

APPENDIX B

RESEARCH NARRATIVES BY DIVISION

Behavioral Science Division

The Behavioral Science Division (BSD) in Boston, Massachusetts, conducts research on life adjustment after military deployment and other traumatic stressors, methods to assess trauma and posttraumatic stress disorder (PTSD), innovative approaches to clinical intervention and treatment delivery and the potential neurobiological and genomic basis of PTSD and its comorbidities.

BIOMARKERS

The Division has an active portfolio of genetic and neuroimaging studies involving collaborations with investigators in the [Translational Research Center for Traumatic Brain Injury and Stress Disorders \(TRACTS\)](#), the [Department of Veterans Affairs \(VA\) National PTSD Brain Bank](#), the Million Veteran Program, the Psychiatric Genomics Consortium (PGC), Brigham and Women's Hospital and the PTSD Working Group of the ENIGMA (Enhancing Neuroimaging Genetics through Meta-Analysis) Consortium. During FY 2020, Division investigators have focused on the role of inflammation and oxidative stress in the biology of PTSD, and on the role of PTSD and other trauma-associated symptoms in accelerated aging. This has included publication of an epigenome wide association study (deoxyribonucleic acid (DNA) methylation) of PTSD across blood and brain tissue which yielded replicable findings with PGC collaborators.

Ongoing studies that examine PTSD and blast-related traumatic brain injury (TBI) in Veterans of Iraq and Afghanistan war zones aim to clarify the relative contribution of mild TBI (mTBI) and psychiatric conditions to deficits in current functioning and health outcomes. Investigators are now in the process of expanding this work to an older longitudinal cohort to study how psychiatric stress, genetic risk and peripheral biomarkers of inflammation, including as measured via small molecule array technology, are associated with subsequent health decline and neurodegeneration, including as evidenced in magnetic resonance spectroscopy.

The biomarkers examined by Division studies include brain features measured by neuroimaging, peripheral markers of inflammation and metabolic pathology, as well as specific genes, and polygenic risk scores. Also under investigation are genomic biomarkers drawn from both blood and post-mortem brain tissue, including epigenome wide-DNA methylation levels and transcriptome-wide messenger ribonucleic acid (mRNA; i.e., gene expression).

During FY 2020, Division researchers continued to use functional (resting state and task-based) and structural magnetic resonance imaging (MRI) to identify neural circuitry involved in PTSD. This includes work identifying neuroimaging and neurocognitive subtypes of PTSD and determining how these subtypes predict recovery from PTSD. Other neuroimaging work is examining how brain responses to reward and punishment can reveal circuits impacted by PTSD. They have also used magnetic resonance spectroscopy to examine neurodegeneration and neuroinflammation. Recent work also includes examining neuroimaging metrics to understand central markers of metabolic health such as cerebrovascular dysfunction in mTBI and PTSD as well as genetic and environmental moderators of these relationships. Investigators are also in the process of expanding longitudinal work to examine predictors of brain morphology and function.

TREATMENT EFFICIENCY, EFFECTIVENESS AND ENGAGEMENT

The Division's pioneering research on treatments for PTSD is focused on overcoming barriers to seeking care, reducing dropout and increasing the efficiency of care delivery. One example is the internet-based treatment [VetChange](#), which was originally designed for Iraq and Afghanistan combat Veterans who report both risky use of alcohol and PTSD-related distress. A [mobile app](#) that has key VetChange features was developed recently, in conjunction with the Dissemination and Training Division, and efforts are currently underway to integrate the mobile app and web versions to increase mobile access for real-time intervention support. In addition, a major extension of the VetChange web intervention allows for its seamless integration with in-person and virtual care with VA providers.

Other Division efforts include developing and testing efficient, therapist-delivered interventions or treatment extenders, with the goals

of finding approaches that require less professional staff time and that are easier for patients to complete. A prime example is Written Exposure Therapy (WET), a five-session exposure-based treatment for PTSD that has been shown to be highly effective with non-Veteran patients. One study comparing WET with Cognitive Processing Therapy (CPT) for PTSD among active duty Service members just finished and data analyses are in progress. Another ongoing VA-funded study is examining the efficacy of WET in comparison to Prolonged Exposure (PE) with Veterans. An implementation study is also being conducted in which VA mental health providers are being trained to deliver WET.

