficacy of such regulation is unclear.

Pharmacies have a role to play in the oversight of prescriptions for controlled substances, and opioid analgesics in particular. Under the Controlled Substances Act, pharmacists must evaluate patients to ensure the appropriateness of any controlled-substance prescription. In addition, state boards of pharmacy regulate the distribution of opioid analgesics and other controlled substances through the discretion of pharmacists. Yet in the majority of cases of potential abuse, pharmacists face a patient who has a legal prescription from a licensed physician, and they have access to very little other background information. That makes it difficult for individual pharmacists to use their own partially informed judgment to identify prescriptions that have come from a pill-mill doctor.

Chain pharmacies, however, have the advantage of aggregated information on all prescriptions filled at the chain. At CVS, we recently instituted a program of analysis and actions to limit inappropriate prescribing. Our program was intended to identify and take action against physicians and other prescribers who exhibited extreme patterns of use of "high-risk drugs" relative to other prescribers. We aimed to minimize the potential for falsely identifying legitimate prescribers (false positives), accepting that doing so might result in a failure to identify some suspicious prescribers.

August 2013

We identified high-risk prescribers by benchmarking them against others on several parameters. We used data from submitted prescriptions from March 2010 through January 2012 for hydrocodone, oxycodone, alprazolam, methadone, and carisoprodol. Prescribers were compared with others in the same geographic region who had the same listed specialty. The first parameters were the volume of prescriptions for high-risk drugs and the proportion of the prescriber's prescriptions that were for such drugs, as compared with the volume and proportion for others in the same specialty and region; the thresholds for suspicion were set at the 98th percentile for volume and the 95th percentile for proportion. Next, prescribers were evaluated with regard to the number of their patients who paid cash for high-risk–drug prescriptions and the percentage of their patients receiving high-risk drugs who were 18 to 35 years of age. In both cases, the thresholds for suspicion were set at the 90th percentile among clinicians in the same region and specialty. Finally, we compared the prescriptions for noncontrolled substances with the prescriptions for controlled substances within the prescriber's practice on the same parameters. To minimize the possibility that we would suspend dispensing privileges for clinicians who were appropriately treating patients, we attempted to interview physicians whom we'd identified as outliers to ascertain the nature of their practice and their use of controlled substances.

We initially identified 42 outliers (see table Prescribing Habits of Outlier Prescribers.) from our database of nearly 1 million prescribers; 17 of the 42 failed to respond to our three letters requesting an interview, despite our indication in the second and third letters that we would stop filling the clinician's controlled-substance prescriptions if he or she would not speak with us. Eight prescribers sent a written response, and one response was sufficiently detailed to convince us that the prescribing was appropriate. The other seven responses were inadequate, and the prescribers refused to engage in a telephone discussion. Two prescribers retained an attorney, and future conversation occurred through legal channels. We considered these 26 clinicians nonresponsive.

The remaining 15 were contacted by phone, and 5 gave us legitimate reasons why their practice had the identified characteristics — in particular, that each was the only practitioner in a given geographic area caring for patients with chronic pain. The remaining 10 either maintained that their approach was legitimate but that they didn't have to explain why or averred that they planned to curb their prescribing of narcotics. For all 10 of these clinicians, we decided not to fill their controlled-substance prescriptions through our pharmacy. The same approach was taken for the 26 nonresponsive clinicians. Surprisingly, now 9 months after we stopped filling controlled-substance prescriptions for these clinicians' patients, we've had contact from only 3 of them requesting reinstatement in our pharmacy chain. The table provides details on the 42 outliers' practices, as compared with those of the average prescriber in our database. There was no clear regional concentration of outliers.

Our program is certainly not a comprehensive solution, but it provides some sense of the kind of inappropriate prescribing that is going on in our health care system. We believe that some of these clinicians may be part of pill mills, doing cursory examinations in high volumes of patients, all of whom then receive opioid analgesics. People seeking to abuse these medications will travel long distances to obtain them and often deal in cash only. These patients are generally younger than the average patient with chronic disease. A comprehensive solution would involve the use of a national prescription-drug–monitoring database that would be used by clinicians at the point of prescribing and by all pharmacies at the point of dispensing. This enhanced view of a patient's controlled-substance history and behaviors would support both prescribers and pharmacists in applying their professional judgment regarding the appropriateness of dispensing a controlled substance.

As we noted, pharmacists have an ethical duty, backed by both federal and state law, to ensure that a prescription for a controlled substance is appropriate. A young person traveling a good distance to fill a prescription and paying cash should raise some concerns for a pharmacist. If the prescription is valid, the pharmacist might have limited grounds on which to deny medication to someone who might be in pain. Yet the DEA has

now identified both pharmaceutical distributors and chain pharmacies as part of the problem, encouraging our industry to develop new programs to reduce inappropriate use.

Our findings provide a lens into the problem we face as a country. Programs providing greater transparency regarding controlled-substance prescribing, such as mandatory use of e-prescribing for all controlled substances and a national, uniform program of prescription-drug monitoring, would help pharmacists and clinicians target interventions more accurately to help patients who are abusing medications. Some state solutions, such as the Massachusetts database that allows clinicians to look up their own patients' prescriptions, also have merit. Analyses of aggregated data like ours can also target patterns of abuse by both prescribers and patients. Given the growing use of controlled substances and the resulting illness and deaths, more innovative use of transparent data is only prudent.

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## **Concurrent Naltrexone and Prolonged Exposure Therapy for Patients With Comorbid Alcohol Dependence and PTSD**

Journal of the American Medical Association

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### **ABSTRACT**

**Importance** Alcohol dependence comorbid with posttraumatic stress disorder (PTSD) has been found to be resistant to treatment. In addition, there is a concern that prolonged exposure therapy for PTSD may exacerbate alcohol use.

**Objective** To compare the efficacy of an evidence-based treatment for alcohol dependence (naltrexone) plus an evidence-based treatment for PTSD (prolonged exposure therapy), their combination, and supportive counseling.

**Design, Setting, and Participants** A single-blind, randomized clinical trial of 165 participants with PTSD and alcohol dependence conducted at the University of Pennsylvania and the Philadelphia Veterans Administration. Participant enrollment began on February 8, 2001, and ended on June 25, 2009. Data collection was completed on August 12, 2010.

**Interventions** Participants were randomly assigned to (1) prolonged exposure therapy plus naltrexone (100 mg/d), (2) prolonged exposure therapy plus pill placebo, (3) supportive counseling plus naltrexone (100 mg/d), or (4) supportive counseling plus pill placebo. Prolonged exposure therapy was composed of 12 weekly 90-minute sessions followed by 6 biweekly sessions. All participants received supportive counseling.

