

Appendix A: Fiscal Year 2016 Research Narrative

Executive Division

The Executive Division, located in White River Junction, Vermont, provides leadership, directs program planning, and promotes collaboration to facilitate optimal functioning of the Divisions, both individually and collectively. The Executive Division specializes in the development of innovative and authoritative educational resources, programs that disseminate and implement best management and clinical practices, and the use of technologies to reach a broad range of audiences.

VA National PTSD Brain Bank

Under the direction of Dr. Matthew Friedman, Senior Advisor to the Center and its founding Executive Director, the National Center continued to coordinate the first VA National PTSD Brain Bank. The Brain Bank supports the Presidential Executive Order of August 2012 on deployment health by enabling VA to lead the nation in unique research that will facilitate deeper understanding of the causes and consequences of PTSD, as well as assessment and treatment.

Enrollment of potential post-mortem donors began in May 2015, with the launch of the Brain Bank website. Since then it has expanded to a seven-part consortium, with facilities at the Miami, Durham, Boston, San Antonio, West Haven, and White River Junction VA Medical Centers and the Uniformed Services University of the Health Sciences (USUHS). As of the end of FY 2016, the Brain Bank had 149 PTSD and comparison tissue specimens. Currently 44 prospective donors have volunteered to be followed over their lifetimes and another six are expected to volunteer soon.

The Clinical Neurosciences Division in West Haven, Connecticut, serves as the primary research site for the Brain Bank. Publications from Brain Bank data have so far identified SGK1 (serum and glucocorticoid-regulated kinase) as a molecular mechanism of PTSD and found that metabotropic glutamatergic receptors, a key signaling molecule, are increased in several brain regions, including the prefrontal cortex, in PTSD patients. Planned analyses at the genetic, cellular, and molecular levels, as well as work in neuroproteomics (i.e., related to synaptic connections) and preclinical rodent models, could lead to the identification of long-term neurobiological changes induced by chronic stress.

Treatment Research

The Executive Division has a long history of participation in VA's Cooperative Studies Program (CSP). Enrollment continued for CSP #591, a groundbreaking study comparing two treatments for PTSD: Cognitive Processing Therapy (CPT) and

Prolonged Exposure (PE). The study, which to date has enrolled over 600 male and female Veterans, will eventually enroll 900 Veterans at 17 sites across the country. The study's findings will help VA leadership, clinicians, and Veterans make informed choices about the delivery of PTSD care in VA, and will also be broadly relevant to the scientific and clinical communities outside VA.

The Executive Division also participates in trials to investigate new treatment approaches for trauma-exposed individuals; the primary outcome paper for the Acceptance and Commitment Therapy (ACT) trial is online ahead of print.

Investigators continue to focus on disorders that frequently co-occur with PTSD. Recruitment was completed for a trial comparing two treatment approaches for Veterans with PTSD and substance use disorders: CPT plus usual outpatient addiction care versus usual care alone. A second trial, which has 115 of 120 participants randomized, compares two psychotherapies — Prolonged Exposure (PE) and Seeking Safety — for comorbid alcohol use disorder and PTSD.

Recruitment was recently launched for a trial to evaluate a brief protocol to reduce guilt and shame related to a traumatic event among Veterans who served in Iraq and Afghanistan. Investigators also continue collaborations with the PTSD specialty clinics and the residential PTSD/substance use treatment program at the San Diego VA to develop ways to use clinical data for research.

Implementation Research

The Executive Division continues work on several initiatives aimed at assessing models of care and improving evidence-based practice. In one study, investigators surveyed a national sample of Veterans and civilians to assess their decision-making needs and preferences for PTSD treatment; the recently published results are informing the development of the first publicly available online decision aid for PTSD.

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Another recent initiative examined the impact of an academic detailing model to reduce inappropriate prescribing practices for PTSD patients and uses decision support tools to encourage the use of shared decision making. An extension of that initiative will examine whether using telehealth and a clinical pharmacist in an academic detailing model can improve local PTSD prescribing practices in rural clinics

throughout Vermont and New Hampshire.

In addition to projects aimed at improving clinical practices, investigators are continuing to assess the state of VA care for PTSD. Work is continuing on a project that applies novel informatics and operational methods to medical and administrative data in order to understand multiple dimensions of quality of PTSD care.

Behavioral Science Division

The Behavioral Science Division in Boston, Massachusetts, conducts research on post-deployment adjustment, aging and health, assessment, genomic and neuroscience mechanisms of psychopathology, and innovative approaches to intervention and treatment delivery.