Research on factors that link PTSD with aggression toward intimate partners has led to the development and evaluation of an intervention, Strength at Home, that reduces or prevents aggression within at-risk military and Veteran families. Positive clinical trials have been published, and the intervention continues to be implemented across the VA health care system, with full implementation expected by summer 2021, as well as on several military installations. A randomized controlled trial of couples Strength at Home on a military installation is near completion, and a follow-up study to examine sexual aggression outcomes and suicidality was recently funded. A recent pilot study in an underserved urban civilian setting also demonstrated promising results in reducing not only intimate partner violence, but also PTSD and alcohol use problems. Another pilot study of the program for civilians is now in progress.

Division investigators have recently completed a small randomized controlled trial examining the impact of a two-session family intervention to complement the delivery of CPT or PE. The goals of the intervention are to increase family members' support for and understanding of trauma-focused treatment and to reduce levels of family accommodation around PTSD symptoms. Initial results from this small trial indicated a positive impact of the family intervention on Veterans' treatment retention, and the investigators are currently pursuing funding for a larger study.

In the area of complementary interventions, a continuing five-year study examining the impact of two 12-week group treatments on chronic pain in Gulf War Illness has converted to remote delivery in response to coronavirus disease (COVID-19) restrictions. A one-year pilot study is examining the same interventions for older, sedentary, trauma-exposed Veterans, and is the process of converting to telehealth delivery. In both studies, Tai Chi, a mind-body exercise that has been associated with physical and mental health benefits, is compared with a wellness promotion intervention that is based on an existing VA model of care entitled Whole Health.

Division investigators are partnering with researchers in the Women's Health Sciences Division to examine the effects of trauma and other high-impact stressors on PTSD and related sequelae such as substance use disorders among lesbian, gay, bisexual and transgender (LGBT) Veterans. This research aims to develop and refine conceptual models of trauma, PTSD and related impairment to inform research, treatment development and treatment planning for LGBT Veterans.

CARE DELIVERY, MODELS OF CARE AND SYSTEM FACTORS

Division investigators are examining access to VA PTSD care. Initial results suggest that only 60% of Veterans initially screened for PTSD in primary care are referred to VA mental health care, with women and minorities being more likely to be initially referred to VA care than their White male counterparts. However, primary care clinics located in rural areas are significantly less likely to refer Veterans to VA follow-up care than urban clinics, across gender and race.

Division investigators (in partnership with the Women's Division) recently received pilot funding for a study examining barriers to and facilitators of family involvement in PTSD in VA. The researchers will conduct qualitative interviews with clinicians and administrators at 10 Veterans Health Administration (VHA) facilities, half of which are performing particularly well with regard to family-inclusive PTSD care and half of which are engaging in lower rates of involvement. Interviews will allow for the identification and understanding of key determinants of family involvement and the process of implementing family involvement. Interview data will be used to inform discussions with a Stakeholder Advisory Board regarding promising implementation strategies for future testing, and a list of recommendations for providers/facilities will be generated.

PTSD AND SUICIDE

Division researchers are actively contributing to knowledge about PTSD and suicide, particularly in the domain of identifying risk factors. One recently completed project examined patterns of change in suicidal ideation over time among active duty personnel following discharge from suicide risk-related psychiatric hospitalization. Results identified discrete groups that differed in patterns of change in suicidal ideation over time and risk for subsequent suicide attempts.

In another project, in collaboration with the South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (STRONG STAR) Consortium, Division investigators are continuing to test a modified version of WET for Suicide with a sample of Army soldiers and Veterans with PTSD symptoms who have been hospitalized for suicide risk. The study seeks to determine whether treating PTSD symptoms reduces the likelihood of future suicidal behavior.