**Main Outcomes and Measures** The Timeline Follow-Back Interview and the PTSD Symptom Severity Interview were used to assess the percentage of days drinking alcohol and PTSD severity, respectively, and the Penn Alcohol Craving Scale was used to assess alcohol craving. Independent evaluations occurred prior to treatment (week 0), at posttreatment (week 24), and at 6 months after treatment discontinuation (week 52).

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**Results** Participants in all 4 treatment groups had large reductions in the percentage of days drinking (mean change, -63.9% [95% CI, -73.6% to -54.2%] for prolonged exposure therapy plus naltrexone; -63.9% [95% CI, -73.9% to -53.8%] for prolonged exposure therapy plus placebo; -69.9% [95% CI, -78.7% to -61.2%] for supportive counseling plus naltrexone; and -61.0% [95% CI, -68.9% to -53.0%] for supportive counseling plus placebo). However, those who received naltrexone had lower percentages of days drinking than those who received placebo (mean difference, 7.93%;  $P = .008$ ). There was also a reduction in PTSD symptoms in all 4 groups, but the main effect of prolonged exposure therapy was not statistically significant. Six months after the end of treatment, participants in all 4 groups had increases in percentage of days drinking. However, those in the prolonged exposure therapy plus naltrexone group had the smallest increases.

**Conclusions and Relevance** In this study of patients with alcohol dependence and PTSD, naltrexone treatment resulted in a decrease in the percentage of days drinking. Prolonged exposure therapy was not associated with an exacerbation of alcohol use disorder.

**Trial Registration** [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: NCT00006489

Alcohol dependence and posttraumatic stress disorder (PTSD) are highly comorbid, yet little is known about how best to treat this large, highly dysfunctional, and distressed population. Even though studies of treatments for alcohol dependence do not exclude patients with PTSD, symptoms of PTSD are not targeted with these treatments. The failure to address PTSD is deleterious because patients with alcohol dependence and PTSD relapse sooner than patients with alcohol dependence and other comorbid Axis I psychiatric diagnoses. In contrast, treatment studies for PTSD typically exclude patients with comorbid alcohol dependence because of the concern that alcohol dependence will interfere with the patient's ability to benefit from PTSD treatment or fear that the PTSD treatment will exacerbate drinking behavior.

Previous trials of concurrent therapies for substance use disorders and PTSD have demonstrated improvements in PTSD, but have not shown clear benefits for the treatment of substance use disorder. Only 1 published randomized trial used cognitive behavioral therapy for alcohol dependence plus 150 mg of sertraline (or placebo) for PTSD. Alcohol use and PTSD symptoms decreased during treatment, but the study design did not allow separating the unique effects of cognitive behavioral therapy from the effects of the medication.

We compared the efficacy of naltrexone, which is an evidence-based treatment for alcohol dependence, and prolonged exposure therapy, which is an evidence-based treatment for PTSD, separately and in combination, along with supportive counseling. Naltrexone is hypothesized to decrease drinking via attenuation of craving for alcohol, and prolonged exposure therapy is hypothesized to reduce drinking via amelioration of PTSD symptoms that can lead to self-medication with alcohol. Our 2 × 2 study design tested the hypotheses that (1) participants receiving naltrexone would show significantly greater reductions in drinking than those receiving placebo; (2) participants receiving prolonged exposure therapy would show greater reductions in PTSD symptom severity than those who do not receive prolonged exposure therapy; and (3) participants receiving combined treatment would show superior outcomes in both decreased drinking and PTSD severity.

## METHODS

### Participants

Participants were treatment-seeking individuals recruited through advertisements and professional referrals to the University of Pennsylvania's Center for the Treatment and Study of Anxiety and the Philadelphia Veterans Affairs Hospital. The demographic and trauma information collected at baseline appear in Table 1. Inclusion criteria were (1) current PTSD and alcohol dependence according to the *Diagnostic and Statistical Manual*

of *Mental Disorders* (Fourth Edition) (*DSM-IV*); (2) clinically significant trauma-related symptoms, as indicated by a score of at least 15 on the PTSD Symptom Severity Interview (PSS-I); and (3) heavy drinking in the past 30 days, defined as an average of more than 12 standard alcohol drinks per week with at least 1 day of 4 or more drinks determined by the Timeline Follow-Back Interview (TFBI). Exclusion criteria were (1) current substance dependence other than nicotine or cannabis; (2) current psychotic disorder (eg, schizophrenia, bipolar disorder); (3) clinically significant suicidal or homicidal ideation; (4) opiate use in the month prior to study entry; (5) medical illnesses that could interfere with treatment (eg, AIDS, active hepatitis); or (6) pregnancy or nursing.

Table 1. Baseline Characteristics

	PTSD Exposure Therapy		Supportive Counseling	
	Plus Naltrexone (n = 40)	Plus Placebo (n = 40)	Plus Naltrexone (n = 42)	Plus Placebo (n = 43)
Age, mean (95% CI), y	40.1 (36.7-43.5)	44.7 (41.8-47.7)	44.9 (41.8-47.9)	41.2 (38.6-43.9)
Sex				
Female	13 (32.5)	13 (32.5)	16 (38.1)	15 (34.9)
Male	27 (67.5)	27 (67.5)	26 (61.9)	28 (65.1)
Race/ethnicity				
Black	30 (75.0)	28 (70.0)	21 (50.0)	26 (60.5)
White	9 (22.5)	8 (20.0)	19 (45.2)	14 (32.6)
Hispanic	1 (2.5)	3 (7.5)	2 (4.8)	1 (2.3)
Native American	0	0	0	1 (2.3)
Other	0	1 (2.5)	0	1 (2.3)
Types of trauma				
Sexual assault	12 (30.0)	11 (27.5)	11 (26.2)	8 (18.6)
Physical assault	16 (40.0)	12 (30.0)	18 (42.9)	16 (37.2)
Combat	4 (10.0)	7 (17.5)	4 (9.5)	4 (9.3)
Other	8 (20.0)	10 (25.0)	9 (21.4)	15 (34.9)
Time since trauma, mean (SD), y	12.3 (13.5)	10.3 (13.0)	12.2 (13.2)	10.3 (12.2)

Abbreviation: PTSD, posttraumatic stress disorder.

\* Values are expressed as number (percentage) unless otherwise indicated. All participants received supportive counseling.