Longitudinal Studies

Project VALOR (Veterans After-Discharge Longitudinal Registry) is a prospective cohort study involving a registry of 1,649 male and female combat Veterans who became users of VA services after 2002. The project is collecting data about health outcomes associated with PTSD, supplemented by clinical information from VA electronic medical records. Data collection for the third sampling wave is now complete, with retention of 89% of the second wave (1202 of 1340 participants). The next phase of data analyses will begin soon.

The Neurocognition Deployment Health Study began collecting data at the outset of the Iraq War in 2003. Military personnel were assessed before deployment and at several intervals afterward, making it the first prospective longitudinal study to address the psychological impact of war zone stress. The study design allows examination of long-term emotional and neuropsychological outcomes, as well as health-related quality of life and occupational functioning. Initial papers stemming from this research have described PTSD outcomes, neuropsychological outcomes, and the relationships among these outcomes, PTSD symptoms, and traumatic brain injury (TBI). Data collection on an associated study that examines the adjustment of both partners and children of the Servicemembers and Veterans in the cohort was completed in June 2016.

Collaboration with other investigators from the VA Boston Healthcare System is advancing a multidisciplinary approach to research focused on the long-term effects of military service on health and well-being, including PTSD, in later life. This effort has led to the creation of a [website](#) that provides researchers with information about military service variables found in several publicly accessible longitudinal data sets. Research prompted by this effort has appeared in publications and in presentations at national and international conferences.

Biomarkers

Division investigators are examining neural biomarkers of

PTSD and blast-related TBI in Veterans who served in Iraq and Afghanistan. The research aims to clarify the contribution of mild TBI (mTBI) and psychiatric conditions to the various deficits experienced by military personnel with blast injury, as well as long-term negative consequences such as neurodegenerative disease. Results have shown that mTBI accompanied by genetic risk for Alzheimer's disease is associated with measures of brain and cognitive domains that are the first to show signs of decline in Alzheimer's disease. Other work has implicated the gene COMT in explaining the relationship between PTSD and hippocampal volume. This research has also uncovered patterns of white and gray matter changes differentially associated with PTSD and mTBI.

Biomarker research at the Division also includes a rapidly growing portfolio of genetic and epigenetic studies in collaboration with the Translational Research Center for TBI and Stress Disorders (TRACTS) Center of Excellence, the Brain Bank, and the Psychiatric Genomics Consortium PTSD Workgroup. These studies have revealed that PTSD-related metabolic syndrome is associated with widespread reductions in cortical thickness, along with evidence for a genetic contribution to this association. Meta-analytic findings have shown that PTSD is associated with reduced amygdala and hippocampal volume, and confirmed previous findings that PTSD is associated with accelerated cellular aging in the epigenome. Related research based on data from the Vietnam Era Twin Registry suggests matching genetic architecture for PTSD and resilience, implying that there is need to refine the construct of traumatic stress to align with its genetic structure.

Finally, Division researchers are conducting functional and structural magnetic resonance imaging (MRI) studies to identify neural circuitry involved in PTSD. Structural MRI data point to specific hippocampal subfield volumes that are negatively correlated with PTSD and that may be related to the persistence of PTSD symptoms. Preliminary data for functional MRI (fMRI) projects also suggest specific brain regions within the prefrontal cortex that are active when individuals with

(Behavioral Science Division Continued)

PTSD manage negative emotions. The findings suggest brain pathways that could be targeted to enhance emotional regulation and cognitive performance.

Treatment Research

The Division continues to conduct pioneering research on treatments for PTSD, with the key aims of overcoming barriers to seeking care, reducing dropout, and increasing efficiency of care delivery. A prime example is the Internet-based treatment, VetChange, designed for Iraq and Afghanistan combat Veterans who report risky use of alcohol and PTSD-related distress. The initial trial produced evidence of effectiveness in reducing both drinking and PTSD symptoms. A second version was constructed as a mobile-friendly public website, and this version is now under evaluation. A mobile app with key VetChange features, developed in conjunction with the Dissemination and Training Division, will begin a pilot test phase soon. In addition, a major extension of the VetChange web intervention is underway, with investigators looking to integrate VetChange directly into clinical care delivered by VA providers and to evaluate its effectiveness in VA clinics.

Researchers are working to develop and test efficient therapist-delivered interventions or treatment extenders, with the expectation that these new approaches will require less professional staff time and will be easier for patients to complete. One example is a brief, exposure-based treatment for PTSD that in the past has demonstrated strong effectiveness with non-Veteran patients. Current and future studies are testing whether this brief intervention is as effective as CPT and whether it can be implemented successfully with Veterans and active duty Servicemembers.