OTHER IMPORTANT RESEARCH

The Division has a great deal of expertise in longitudinal, observational studies that inform the understanding of the course of PTSD and associated conditions over time. Division researchers are working on two large prospective cohort studies that collect information from strategically selected Veteran and Service member groups. The first, [Project VALOR](#) (Veterans After-Discharge Longitudinal Registry), has been working with a registry of 1,649 male and female combat Veterans who became users of VA services after 2002. The project collects data about health outcomes associated with PTSD, supplemented by clinical information from VA electronic medical records. The primary aim of Project VALOR was to examine the long-term course of PTSD symptoms. Recently published results revealed symptom course is most appropriately characterized by substantial heterogeneity. On average, Veterans experienced initial PTSD symptom severity above the diagnostic threshold following trauma exposure, which was initially stable over time and later began to gradually improve. Although results indicated symptoms eventually began to decline, this effect was gradual; most Veterans continued to meet or exceed the PTSD provisional diagnostic threshold long after trauma exposure. Predictors of symptom course included Hispanic ethnicity, postdeployment social support and cooccurring psychopathology. Findings highlight the heterogeneous nature of PTSD symptom course, the urgent need to ensure access to evidence-based care and to improve available treatments.

The second large investigation, the [Neurocognition Deployment Health Study \(NDHS\)](#), began data collection at the outset of the Iraq War in 2003. Military personnel were assessed before deployment and at several intervals afterward including a long-term follow-up, making this 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. Papers have described PTSD outcomes; longitudinal neuropsychological outcomes; and relationships among emotional distress, including PTSD, TBI and neuropsychological outcomes. A related study examining family mental health outcomes had documented poorer family relationships and partner distress as a function of Service member/Veteran mental health concerns. A manuscript describing child outcomes as a function of parental PTSD and depression is under review.

Division researchers recently launched the Boston Early Adversity and Mortality Study (BEAMS), which aims to advance research on how early life conditions affect later-life health outcomes, including Alzheimer's disease and related dementias, cardiometabolic disease and mortality risk. The BEAMS team is conducting novel linkages to multiple large-scale administrative databases to gather prospective information on the early-life health, family and environmental hazards for participants and siblings from three longitudinal cohorts of men who have been followed since 1938 or 1961 to the present day. Inclusion of siblings allows the researchers to extend the cohorts to include women and allow within-family comparisons. Using the cradle-to-grave dataset created from this project, the BEAMS team will examine prospective associations linking early adversities in the psychosocial, socioeconomic and environmental domains to health outcomes in old age.

Division investigators have partnered with Boston VA Research Institute, IBM Watson, Boston University School of Public Health, Massachusetts Veterans Epidemiology Research and Information Center and the Center for Healthcare Organization and Implementation Research to conduct research on the impact of COVID-19 on opioid use disorder treatment. This research will examine rapidly evolving trends regarding treatment access and adverse outcomes among Veteran patients, and identify vulnerable subgroups, including patients with PTSD, using national medical record and administrative claims data. This work will inform policy and best-practice recommendations to improve care delivery in the COVID-19 and post-pandemic era.

Finally, one ongoing project is examining the feasibility of using automated facial affect coding software for PTSD diagnostic assessment. This study is gathering facial affect coding during a standardized trauma prompt and diagnostic assessment. Researchers will examine dynamic changes in distinct affect domains in response to the trauma prompt to examine diagnostic utility.

Clinical Neurosciences Division

The Clinical Neurosciences Division (CND) in West Haven, Connecticut, focuses on research to establish novel treatments, uncover biomarkers of disease mechanisms related to traumatic stress and investigate paradigms of risk and resilience. By leveraging an interdisciplinary approach that includes genetics, neuroimaging, treatment interventions and epidemiological studies, the CND maximizes efforts to translate discoveries into therapeutic targets for PTSD and associated comorbid conditions.

BIOMARKERS

Neurogenomics and neuroimaging guide biomarker development, including molecular, biochemical, structural and functional approaches to investigate stress-related phenotypes and to better understand the sequence of pathological events associated

with posttraumatic stress. Integrating multiple markers into a comprehensive panel, combined with behavioral data, enables faster identification of putative biomarkers, biomarker validation, earlier detection of at-risk individuals and informed decisions regarding treatment planning.