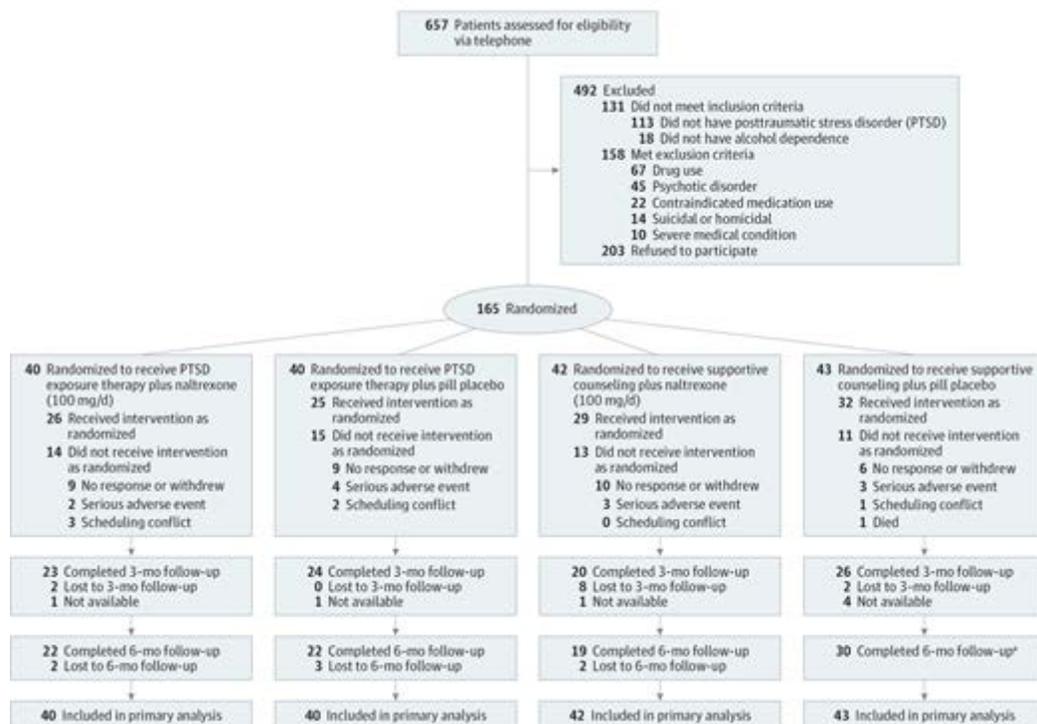
## Procedure

The University of Pennsylvania institutional review board approved the protocol. After receiving written informed consent, participants completed an intake assessment, which included a physical examination, laboratory assessments, and a psychiatric evaluation. Eligible participants completed a baseline evaluation and were then randomly assigned to 1 of 4 treatment groups in which they received 100 mg/d of naltrexone or placebo plus prolonged exposure therapy or no prolonged exposure therapy. Prior to beginning treatment, participants completed outpatient medical detoxification ( $\geq 3$  consecutive days of abstinence from alcohol) measured via self-report and breath testing for alcohol. During detoxification, oxazepam was administered as needed to manage symptoms of alcohol withdrawal. All patients received supportive counseling focused on medication management (see treatment descriptions below). Participant enrollment began on February 8, 2001, and ended on June 25, 2009 (Figure 1). Data collection was completed on August 12, 2010.

Figure 1.

## Flow of Participants Through the Trial

All participants received supportive counseling. <sup>a</sup>Some participants who did not complete the 3-month follow-up returned to complete the 6-month follow-up.



## Measures

The PSS-I is a clinician-rated interview corresponding to the *DSM-IV* symptom criteria. It was administered by evaluators, who were blinded to group assignment, prior to treatment, every 4 weeks during treatment, at posttreatment (week 24), and at follow-up (weeks 38 and 52). The PSS-I has a range of scores from 0 to 51 with higher scores indicating more severe PTSD symptoms.

The TFBI is an interview that uses a calendar method to assess when and how much alcohol was consumed. The TFBI was used to calculate the percentage of days drinking (PDD) at pretreatment, each visit during treatment, posttreatment (week 24), and 6 months after treatment discontinuation (week 52). Because the number of days between assessment points varied, we presented drinking days as a percentage of total

days. For descriptive purposes, we also calculated the number of days drinking in the past 90 days at baseline and week 52. Higher scores for PDD and drinking days in the past 90 days indicate worse drinking outcomes.

The Penn Alcohol Craving Scale is a 5-item self-administered measure of alcohol craving during the prior week that was completed at every visit. The range of possible scores is 0 to 30, with higher scores indicating a higher level of craving.

### **Treatments**

Naltrexone is an opiate antagonist approved by the US Food and Drug Administration to treat alcohol dependence. The target dose of naltrexone was 100 mg/d, starting with 50 mg/d for a minimum of 3 days and titrating up within 1 week; 3 patients were unable to tolerate the 100-mg/d dose and were titrated down to 50 mg/d. The 100-mg/d dose of naltrexone used in this study is higher than the 50-mg/d dose recommended for treatment of alcohol dependence, but much lower than the 300-mg/d dose that has been associated with elevations in liver enzyme levels. Compliance with the dosing regimen was monitored by weekly pill counts during the first 3 months and by biweekly counts for the next 3 months.

Prolonged exposure therapy consisted of 12 weekly 90-minute sessions followed by 6 biweekly sessions and included repeated imaginal exposure (ie, revisiting and recounting traumatic memories) and processing the memory (ie, discussing thoughts and feelings related to revisiting the memory). Participant homework consisted of repeated listening to a recording of the recounting made during the session, and repeated in vivo exposure to safe situations he/she avoided because of trauma-related distress. When the participant demonstrated no or minimal distress when recounting the traumatic memory and confronting traumatic reminders, any remaining sessions focused on other psychosocial problems.

Supportive counseling was based on the BRENDA model, which combines medication management with compliance enhancement techniques based on motivational interviewing. All participants received eighteen 30- to 45-minute sessions of supportive counseling, administered by a study nurse, which included dispensing medication, monitoring compliance, assessing and providing education about alcoholism, and offering support and advice concerning drinking. Visits were weekly during the first 3 months and biweekly during the remaining 3 months.

For more details about the treatment methods and sample, see Foa and Williams.

### **Data Analyses**

Two-tailed tests adopting an  $\alpha$  level of .05 were conducted to test differences in change in outcomes among treatment groups. We conducted piecewise growth modeling using hierarchical linear and nonlinear modeling (version 6.34) to estimate different slopes during the treatment phase and the follow-up phase. Hierarchical linear and nonlinear modeling is robust to missing data due to dropout during treatment and follow-up. Using hierarchical linear and nonlinear modeling does not exclude any data, thus rendering replacement or imputation for missing values unnecessary. A nonlinear model (natural log number of weeks) fit the data best for the PSS-I and alcohol craving outcomes; for PDD, a piecewise model with a hyperbolic transformation of the number of weeks fit the data best.