Research on factors that link PTSD with aggression toward intimate partners has led to the development and evaluation of interventions to reduce and prevent aggression within families of Iraq and Afghanistan Veterans. Clinical trials examining two such interventions were completed and positive results were published in 2016. These intervention programs are currently being implemented at multiple sites in the VA and on one military installation. A new pilot study will focus on adapting and examining one of these programs in an underserved urban civilian setting.

In the area of complementary interventions, a pilot study investigating Tai Chi exercise for PTSD-related distress has demonstrated high satisfaction and enthusiasm on the part of Veteran participants. An upcoming five-year study will compare Tai Chi with a wellness intervention and measure the impact of these two interventions on chronic pain experienced by Veterans with Gulf War Illness, a set of chronic, medically unexplained symptoms that afflicts some Veterans of that service era.

Division investigators are examining a phenomenon termed later-adulthood trauma re-engagement (LATR), in which older combat Veterans actively re-engage with wartime memories in an effort to build coherence or find meaning; the LATR process could have the potential to lead to either growth and positive outcomes or to increased symptomatology. A current study of LATR is examining the utility of a 10-week psychosocial discussion group for older combat Veterans who report experiences consistent with the LATR process. Two cohorts are complete, and recruitment for the third cohort is ongoing.

Research is being conducted into the efficacy of transcranial, low-level light (t-LLLT) as a treatment for PTSD and comorbid conditions. Some preclinical studies have shown that exposure to red and near-infrared light re-establishes normal mitochondrial functioning in damaged brain cells. This approach is used to treat a variety of animal and human conditions, but application to psychiatric and neurological conditions is a relatively recent undertaking. The therapy t-LLLT intervention is being tested in two studies, one involving Veterans with Gulf War Illness and another involving Veterans with PTSD and TBI.

Assessment

A recent study looked at proposed revisions to the PTSD diagnosis in the International Classification of Diseases (ICD-11) using network models. Another study evaluated the new Minnesota Multiphasic Personality Inventory (MMPI-2) Restructured Form scales in relation to the assessment of DSM-5 PTSD, the dissociative subtype of PTSD, and PTSD-related malingering. New data collection also is underway that will evaluate the utility of the MMPI-2 Restructured Form scales in relation to PTSD-related chronic pain and other chronic pain outcomes. A product of past work is a new published measure to assess the dissociative subtype of DSM-5 PTSD (Dissociative Subtype of PTSD Scale); it is available for download on the National Center's website.

Division investigators are participating in a consortium of private industries, universities, and government agencies that are working with the Defense Advanced Research Projects Agency (DARPA) to develop analytical tools to assess the psychological status of Warfighters. The current effort applies machine learning methods developed from the initial project to the extensive TRACTS dataset. The primary aim is to be able to predict various outcomes, including PTSD, TBI, and suicide risk. In addition, a collaborative study with investigators from Harvard University tests new methods for measuring and modifying cognitive processes related to suicidal behavior among Veterans.

A pilot study has been completed for a project designed to inform postmortem donor classification for the Brain Bank. Individual incidence of PTSD and comorbid disorders is

(Behavioral Science Division Continued)

determined on the basis of data collected directly from living elderly Veterans. This information is then used to evaluate the predictive potential of information drawn from an informant

interview and medical record review. The aim is to determine the best predictors from indirect sources and to provide a template for use by the Brain Bank.

Clinical Neurosciences Division

The Clinical Neurosciences Division (CND), located in West Haven, Connecticut, focuses on the neurobiology of traumatic stress, investigating paradigms of risk and resilience, and pharmacotherapeutic interventions for the treatment of PTSD and comorbid conditions. Publications and presentations are also an important part of CND's work, and in FY 2016 the Division launched *Chronic Stress*, a new peer-reviewed scientific journal that focuses on the neurobiology, assessment, and treatment of the behavioral and biological effects of stress.

Molecular Neuroimaging

The Division has been in the forefront of the development of new technologies and methods to non-invasively investigate human brain chemicals, structure, and function. CND was the first group to identify alterations in specific signaling molecules in Veterans using single-photon emission computed tomography (SPECT) and positron emission tomography (PET) technologies.

Recent work in this area has shown that a key signaling molecule, metabotropic glutamatergic receptor (mGluR5), is present at higher levels in people with PTSD. Work continues in this area, examining ketamine-induced changes within mGluR5 and studying how these changes may be related to disruptions in behavioral and cognitive functioning, resting state connectivity, and receptor internalization. This novel paradigm has been studied in healthy control participants and in PTSD and depressed patients.