Genome-wide association studies (GWAS) are used to screen for genetic variations across large numbers of research participants with goal of uncovering markers associated with complex disease. CND researchers conducted a GWAS analysis of 166,643 United States Veterans from the Million Veteran Program (MVP) to identify genetic risk factors relevant to intrusive reexperiencing of trauma, the most characteristic symptom cluster of PTSD. This work, published in *Nature Neuroscience*, identified eight distinct regions containing risk variants for intrusive reexperiencing symptoms. Three highly significant regions include: 1) CAMKV, a synaptic protein crucial for dendritic spine maintenance; 2) chromosome 17, a region closest to KANSL1 (a chromatin regulator influencing gene expression and deoxyribonucleic acid (DNA) packaging in chromosomes) but also within a region that includes CRHR1 (the gene encoding Corticotropin Releasing Hormone Receptor 1); and 3) TCF4, a gene associated with schizophrenia and other psychiatric traits. A larger study considering all three PTSD symptom clusters, reexperiencing, hyperarousal and avoidance, is underway.

The [VA National PTSD Brain Bank](#) studies postmortem brain tissue of PTSD and major depressive disorder (MDD) donors to characterize gene expression associated with stress and suicide. This year, researchers completed work on the largest postmortem ribonucleic acid (RNA) transcriptomic study of PTSD to date. Results published in *Nature Neuroscience*, identified a highly connected set of interneuron transcripts within the most significant gene network associated with PTSD. Integration of this data with genotype data from the MVP project, identified the interneuron synaptic gene ELFN1 and a proinflammatory marker, UBA7, as conferring significant genetic liability for PTSD. DNA methylation profiles identified several other significant biomarkers for PTSD including HDAC4 and a transcriptomic sexual dimorphism, which could contribute to a higher incidence of PTSD in women. Significant divergence in molecular profiles of subjects with PTSD and MDD was observed despite high comorbidity of these disorders. These functional genomic studies link heritability for PTSD with disease state and are critical for identifying the neurobiological underpinnings of PTSD.

The CND uses multimodal neuroimaging, such as positron emission tomography (PET), magnetic resonance imaging (MRI) and spectroscopy, to investigate functional activation patterns, concentrations of neurotransmitters, the structure and shape of brain regions, brain network connections and energy demands throughout the brain. This work includes developing medically informed bioengineering approaches such as machine learning and artificial intelligence. This year, CND researchers addressed a major limitation in the field of network connectivity mapping by establishing a whole-brain connectivity atlas. This PTSD brain connectome hierarchically maps brain network architecture and enables novel machine learning and imaging methods related to behavioral outcomes, with the goal of discovering a PTSD-specific fingerprint.

CND researchers also established a robust and reproducible brain connectome fingerprint to predict treatment response of traditional and rapid acting antidepressants using longitudinal pharmaco-imaging challenges. Data suggested that both slow-acting and rapid-acting antidepressants, such as sertraline and ketamine, exert therapeutic effects by reducing internal connectivity within primary brain cortices and by increasing connectivity between executive networks and the rest of the brain.

CND researchers used spectroscopy to measure glutamate neurotransmitters and synaptic strength, as well as to determine cortical glial function. White matter microstructural alterations were uncovered in PTSD patients, including higher white-matter integrity in the inferior frontal-occipital fasciculus but lower integrity in the genu of corpus callosum. These findings are consistent with decreased association and cognition, impairments in emotion regulation and abnormal visual processing.

CND researchers previously demonstrated that Veterans have widespread reduction in cortical thickness corresponding to PTSD and severity of combat exposure. New findings revealed that antidepressant treatment increases cortical thickness, suggesting that successful treatment may reverse this abnormality.