All change parameters were modeled as random effects. The main effects of treatment were evaluated by coding time variables such that intercept terms of the piecewise growth models represented posttreatment outcome levels (ie, centering the time variables at posttreatment), and by including dummy-coded treatment group variables as predictors of the intercept. A graphical examination of the growth curve results revealed potential treatment differences in change over time during the follow-up period. Therefore, we conducted exploratory tests for the following

interactions during follow-up: prolonged exposure therapy × time, naltrexone × time, and prolonged exposure therapy × naltrexone × time. Dummy-coded variables and interaction terms for prolonged exposure therapy and naltrexone were included in the level 2 component of the model as predictors of the change parameter during follow-up. The Cohen *d* statistic is reported for between-group effect sizes (*d* = 0.25 for small, *d* = 0.50 for medium, and *d* = 0.80 for large). All analyses were conducted with the intent-to-treat sample.

The Mplus statistical software version 5.1 was used for a Monte Carlo simulation post hoc power analysis, which used parameter estimates from the data analysis to provide estimates of obtained power. These analyses produced power estimates of 0.90 or higher to detect medium (*d* = 0.50) effect size differences of 20.6 to 22.8 for change in PDD and 7.1 to 10.2 for change in PTSD severity (on the PSS-I) during treatment. The analyses also produced power estimates of 0.90 or higher to detect medium effect size differences of 17.4 to 18.1 for PDD and 7.1 to 8.4 for PTSD severity (PSS-I) during follow-up. Exploratory  $\chi^2$  analyses were conducted to examine differences in the percentage of participants classified as having achieved low PTSD severity (ie,  $\leq 10$  on the PSS-I at 6 months after treatment discontinuation).

## RESULTS

### Preliminary Analyses

There were 165 participants with PTSD and alcohol dependence. Fifty-three participants (32.1%) dropped out of the study prior to the end of the treatment period. This rate did not significantly differ ( $\chi^2_3 = 1.55$ ;  $P = .67$ ) across treatment groups ( $n = 165$ ): 35% for prolonged exposure therapy plus naltrexone, 38% for prolonged exposure therapy plus placebo, 31% for supportive counseling plus naltrexone, and 26% for supportive counseling plus placebo. Twelve participants were removed from the study because of serious adverse events (serious suicidal ideation,  $n = 7$ ; serious medical illness,  $n = 3$ ; psychotic symptoms,  $n = 1$ ; death,  $n = 1$ ; however, none of these events was determined to be related to the study). Analysis of variance and  $\chi^2$  analysis revealed no significant differences for demographic and pretreatment outcome variables across groups (Table 1). The median number of years since the index trauma was 5.15 (25th percentile, 1.34; 75th percentile, 20.21).

### Treatment Adherence

#### Prolonged Exposure Therapy

On average, participants completed a mean of 6.18 (SD, 3.86) exposure sessions in the prolonged exposure therapy plus naltrexone group vs a mean of 6.48 (SD, 3.49) sessions in the prolonged exposure therapy plus placebo group ( $P = .73$ ). Treatment adherence for prolonged exposure therapy was monitored by 3 doctoral-level clinicians. Of the total prolonged exposure therapy sessions provided, 15% were randomly selected to assess treatment adherence. The overall adherence rate was 96%. Three adherence raters performed separate ratings on 10% of the sessions. Interrater reliability was 97.8% (95% CI, 91.7%-99.9%).

#### Medication

The average number of days of detoxification was 4.45 (range, 3-14 days). All but 10 participants were able to reach and remain on 100 mg/d of naltrexone; 9 were titrated down to 50 mg/d and 1 participant refused medication and dropped out of the study. There were 141 participants (85%) who met criteria for adherence to medication and supportive counseling (defined as  $\geq 80\%$  adherence to medication and attendance to supportive counseling): 34 (85.0%) in the prolonged exposure therapy plus naltrexone group, 34 (85.0%) in the prolonged exposure therapy plus placebo

group, 36 (85.7%) in the supportive counseling plus naltrexone group, and 37 (86.0%) in the supportive counseling plus placebo group. Differences between groups were not statistically significant ( $P = .99$ ).

### Drinking Outcome

Participants in all groups reported reductions in PDD during treatment (Table 2). At posttreatment, a significant main effect of naltrexone emerged (mean difference = 7.93%,  $P = .008$ ,  $d = 0.42$ ) such that patients receiving naltrexone had lower PDD (mean, 5.38%; 95% CI, 2.23% to 8.54%) than patients receiving placebo (mean, 13.29%; 95% CI, 8.45% to 18.12%). At posttreatment, the main effect of prolonged exposure therapy ( $P = .51$ ) and the interaction of naltrexone  $\times$  prolonged exposure therapy ( $P = .53$ ) were not statistically significant. During the 6 months following treatment discontinuation, a significant prolonged exposure therapy  $\times$  time interaction emerged ( $P = .01$ ,  $d = 0.41$ ) such that patients receiving prolonged exposure therapy had a mean change in PDD during follow-up of 3.6% (95% CI, -2.2% to 9.5%), which was not significant, whereas patients not receiving prolonged exposure therapy exhibited a mean increase in PDD during follow-up of 15.9% (95% CI, 8.8% to 23.1%). The interactions of naltrexone  $\times$  time ( $P = .98$ ) and prolonged exposure therapy  $\times$  naltrexone  $\times$  time ( $P = .39$ ) were not statistically significant during follow-up.

Table 2. Summary of the Piecewise Growth Curve Models for Percentage of Days Drinking and Craving to Drink

	Mean (95% CI), % of Days				
	Pretreatment (Wk 0)	Posttreatment (Wk 24)	Change Between Pretreatment and Posttreatment	Follow-up (Wk 52)	Change Between Posttreatment and Follow-up
<b>Drinking</b>					
PTSD exposure therapy					
Plus naltrexone	71.2 (62.5 to 79.9)	7.3 (1.9 to 12.7)	-63.9 (-73.6 to -54.2)	8.8 (3.3 to 14.3)	1.5 (-0.9 to 3.8)
Plus placebo	78.6 (71.4 to 85.6)	13.4 (5.5 to 21.1)	-63.9 (-73.9 to -53.8)	18.9 (8.8 to 29.1)	5.6 (0.2 to 11.0)
Supportive counseling					
Plus naltrexone	75.4 (67.1 to 83.5)	3.5 (0.1 to 6.8)	-69.9 (-78.7 to -61.2)	21.5 (10.6 to 32.4)	18.0 (13.2 to 22.8)
Plus placebo	74.1 (66.4 to 81.8)	13.2 (7.3 to 19.2)	-61.0 (-68.9 to -53.0)	27.3 (14.7 to 40.0)	14.1 (8.8 to 19.4)
<b>Craving to drink</b>					
PTSD exposure therapy					
Plus naltrexone	17.9 (15.8 to 20.1)	5.1 (3.4 to 6.7)	-13.6 (-16.1 to -11.2)	6.0 (4.0 to 8.1)	1.0 (-1.2 to 3.2)
Plus placebo	19.2 (16.3 to 22.1)	9.1 (6.1 to 12.2)	-10.1 (-13.5 to -6.63)	6.9 (4.2 to 9.7)	-2.1 (-5.2 to 1.0)
Supportive counseling					
Plus naltrexone	17.7 (15.3 to 20.0)	8.0 (6.0 to 10.1)	-9.8 (-12.3 to -7.2)	7.4 (4.2 to 10.6)	-0.6 (-3.4 to 2.3)
Plus placebo	18.7 (16.7 to 20.7)	10.3 (8.2 to 12.4)	-8.7 (-11.4 to -6.1)	8.9 (6.4 to 11.4)	-1.4 (-3.4 to 0.7)

Abbreviation: PTSD, posttraumatic stress disorder.