Research in this area is providing a better understanding about alterations in specific regulatory processes involved in PTSD — that is, the “switches” that might correct and normalize aberrant biochemical changes. Division investigators intend to continue this work by linking patient data to post-mortem data from the Brain Bank. This approach will determine whether increases in mGluR5 occur in conjunction with increased gene expression by a protein holding mGluR5 in the synapse but not by an increase in gene transcription. Other projects are investigating mGluR5 availability in comparative samples of PTSD, major depression, bipolar disorder, and healthy control participants to look for similarities and differences across these disorders.

Neuroinflammation is the focus of another study using PET technology. A neuroimmune challenge is being used to evaluate the role of activated microglia in mediating the expression of PTSD, as well as to study the relationship between peripheral inflammatory markers such as TNF- α , and trauma-related symptoms. Measuring the distribution of activated microglia in the brain is made possible using a new PET tracer for the translocator protein, so that components of the neuroinflammatory process can be studied non-invasively.

By characterizing the type and extent of neuroinflammation in PTSD, it may be possible to uncover new mechanisms of treatment with anti-inflammatory agents.

Division investigators are conducting a number of synaptic protein level (SV2a) studies, using both preclinical and clinical participants in stress models. Synaptic loss is known to be a contributor to treatment failure in PTSD, and this research explores whether stress-related loss of synaptic connectivity compromises the circuits involved in mood regulation. By using a PET tracer for SV2a, researchers are able to quantify the density of synapses in the brain. Preclinical work with SV2a includes examination of synaptic density in nonhuman primates after administration of drugs that have been shown to rapidly increase synaptic density in rodent models. Clinical work includes measuring SV2a levels in patients diagnosed with depression and PTSD, as well as examining postmortem samples.

Another area of focus during the year included a series of projects utilizing a novel Carbon-13 magnetic resonance spectroscopy (^{13}C -MRS) paradigm, providing for a non-invasive measurement of glutamate neurotransmission. This work revealed two important findings: global brain connectivity was identified as a putative marker for stress-related synaptic pathology and as one possible mechanism of action for antidepressants; and anterior hippocampal dysconnectivity (functional and anatomical) was observed in Veterans with high PTSD symptoms. Based on these results, the Division will continue research that tests the efficacy of glutamate based drugs, while also investigating underlying neural mechanisms and synaptic strength in the pathophysiology and treatment of PTSD and depression.

Additionally, CND investigators plan to establish graph network based measures and machine learning approaches to identify disorder-specific biomarkers related to PTSD and depression. Graph theory can be used to evaluate changes in the way that brain networks communicate and interact, as well as the consequence or cause of some changes. Similarly, investigators will attempt to characterize psychopathology by investigating patterns of connectivity. Preliminary work

(Clinical Neurosciences Division Continued)

in this area was conducted over the past year via univariate analyses that distinguished between dimensions of PTSD. To expand upon this work, investigators will employ high quality multimodal neuroimaging scans and well established functional and connectivity measures to conduct a proof of concept study using artificial intelligence to predict diagnoses and PTSD severity. This study will be the first to combine state-of-the-art graph-based and voxel-wise data-driven measures (as opposed to cluster- or seed-based, *a priori* measures) of anatomical and functional connectivity along with current multi-voxel pattern analysis algorithms.

The Division is also participating in the PTSD research efforts of the Psychiatric Genomics Consortium and ENIGMA, which together have assembled the largest collection of MRI data in PTSD patients. The initial results from this collaboration replicate CND's first MRI study in showing evidence of smaller hippocampal volume in PTSD.

Genetic Studies

Genetic and epigenetic research in support of the Research Domain Criteria (RDoC) initiative of the National Institute of Mental Health (NIMH) continued. This work aims to characterize psychosocial, genetic, environmental, and genetic/environmental determinants of PTSD. A major focus is identification of risk factors for PTSD, as well as protective psychosocial factors that promote resilience.

One recent genetic study using data from the National Health and Resilience in Veterans Study (NHRVS) examined the relationship between forms of FK506 binding protein 5 (FKBP5), childhood abuse, and the risk for PTSD in Veterans. It was found that these substances directly interacted with childhood abuse and were associated with increased severity of PTSD symptoms. These findings further suggested that the associations are specific to the hyperarousal symptoms of PTSD.

Other work examining associations between oxytocin receptor gene (OXTR) polymorphisms and PTSD revealed that the OXTR single nucleotide polymorphism (SNP) rs53576 minor A allele is associated with increased risk for PTSD, and that this relationship was especially strong for individuals who reported insecure adult attachment. Investigators also examined psychosocial determinants of accelerated cellular aging in Veterans. Results revealed that accelerated cellular aging is associated with hostility, particularly difficulties controlling anger, as well as negative age stereotypes, such as believing that depression is an inevitability of aging.

Treatment Research

The Division's clinical trials program has continued to grow. By combining neuropharmacology and neuroimaging to study mechanisms of action and treatment response, researchers aim to develop biomarkers that lead to better

matching of patients to treatments. Pharmacotherapeutic agents currently under study include riluzole, a glutamate modulating agent; ketamine, a N-Methyl-D-Aspartate (NMDA) receptor antagonist drug; neuropeptide Y, an endogenous neuropeptide; intranasal oxytocin, a peptide hormone; and the immunosuppressant rapamycin.

Ketamine, an agent known to interact with glutamate and to rapidly reverse the damaging effects of stress on neurons, is being studied specifically for its effects in treatment-resistant PTSD. Ketamine is also the subject of a number of other trials, including an assessment of the potential benefit of intense seven-day PE therapy combined with a single ketamine infusion; a study of ketamine's ability to improve cognitive functioning using a single intravenous dose to study visual, verbal, and working memory in PTSD; and a study of the interactive effects of ketamine and guanfacine on activation and connectivity of the locus coeruleus, a prominent brain region for hyperarousal in PTSD.

As part of the National Center's work on NMDA receptor antagonist drugs, including ketamine and lanicemine, Division researchers also completed a scholarly review looking at the potential use of these medications to prolong the therapeutic effects of cognitive behavioral therapy, as well as their effects as rapid-acting antidepressants for the treatment of suicidal thoughts. This work has led to consultation with the American Psychiatric Association to develop consensus guidance on the clinical use of ketamine for the treatment of psychiatric disorders.

Investigations continue studying the neural mechanisms of fear and safety learning in Veterans with PTSD in order to better understand the process of fear extinction and to develop treatment strategies. Data collected from a study of the neural correlates of decision making in PTSD patients demonstrated that aversion to ambiguity helped to explain the relationship between combat exposure and the level of anxious arousal in PTSD. One component of this research is using fMRI technology, and preliminary findings are promising. The team is now expanding this work to further study the relationship between substance use and PTSD symptoms.

Finally, the pilot phase of a study utilizing real-time fMRI neurofeedback for the treatment of PTSD has been completed and published. Examination of changes in resting-state functional connectivity patterns in the pilot data revealed normalization of brain connectivity consistent with clinical improvement. These preliminary results suggest that this emerging technique has potential clinical utility in treatment of PTSD. Additionally, a treatment trial comparing standard care to an intensive integrated treatment for Veterans with PTSD and comorbid chronic pain completed enrollment and is scheduled for data analysis.

(Clinical Neurosciences Division Continued)

Epidemiology

Several additional studies using data from the NHRVS and the World Trade Center (WTC) Health Program were conducted during 2016. Recent projects have focused on the epidemiology of DSM-5 PTSD in U.S. Veterans, and on trajectories and latent typologies of PTSD in WTC responders. Other work looked at the prevalence and determinants of late-life re-emergence or exacerbation of PTSD symptoms in older Veterans, and revealed that approximately 10% have these experiences on average nearly 30 years after the trauma. Greater executive dysfunction, trauma burden, loneliness, and reductions in social support were associated with this re-emergence or exacerbation of symptoms.

A series of studies using the NHRVS data were conducted on

the prevalence, course, and determinants of posttraumatic growth (PTG) in Veterans. Results revealed that 50% of Veterans, including 72% of those with PTSD, experienced PTG in relation to what they described as their “worst” traumatic event; specifically, those with PTSD reported better mental functioning and quality of life. Key predictors of PTG included experiencing a life-threatening illness or injury, having greater severity of re-experiencing symptoms, and enjoying higher levels of social connectedness, purpose in life, and altruism. PTG, particularly perceptions of greater personal strength following one’s “worst” traumatic event, was also associated with lower risk of developing PTSD in response to a new trauma, suggesting that PTG may help trauma survivors develop coping skills to better manage subsequent traumas and stressful life events.

Dissemination and Training Division

The Dissemination and Training Division in Palo Alto, California, conducts research on patient needs and preferences; development and testing of novel or adapted treatments; development and testing of treatments that employ technology-based delivery of services; and implementation science.