\* All participants received supportive counseling.

All groups showed reductions in alcohol craving during treatment (Table 2). A significant main effect of naltrexone emerged (mean difference = 3.14,  $P = .008$ ,  $d = 0.43$ ) at posttreatment such that the 2 naltrexone groups had less alcohol craving (mean craving, 6.6; 95% CI, 5.2-7.9) than the 2 placebo groups (mean craving, 9.7; 95% CI, 7.9-11.6). Neither the main effect of prolonged exposure therapy ( $P = .08$ ) nor the interaction of prolonged exposure therapy  $\times$  naltrexone ( $P = .44$ ) was significant at posttreatment. During follow-up, the interactions of prolonged

exposure therapy × time ( $P = .55$ ), naltrexone × time ( $P = .66$ ), and prolonged exposure therapy × naltrexone × time ( $P = .63$ ) were not statistically significant, with none of the groups exhibiting significant changes in alcohol craving during follow-up.

### PTSD Outcome

All 4 groups showed reductions in PSSI (or PTSD symptoms) during the treatment period (Table 3). The main effect of prolonged exposure therapy at posttreatment was not significant (mean difference = 2.63,  $P = .15$ ,  $d = 0.23$ ). At posttreatment, the main effects of naltrexone ( $P = .70$ ) and the interaction of prolonged exposure therapy × naltrexone ( $P = .80$ ) were also not significant. The interactions of prolonged exposure therapy × time ( $P = .55$ ), naltrexone × time ( $P = .66$ ), and prolonged exposure therapy × naltrexone × time ( $P = .63$ ) were not statistically significant for the follow-up period.

Table 3. Summary of the Piecewise Growth Curve Models for Posttraumatic Stress Disorder (PTSD) Symptoms

PTSD Symptom Severity Interview	Mean (95% CI), % of Days				
	Pretreatment (wk 0)	Posttreatment (wk 24)	Change Between Pretreatment and Posttreatment	Follow-up (wk 52)	Change Between Posttreatment and Follow-up
PTSD exposure therapy					
Plus naltrexone	30.3 (27.7 to 32.9)	12.2 (8.2 to 16.1)	-19.1 (-23.1 to -15.09)	7.9 (4.1 to 11.8)	-4.1 (-7.6 to -0.6)
Plus placebo	27.7 (24.7 to 30.8)	13.3 (9.3 to 17.3)	-16.1 (-20.8 to -11.3)	10.8 (6.3 to 15.2)	-2.5 (-6.3 to 1.3)
Supportive counseling					
Plus naltrexone	27.1 (24.7 to 30.8)	15.3 (12.2 to 18.3)	-12.40 (-15.79 to -8.97)	10.9 (7.2 to 14.6)	-4.2 (-8.1 to -0.3)
Plus placebo	27.5 (25.4 to 29.6)	15.5 (12.4 to 18.6)	-11.6 (-14.1 to -9.1)	11.1 (8.2 to 14.1)	-4.3 (-6.9 to -1.6)

\* All participants received supportive counseling.

In an exploratory analysis, 70.0% of participants in the prolonged exposure therapy plus naltrexone group achieved a low level of PTSD severity (ie,  $\leq 10$  on the PSS-I at 6 months after treatment discontinuation) vs 55.0% of participants in the prolonged exposure therapy plus placebo group, 43.9% of the supportive counseling plus naltrexone group, and 37.2% of the supportive counseling plus placebo group ( $P = .02$ ).

### DISCUSSION

This is the first study, to our knowledge, that used a design which allowed for separate examination of the effects of an evidence-based medication for alcohol dependence (naltrexone), an evidence-based psychotherapy for PTSD (prolonged exposure), and their combination, on both drinking and PTSD symptoms among individuals with comorbid alcohol dependence and PTSD. Participants in all 4 groups showed a significant reduction in PDD. However, at posttreatment, participants who received naltrexone showed significantly lower PDD than participants who received placebo. This finding is consistent with previous studies showing that naltrexone is an effective treatment for alcohol dependence. One hypothesized mechanism of naltrexone's effect on drinking is through the attenuation of alcohol craving. The results of the current study support this hypothesis; participants who received naltrexone had lower cravings for alcohol than those who received placebo.

All 4 groups showed a significant reduction in PTSD symptoms during treatment. However, there was no increased improvement in PTSD symptoms from prolonged exposure therapy compared with supportive counseling, which is inconsistent with a large body of evidence that

prolonged exposure is an effective treatment for PTSD. This null finding may be due to the fact that all participants received supportive counseling. Perhaps the nonspecific factors involved in supportive counseling masked some of the unique effects of prolonged exposure therapy. In addition, attendance to prolonged exposure therapy sessions was lower in this study than in other trials of prolonged exposure therapy. The relatively low number of prolonged exposure therapy sessions received by the participants, combined with the fact that all participants received supportive counseling, prevents strong conclusions about the efficacy of prolonged exposure therapy on PTSD in patients with alcohol dependence and PTSD.

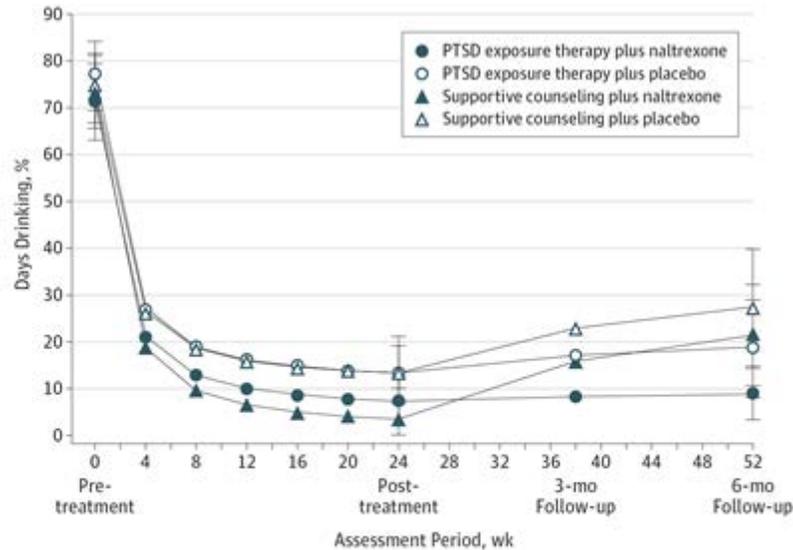
Importantly, our findings indicated that prolonged exposure therapy was not associated with increased drinking or alcohol craving, a concern that has been voiced by some investigators. In fact, reduction in PTSD severity and drinking was evident for all 4 treatment groups. This finding contradicts the common view that trauma-focused therapy is contraindicated for individuals with alcohol dependence and PTSD because it may exacerbate PTSD symptoms and thereby lead to increased alcohol use.