Patient Needs and Preferences

The Division has undertaken several studies on the development and evaluation of strategies to quickly identify patient needs, patients at risk, and patient preferences. A current study funded by Health Services Research & Development (HSR&D) is developing a brief measure of patient characteristics associated with effective engagement in care; the measure is expected to guide identification of the type and amount of resources needed to engage Veterans and encourage them to continue with treatment. A second and related study is focusing on the development and cross-validation of a hospital risk screening tool that can provide guidance about the type and intensity of mental health services that might benefit patients.

Two studies concern substance use: one is evaluating a brief screen for drug use among primary care patients with and without PTSD. The other examines barriers to cannabis treatment among Veterans with PTSD. Along with collaborators at the Women’s Health Sciences Division, staff at the Division also completed research and evaluation work on screening and treatment of military sexual trauma (MST).

Treatment Research

Randomized controlled trials that are evaluating patient outcomes under various delivery strategies in a variety of treatment settings and using novel interventions are underway. One large multisite clinical trial has been completed and will assess the effectiveness of a flexibly delivered evidence-based PTSD skills-plus-exposure treatment among civilian public sector women and will examine how

variations in delivery affect patient outcomes. Another study is evaluating adaptive changes in cardiac autonomic status, physical activity, social cognition, and social interaction in real time among Veterans participating in the VA Service Animal Training Intervention program.

Three new trials address substance use disorders: a project evaluating cognitive remediation for alcohol abuse and PTSD; an evaluation of ACT in patients with comorbid PTSD and substance use problems; and an evaluation of the effectiveness of exercise in resolving cannabis dependence. Evaluation of the national rollout of PE therapy continued, with recent results confirming PE’s effectiveness in a national sample of more than 1,800 Veterans.

Technology-based Treatments and Treatment Delivery

Several ongoing studies are assessing the benefits of phone and web-based technology to increase Veteran access to mental health care and to enhance outcomes. Following two successful pilot studies of PTSD Coach, a new project will assess the efficacy of this treatment compared to treatment as usual in reducing PTSD symptoms in Veterans who are receiving service in a primary care setting. Other mobile phone apps under study include PTSD Family Coach, an app for family members of individuals with PTSD intended to reduce stress among family members; Parenting2Go; Mindfulness; and Cognitive Behavioral Therapy for Insomnia (CBTi).

A study in a national sample of trauma-exposed individuals compared the effectiveness of web-based “brain games” versus “games as usual.” The brain games were more effective for PTSD symptoms and emotion regulation than “games as

(Dissemination and Training Division Continued)

usual,” but this effect was only observed in individuals with low to moderate PTSD symptoms. The first investigation of Moving Forward, a web-based problem-solving intervention, has been completed; findings suggested that it was helpful in reducing PTSD symptoms.

In collaboration with investigators from the Minneapolis VA Medical Center, Division researchers are testing a web-based intervention to help National Guard families encourage their loved ones to seek mental health care. Key questions concerning the ways and extent to which social networks can be utilized to increase treatment engagement and improve mental and physical health outcomes is being investigated in a study of a highly stressed population — cancer survivors.

Implementation Research

A current implementation project is evaluating competing strategies intended to enhance and sustain the delivery of a PTSD treatment, where one strategy emphasizes fidelity to the protocol through expert consultation and the other focuses on improving fit of the intervention to the environment through continuous quality improvement. Division researchers are also conducting a trial that focuses on increasing awareness of, receptivity to, and implementation of clinical practice

guidelines for management of traumatic stress. Investigators from the Division and the Minneapolis VA have completed a study that identifies organizational factors that differentiate VA PTSD clinics with high and low reach of evidence-based psychotherapies.

The Department of Defense (DoD) is funding an investigation of the use of Web technology to train clinicians in evidence-based treatments, and testing variations in training procedures as they affect quality of skills in implementing the treatments. A long-term project is working to develop a practitioner network across both VA and DoD that will assess the benefits of the implementation of measurement-based care (MBC), specifically on the use of symptom measures during the course of treatment to guide treatment planning.

New efforts are underway to improve patient access to care, including reduced patient wait times, by using participatory systems dynamics, a collaborative stakeholder model in which specific system problems are identified, changes are proposed, and the impact of the changes on the outcome of interest is predicted in a data-driven fashion. The model has the potential to guide decisions about system changes in a manner that is collaborative, evidence-based, and cost effective.

Evaluation Division

The Evaluation Division, headquartered in West Haven, Connecticut, is linked to VA’s Northeast Program Evaluation Center (NEPEC). NEPEC has broad responsibility within the Office of Mental Health Operations (OMHO) to evaluate their programs, including those for specialized treatment of PTSD.

Treatment Research

NEPEC has continued to monitor and assess PTSD treatment at VA, including residential and outpatient specialty treatment programs and PTSD treatment by trained providers not working within one of the specialty programs. The Evaluation Division also monitors the efforts to improve psychotropic medication prescribing practices at the Veterans Health Administration (VHA). Two of the measures being investigated in this initiative are the use of off-label antipsychotics to treat PTSD and the use of benzodiazepines.

The Evaluation Division continues research on PTSD health services, pain management, and the role of pain in the treatment of PTSD. Data collection has been completed for a NIMH project investigating the implementation of CPT and PE in 38 VA residential treatment programs. Published findings include provider perspectives on perceived effective residential treatment ingredients, provider perceptions of factors that support the use of CPT and PE, and changes in implementation of CPT and PE over time.

A number of investigators are using administrative data to explore treatment patterns and outcomes of PTSD care.

Studies have been published on medication use for the treatment of PTSD, as well as factors that correlate with self-reported PTSD symptoms over time. Over the next year the Evaluation Division will examine further the role of pain in specialized PTSD treatment and in the treatment of comorbid disorders.

The national psychotropic drug safety initiative (PDSI) has entered its third year and has been tracking data on changes in prescribing practices for PTSD. The Division continues to work with the Mentoring Program and OMHO to provide technical assistance and to respond to requests from specialized programs and staff in the field on policy, operations, handbook implementation, and the use of evidence-based practices.

Gender-Related Issues

The Division is involved in research on gender-related issues. Recruitment has been completed for the Survey of Returning Veterans (SERV), a repeated panel study of gender differences in psychiatric status and functioning among Veterans of Iraq and Afghanistan. The 850 participants — more than 40% of whom are female — were interviewed at three-month intervals for at least a year, and a sizable subset continued for

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as long as three years. Analyses of the data have begun, and the Division is making the data available to investigators who want to do add-on or other primary data collection studies.

Papers have been published on MST and PTSD as they relate to unit cohesion, gender differences in prevalence rates of disorders over time, and characteristics of Veterans reporting sex addiction.

Measurement Based Care

A new national VA initiative, Measurement Based Care in Mental Health, was formally launched by Mental Health Services and OMHO, and now has 58 hospitals and 179 mental health clinics enrolled as Champion Sites for implementation. Two Division staff members are supporting the initial pilot program evaluation; members of both the Executive and Dissemination and Training Divisions are involved in the senior leadership of the initiative. Additional investigators from within the National Center may be closely involved in the evaluation study itself.

Pacific Islands Division

The Pacific Islands Division in Honolulu, Hawaii, advances PTSD work in the Pacific Rim. The Division also focuses on improving understanding of cultural attitudes and using advanced technologies to reach out to Veterans in remote locations who are unable to access evidence-based care.

Specific Populations

Several ongoing studies examine ethnic minority populations with regard to prevalence of PTSD, response to treatment, and related mental health comorbidities. The studies identify unique risk and resilience correlates of PTSD among ethnically and racially diverse Veterans, as well as identifying their response to evidence-based PTSD treatments.

Researchers have also studied whether there are racial and ethnic differences between patients who drop out and those who continue with VA psychotherapy and pharmacotherapy for PTSD, and in providers' perceptions of reasons for patient dropout from treatment. An ongoing study using the same database examines racial and ethnic disparities in PTSD symptoms and mental health quality of life among Veterans six

months after the PTSD diagnosis.

Treatment Research

Investigators are in the final year of completing a large trial that examines Veterans' preferences for different methods of delivery of treatment. The project is also evaluating the clinical efficacy of three different approaches to providing PE: two involving technology, and one involving providers going to the Veteran's home. Division researchers also launched a new trial examining the clinical efficacy of Cognitive-Behavioral Conjoint Therapy (CBCT), a couples-based intervention for PTSD, and the use of home-based care, as compared to traditional office-based care, when working with Veterans and their partners.

Women's Health Sciences Division

The Women's Health Sciences Division, located in Boston, Massachusetts, specializes in the study of women Veterans, with an additional focus on understanding gender differences in trauma exposure and post-trauma psychopathology.

Biomarkers

Division investigators have undertaken a number of studies aimed at understanding the basic biological processes underlying PTSD. Recently completed projects include data analysis on a study of sex hormones and derivatives associated with decreased extinction retention across the menstrual cycle in PTSD; a study of GABAergic neuroprotective steroids in men and in women across the menstrual cycle; a study of the role of stress-modulating biological factors in reducing symptoms of withdrawal and negative mood during smoking cessation in trauma-exposed individuals with and without PTSD; an analysis of plasma predictors of PTSD and comorbid psychiatric, substance abuse, and medical conditions in the longitudinal cohort of Iraq and Afghanistan Veterans; and a series of studies of the gene-environment interplay in the

comorbidity of PTSD and eating disorders.