Participants in this study were followed up for 6 months after treatment discontinuation. During this follow-up period, participants who received prolonged exposure therapy retained low drinking levels, whereas participants who did not receive prolonged exposure therapy had a higher relapse rate. Exploratory analyses suggest that naltrexone plus prolonged exposure therapy vs naltrexone alone, prolonged exposure therapy alone, or supportive counseling alone was associated with a lower rate of relapse of alcohol dependence, as measured by PDD (Figure 2). Further evidence that prolonged exposure therapy may reduce the rate of relapse comes from our findings of the main effect of prolonged exposure therapy on PDD during follow-up. This finding suggests that receiving prolonged exposure therapy plus naltrexone protects patients with alcohol dependence and PTSD from relapse in drinking after treatment discontinuation.

Figure 2.

### **Mean Percentage of Days Drinking During Treatment and Follow-up**

Preliminary growth curve analyses indicated that change during treatment was nonlinear and modeling time using a hyperbolic transformation of the number of weeks ( $\text{time} = 1 - [1/\{\text{weeks} + 1\}]$ ) yielded the best fit to the data with drastic decreases in percentage of days drinking during the earlier part of treatment that flattened out over time. Error bars indicate 95% confidence intervals; PTSD, posttraumatic stress disorder.



No. of patients  
 PTSD exposure therapy  
 Plus naltrexone  
 Plus placebo  
 Supportive counseling  
 Plus naltrexone  
 Plus placebo

40	40	38	34	34	31	28	26	21
40	40	39	34	33	29	28	25	23
42	41	37	34	34	31	31	28	19
43	41	40	36	36	35	34	32	26

To our knowledge, this study is the first randomized trial of patients with comorbid alcohol dependence and PTSD to demonstrate significant differences in outcomes between an active treatment and a control comparison. This may be due to differences between the treatments that were used in the current study and those used in the other studies. Brady et al used sertraline for treating PTSD and cognitive behavioral therapy for treating alcohol dependence, neither of which have been found to have strong effects on the respective target disorder. Hien et al used the Seeking Safety treatment program, a type of cognitive behavioral therapy that targets substance use disorders and comorbid PTSD, which has not gained strong support for its efficacy with either disorder. Our results highlight the importance of selecting treatments with strong evidence for their efficacy with both disorders when treating patients with alcohol dependence and PTSD.

As noted above, attendance to prolonged exposure therapy sessions was low relative to our previous PTSD treatment studies. However, our previous studies excluded patients with PTSD and comorbid alcohol dependence. Low adherence to therapy has been found in other studies of patients with PTSD and substance use disorders. For example, Hien et al found that only 12.2% of patients completed all 12 sessions of the Seeking Safety treatment program. The relatively low adherence to prolonged exposure therapy sessions may be explained in part by our clinical observation that participants in the study experienced multiple life difficulties (eg, homelessness, health problems). This observation is consistent

with Drapkin et al's findings. It is encouraging to note, however, that patients who received 6 or more sessions of prolonged exposure therapy benefitted substantially from treatment, suggesting that a relatively low dose of prolonged exposure therapy is effective in this population.

Several caveats should be noted. First, because of concern for the safety of these highly impaired patients, supportive counseling was provided for all 4 treatment groups. As a result, we were unable to evaluate the separate contribution of this intervention to the overall outcome. Second, attendance to prolonged exposure therapy sessions was relatively low, therefore the efficacy of a full treatment dose of prolonged exposure therapy on PTSD and drinking behavior could not be evaluated. Future research should examine ways to increase treatment adherence in this population. Third, we relied on pill counting to assess adherence to medication; the use of more sophisticated methods may have increased the reliability of assessing adherence to medication. Fourth, medication management and prolonged exposure therapy were delivered by separate clinicians. This model may be less readily applicable in mental health community clinics or primary care settings because it requires greater logistical coordination than an integrated model in which both interventions would be delivered by the same clinician. Despite these limitations, our trial demonstrates that (1) patients with comorbid alcohol dependence and PTSD benefit from naltrexone treatment; (2) prolonged exposure therapy is not associated with exacerbation of alcohol dependence; and (3) combined treatment with naltrexone and prolonged exposure therapy may decrease the rate of relapse of alcohol dependence for up to 6 months after treatment discontinuation.

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***TBI***

## **Traumatic Brain Injury An International Knowledge-Based Approach**

Journal of the American Medical Association

Tracy Hampton, PhD

7 August 2013

Traumatic brain injury (TBI) is a multifaceted condition, not an event. Traumatic brain injury is broadly defined as an alteration in brain function or other evidence of brain pathology caused by an external force that can occur in traffic, at home, at work, during sports activities, and on the battlefield. Traumatic brain injury is an important cause of death and disability for children and an exponentially increasing source of morbidity and mortality in older adults. Each year in the United States, at least 1.7 million people seek medical attention for TBI; it is a contributing factor in a third of all injury-related deaths. Many more persons, particularly those with mild TBI, are never seen by a clinician. These injuries (at times considered to be "concussions") are often dismissed by the medical community as mild with few or no consequences. Although no single definition of concussion is widely accepted, it typically affects orientation, memory, and may involve loss of consciousness. Often, patients are not carefully followed up over time, despite the increasing appreciation that TBI can affect long-term physical, cognitive, emotional, and social domains of function. The Centers for Disease Control and Prevention estimates that 2% of the US population lives with disabilities directly attributable to TBI, with annual direct and indirect costs estimated at more than \$76.5 billion.

Although the current media attention on TBI in the military and sports has raised awareness, it also has highlighted just how little is known. Many basic questions remain unanswered, such as whether a brain injury has actually occurred, when an athlete can safely return to play, or which individuals with TBI will develop postconcussive syndrome or posttraumatic stress.