Treatment Research

Several intervention studies are examining more efficient treatment formats for CPT. With funding from the South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (STRONG STAR) Consortium, investigators recently completed studies on the relative effectiveness of CPT delivered in a group versus individual format. The Division is also investigating a variable-length CPT protocol, testing the efficacy of the intervention when treatment end is determined by patient progress. In a related effort, investigators are working to improve adherence to existing PTSD treatments; one current study is exploring Veteran and provider perspectives regarding reasons for dropout from CPT and PE in

(Women's Health Sciences Division Continued)

order to create an intervention to increase rates of completion.

Other intervention studies include a recently completed examination of the efficacy of contingency management-supported tobacco cessation in Veterans with and without PTSD, and an examination of a physical exercise intervention to elucidate the shared neurobiology of PTSD and chronic pain. Research is underway on a project to test the effectiveness and fit of the Unified Protocol, a transdiagnostic treatment, for trauma-exposed Veterans with co-occurring diagnoses.

Finally, continued analyses are being conducted on two recently completed trials funded by the National Institutes of Health (NIH). The first set of studies involves further examination of therapist fidelity and client variables that contribute to change in PTSD across administrations of CPT. The second trial examines the role of sleep improvement in augmenting recovery from PTSD and depression in a civilian sample of survivors of interpersonal violence.

The Division is also focused on intervention research targeting women who report subthreshold symptoms, including the development of a national network of peer-facilitated psychoeducation and support groups for women Veterans who want to improve their wellbeing. Another project recently published findings on a brief mindfulness-based training to assist Servicemembers who are coping with post-deployment intrusive thoughts.

Gender Differences

The Women's Health Sciences Division is continuing its research on the Iraq and Afghanistan Veteran cohort, focusing particularly on the experiences of women Veterans. A longitudinal study, supported through a public-private partnership between VA, DoD, academia and industry, was recently initiated to investigate the reintegration experiences and use of VA services by both male and female Veterans. A total of 9,600 Veterans have completed the first assessment, which was administered within three months of military separation. Additional assessments will be conducted at six-month intervals over the next three years. Work with this cohort also includes an examination of gender differences in the effects of deployment stressors and associated mental health conditions on occupational and family quality of life over time.

Investigators are conducting research on the associations between PTSD and suicidal behavior among VA health care users. One cohort study is looking at gender differences in predictors of suicide attempts VHA patients with and without

PTSD; the study is focusing on psychiatric comorbidities and gender differences as moderators of these relationships. Using a different large sample of Iraq and Afghanistan Veterans, investigators recently conducted a gender-stratified examination of risk models for suicidal thoughts, and found critical gender differences among this cohort.

Gender differences are being examined in both a community sample and a sample of law enforcement officers recently exposed to community violence. This prospective study seeks to examine gender differences in both positive and negative mental health outcomes, as well as a host of health-related behaviors. Such differences are being considered within the context of socioeconomic status, racial identity, and prior trauma history. Differences in barriers to seeking treatment across study groups are being investigated as part of this effort.

The Division is conducting research on the health of older women Veterans. A new study is investigating the impact on later life health of military and other early life stress exposures and resulting mental health issues, with a focus on PTSD; the study involves an epidemiologic cohort of Vietnam-era women Veterans.

An important project that is just getting underway is the Longitudinal Investigation of Gender, Health and Trauma (LIGHT) study. This is a large national survey of Veterans that will focus on the impact of trauma and community violence on mental, physical, and reproductive health. Planning for this survey took place in FY 2016, and the survey is expected to be launched in 2017.

Military Sexual Trauma and Intimate Partner Violence

Exposure to different forms of interpersonal violence is a key issue of study at the Division. Research related to MST includes a recent qualitative investigation aimed at identifying unique factors associated with sexual trauma that occurs within a military context. Another effort is a mixed-methods investigation of Veterans' experiences with and preferences for the VHA's universal MST screening program.

Intimate partner violence (IPV) among female Veterans is a strong focus area. Researchers are examining best practices for IPV identification, assessment, treatment, and the targeting of health services within the VHA context. A new study will refine and evaluate the effectiveness of a patient-centered brief counseling intervention for women who experience intimate partner violence. This study incorporates hybrid methodology that will help to facilitate expansion of the intervention in VA.