August 2013

Understanding of the molecular and cellular mechanisms of TBI has improved; however, these advances have failed to translate into a single successful clinical trial or treatment. These failures are largely attributable to the broad classification of TBI as mild, moderate, or severe that does not incorporate newer insights and findings from diagnostic tools, such as imaging and proteomic biomarkers. This classification scheme is derived from the Glasgow Coma Scale (GCS); outcomes are measured using the Glasgow Outcome Scale-Extended (GOSE), which is global and relatively insensitive. This symptom-based approach does not permit mechanistic targeting for clinical trials. A nuanced, more advanced approach requires the transition to a more precise disease classification model that is based on pathoanatomical and molecular features. Clinical research has further been limited by lack of standards for data collection and limited multidisciplinary collaboration. However, the increasing recognition of the complexity of TBI and of the limitations of previous research are beginning to foster collaborative changes in research and clinical approaches for TBI.

The US National Institute of Neurological Disorders and Stroke, US Department of Defense, and the National Institute on Disability and Rehabilitation Research have identified and supported the need for improved TBI classification using diagnostic and outcome tools beyond the GCS and GOSE as well as the need for a standardized approach to data collection. In response, multidisciplinary, international expert panels were convened that comprised clinician-scientists from 49 institutes and agencies across the TBI care spectrum from emergency services to rehabilitation. By consensus, these panels developed the TBI Common Data Elements for clinical data, imaging, biospecimens, and outcomes. Work by various groups has further refined the TBI Common Data Elements and validated the feasibility of collecting these data across sites and across the injury spectrum, ranging from mild to severe. Integrated databases, imaging repositories, biosample repositories, and multicenter expertise have also been developed. This dataset is the first to populate the Federal Interagency Traumatic Brain Injury Research (FITBIR) repository, an informatics system that provides a collaborative platform for imaging, assessment, and genomics research.

The future success of TBI research and clinical care requires interdisciplinary and international collaboration that concentrates concurrently on the following: establishing a new TBI classification and taxonomy, improving outcome assessments, identifying the economic effects, and creating a scalable and sophisticated infrastructure for clinical care and research.

Recent work in each of these areas holds promise. In the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK–TBI) study, magnetic resonance imaging uncovered structural abnormalities in approximately 30% of 135 patients with mild TBI and a normal computed tomographic (CT) scan. The presence of these abnormalities predicted unfavorable outcome at 3 months. This represents an important step toward improved stratification of heterogeneous patient subgroups within the population traditionally classified as having mild TBI or concussion. Additionally, newly validated blood-based glial proteomic biomarkers have been shown to detect reliably the presence and severity of brain injury seen on CT scan. Ongoing work is using the TBI Common Data Elements outcome measures to examine patient-oriented domains, including cognitive, psychosocial, physical function, and quality of life. Combining these more refined outcome data in a multidimensional scale is expected to improve the detection of treatment effects. Large between-center and between-country differences in outcome may facilitate comparative effectiveness of clinical decisions. As with other diseases, patient-, clinician-, and system-level factors may influence outcome and costs.

The European Commission and the Canadian Institutes of Health Research have each announced the first recipients of funds from the International Initiative for Traumatic Brain Injury Research. This initiative was established in 2011 as a collaborative effort of the European Commission, Canadian Institutes of Health Research, and the US National Institutes of Health, with the goals of advancing global clinical TBI research, treatment, and care. The US National Institute of Neurological Disorders and Stroke will soon announce the US recipient of a multicenter award to participate in the International Traumatic Brain Injury Research Initiative. This represents the beginning of an innovative research model,

developed collaboratively through public-private partnerships. The large, international TBI patient database should have sufficient power to identify new diagnostic and prognostic markers of disease, refine outcome assessments, and identify best practices.

The complexity of TBI is such that no single investigator, institution, funding organization, or private company can make progress on its own. Traumatic brain injury needs a broad-based, sustainable, multidisciplinary approach aimed at elucidating mechanisms of TBI biology, identifying risk factors, and developing treatments. First steps should include the design of longitudinal studies to follow the natural history of TBI, which should help prioritize promising avenues for research.

President Obama recently unveiled The BRAIN Initiative—Brain Research Through Advancing Innovative Neurotechnologies. This “big data and team science” approach has been successfully operationalized in the National Institutes of Health’s Alzheimer’s Disease Neuroimaging Initiative and is uniquely applicable to TBI. Traumatic brain injury research and clinical care are decades behind other diseases, such as cancer and cardiovascular disease, and there is an important need to close existing knowledge gaps. Political will and resources are needed to create meaningful change for the global disease that is traumatic brain injury.

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***Other***

## **Researchers Use Human Stem Cells to Build a Functional Liver**

Journal of the American Medical Association  
Tracy Hampton, PhD  
7 August 2013

Researchers in Japan coaxed human induced pluripotent stem cells into becoming a liver bud—an early structure that is seen when livers form—when they recreated cellular interactions that normally occur during bud development (Takebe T et al. Nature. doi:10.1038/nature12271 [published online July 3, 2013]).

The approach involved mixing hepatic progenitors derived from the stem cells with endothelial and mesenchymal cells. Staining and gene-expression analyses revealed a resemblance between the stem cell–derived buds and naturally occurring liver buds.

After transplantation into mice, the buds matured, developed a vascular system, and performed liver-specific functions such as protein production and drug metabolism. Furthermore, transplantation of the newly created liver buds improved survival after drug-induced liver failure in mice.

Until now, no investigators had successfully generated a 3-dimensional vascularized organ from induced pluripotent stem cells. The feat highlights the potential of transplanting organ buds grown from such stem cells for the treatment of organ failure. The researchers are now using their approach to create a functioning pancreas.

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## Perspectives on Complementary and Alternative Medicine Research

Journal of the American Medical Association  
Josephine P. Briggs, MD; Jack Killen, MD  
21 August 2013

For the last 2 decades, the phrase “complementary and alternative medicine” has been used to describe a wide array of treatments, health practices, and practitioner disciplines with historical roots outside conventional medicine. Examples include ancient practices such as acupuncture; herbal remedies; visits to complementary clinicians including naturopaths, homeopaths, and chiropractors; and meditative practices such as mindfulness, yoga, and tai chi. Data from the 2007 National Health Interview Survey show that about 40% of US residents integrate 1 or more of these unconventional health practices into their personal health care,<sup>1</sup> spending about \$34 billion per year out of pocket.<sup>2</sup>

The widespread use of these practices perplexes many physicians. Concerns include scientific implausibility, unjustified claims of benefit, possible adverse effects, interactions with prescribed treatments, adulterated products, and the possibility that vulnerable patients with serious diseases may be misled.

The National Institutes of Health’s (NIH’s) efforts to address these concerns began in earnest in 1999, driven toward 2 ends: filling gaps in scientific evidence about efficacy and safety and exploring the possibility of real benefit in some practices of interest to the public. The efforts have included both large, multicenter clinical trials and a wide-ranging portfolio of exploratory, investigator-initiated, basic and clinical research projects.

That this public sector investment has been the subject of intense debate<sup>3</sup> is not surprising. If well-informed, such debate is welcome. However, some criticisms betray a lack of understanding of scientific progress in this field and how it has shaped a compelling, sharply focused research agenda. In this Viewpoint, we describe the 2013 NIH perspective on investment in research on these interventions and call for a more nuanced conversation about them.

### WHAT HAVE WE LEARNED?

National surveys suggest that approximately half of US residents’ use of these complementary and alternative therapies is to treat symptoms, particularly chronic pain. The other half is used to promote physical health or psychological well-being. Although much of this use is self-administered, it is most often combined with conventional care. Use to replace proven conventional treatment—although of substantial concern—is uncommon.

Moreover, many mainstream institutions, both civilian and military, are integrating some of these approaches into the care they provide. Marketing to consumer demand in the US health care system undoubtedly is driving some of this integration, ahead of evidence about safety and efficacy.

For some mind-body approaches, however, there is mounting evidence of usefulness and safety, particularly in relieving chronic pain. A few examples include acupuncture for osteoarthritis pain; tai chi for fibromyalgia pain; and massage, spinal manipulation, and yoga for chronic back pain. Increasing comfort with this emerging evidence is reflected in practice guidelines from the American College of Physicians, the American Pain Society, and the Department of Defense.

Translational research is also elucidating effects of interventions like meditation and acupuncture on central mechanisms of pain perception and processing, regulation of emotion and attention, and placebo responses. Although not yet fully understood, these effects point toward scientifically plausible mechanisms—often unrelated to the traditional mechanistic explanations—by which these interventions might exert benefit.

Another major focus of past NIH investments has been on rigorous, appropriately powered, placebo-controlled trials of widely used dietary supplements. These include St John's wort for major depression, glucosamine and chondroitin sulfate for knee osteoarthritis, silymarin for chronic liver disease, saw palmetto for benign prostatic hyperplasia, ginkgo for early cognitive decline, and vitamin E and selenium to prevent prostate cancer. The results of these large studies failed to confirm benefits seen in earlier preliminary studies. Although many were disappointed, this body of work has had well-documented influences on consumer use and spending and has contributed evidence to systematic reviews. In addition, high-quality data sets from these studies are being used to examine other important health research questions.

Other research on natural products has yielded important information about safety concerns, including toxicities of specific products, herb-drug interactions, and instances of product contamination or adulteration. This work has contributed to regulatory actions aimed at consumer protection and has arguably heightened awareness that “natural does not mean safe.”

#### PERSPECTIVES ON CURRENT RESEARCH AND FUTURE DIRECTIONS

These investments of a small fraction of public sector health research dollars have begun to meet the need for better evidence about these widely used interventions and clarify the potential of some for integration into patient care. A new set of priorities has evolved, shaped around emerging evidence of efficacy and safety, amenability to rigorous investigation, and practical but important public health needs.

One research priority is focused on symptom management—specifically the role of mind-body interventions in managing pain and other symptoms common to many chronic diseases. All physicians understand the limits of current treatments for chronic pain and the potential value of nonpharmacological interventions. This priority also encompasses research to better understand the mechanisms—including placebo responses—that could be exploited to mediate or modulate these symptoms.

Similarly, research on natural products—dietary supplements, herbal medicines, and probiotics—has also been focused considerably. Priorities now include translational research to elucidate biological actions and provide a sound mechanistic foundation for potential clinical studies and include the development of a strong technological platform for systematic study of herb-drug and herb-herb interactions using state-of-the-art methods of pharmacology, pharmacognosy, genomics, and proteomics.

Debate about NIH efforts in this area is vital to ensuring that valuable research resources are wisely invested. However, the debate requires a more nuanced conversation than has often been the case in the past.

First and foremost, the conversation should reflect current realities, including the evolution of research priorities and the shifts in funding to projects that address them, rather than areas that have less scientific promise or less amenability to scientific investigation. Second, although discussions about complementary and alternative medicine often imply a clear demarcation distinguishing a monolithic alternative domain from conventional medicine, this distinction breaks down in the realities of the pluralistic US health care system. The boundaries also shift—in both directions—as evidence changes. Third, the conversation should recognize the state of current evidence indicating that some of these practices

are useful and can appropriately be integrated into care, some should not, some are dangerous and merit regulatory attention, and many are somewhere in between.

A more nuanced conversation about this field and its research can improve the dialogue between health care professionals and patients, foster better research partnerships, and facilitate patient access to interventions that may be helpful.

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## **Cancer-Causing Infections Decline After HPV Vaccine Introduced**

Journal of the American Medical Association  
Rebecca Voelker, MSJ  
August 7, 2013

Despite low immunization rates, infections with human papillomavirus (HPV) strains that are associated with cervical cancer have declined markedly among adolescent girls since 2006, when HPV vaccination was introduced.

Investigators led by Lauri Markowitz, MD, of the Centers for Disease Control and Prevention (CDC), analyzed HPV prevalence data from 2003 to 2006, before vaccination began, and afterward, from 2007 to 2010. They based prevalence determinations on 4150 cervicovaginal swab samples collected from girls and women aged 14 to 59 years during the earlier time period and 4253 samples taken after HPV vaccination was introduced.

The data collection was part of the National Health and Nutrition Examination Surveys, which use standardized interviews, physical examinations, and laboratory tests to assess the health and nutritional status of US children and adults.

Markowitz and her colleagues found that the prevalence of 4 HPV strains targeted by 2 currently marketed vaccines decreased in 14- to 19-year-old females by 56%, from 11.5% before immunization began to 5.1% during the later data collection period.

“This is exactly the age group [in which] we would expect to first see an impact based on who’s getting vaccinated in the United States,” Markowitz said during a telebriefing on the study, which was published in June (Markowitz LE et al. *J Infect Dis*. doi:10.1093/infdis/jit192 [published online June 19, 2013]). Vaccination is recommended for girls when they’re 11 or 12 years old and women up to age 26 years if they haven’t already been vaccinated. Boys also should be vaccinated at age 11 or 12 years and men up age 21 years.

The study showed no HPV infection decreases in other age groups and didn’t include data for boys or young men. Even though the decreased prevalence was in the age group they expected, Markowitz said she and her colleagues found a surprise in the data.

“The decrease was greater than we thought... based on 3-dose coverage in the United States,” she said.

Human papillomavirus vaccination is increasing in the United States, but a 2010 national survey showed that only 49% of girls aged 13 to 17 years had received at least 1 dose of vaccine and 32% had received all 3 recommended doses (CDC. *MMWR Morb Mortal Wkly Rep*. 2011;60[33]:1117-1123).

CDC Director Tom Frieden, MD, MPH, said the results were striking. “They should be a wake-up call that we need to increase vaccination rates because we can protect the next generation of adolescents and girls against cancer caused by HPV.”

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