PET researchers examined a putative marker of brain cortisol regulation with in vivo imaging of 11b-HSD1 (an enzyme that generates cortisol in the brain) and assessments of PTSD severity, threat and loss. 11b-HSD1 availability in a prefrontal-limbic circuit was significantly higher in the PTSD group compared to matched controls. However, lower prefrontal-limbic 11b-HSD1 availability was related to greater overall severity, and greater threat and loss symptoms, within the PTSD group. These findings may represent neuroadaptation of brain cortisol in individuals with chronic or more severe PTSD symptoms.

PET researchers are developing a novel ligand [¹¹C]MK-3168 to evaluate the endocannabinoid system in stress response. The endocannabinoid system is instrumental in extinction of aversive memories, providing a novel therapeutic target for PTSD. CND researchers are also evaluating the role of the endocannabinoid system in childhood trauma.

Investigators also use electroencephalogram (EEG) to evaluate changes in electrical activity in the brain pre/post pharmacotherapy treatment. Using genomic data and machine learning methods, CNS researchers are working to establish an analytic biomarker pipeline to predict ketamine treatment response via EEG patterns, with promising results from validation samples.

Studies using MRI and computational modeling to examine PTSD related brain dysfunction include: 1) a drug challenge to derive specific biomarkers of ketamine treatment via stimulation of the AMPAR neuroreceptor and to investigate how depression, PTSD and suicidality are related to these biomarkers and how they co-occur; 2) a computational model to understand how cumulative stressful experiences may contribute to PTSD and to identify patient sub-groups susceptible to PTSD; 3) a study using novel pupillary biosensors to examine stress arousal via neuron firing in the locus coeruleus (i.e. this brain region controls changes in the pupil of the eye). Data revealed that the pupillary biomarker conveys different information about brain state depending on stress level and that acetylcholine and norepinephrine interact to produce brain-wide dynamics.

PTSD AND SUICIDE

CNS researchers are investigating the use of pharmacological agents that have an acute antidepressant effect as a strategy to prevent suicide among individuals with PTSD. This work includes several projects that evaluate the anti-suicidal properties of ketamine in both treatment-resistant PTSD and depression and how neural alterations and changes in synaptic connectivity pre/post ketamine treatment, may underlie behavioral changes. Other work includes investigation of suicide risk factors among Veterans who undergo VA specialty care in PTSD clinical teams and PTSD residential treatment programs.

Data from the National Health and Resilience in Veterans Study ([NHRVS](#)), which surveyed a nationally representative sample of U.S. Veterans, demonstrated that only 36% of suicidal Veterans are currently engaged in mental health treatment. Younger age, female gender, current depression, lifetime suicide attempt history, number of traumas and medical problems were associated with increased mental health treatment. Mistrust of mental health professionals and fear that mental health treatment may harm one's reputation were associated with decreased treatment. These findings underscore the importance of multi-modal suicide prevention and engagement efforts that target need-based factors and perceptions of mental health stigma in suicidal Veterans.

NHRVS researchers also found that combat Veterans who experienced childhood sexual abuse were nearly three times more likely to contemplate suicide relative to those without such histories. Childhood sexual abuse also independently predicted lifetime suicide attempts. Further, combat Veterans who witnessed others be killed or wounded in combat had substantially increased risk for suicidal thinking and attempts, even after controlling for psychiatric histories. Collectively, these findings highlight the importance of detailed trauma history assessments in suicide prevention and treatment efforts.

NHRVS researchers employed a novel 'symptomics' approach to identify individual PTSD symptoms associated with suicidal ideation in Veterans. Trouble experiencing positive feelings; negative beliefs about oneself, others or the world; and irritability/aggression were most strongly associated with suicidal ideation. These findings underscore the importance of considering individual PTSD symptoms in assessment, monitoring and treatment approaches for PTSD.

TREATMENT EFFICIENCY, EFFECTIVENESS AND ENGAGEMENT

CNS researchers completed the largest known efficacy study of repeated doses of ketamine in Veterans and active duty Service members diagnosed with treatment resistant PTSD. Data analyses and results are anticipated by the end of 2020. Researchers also demonstrated a new approach to extend the therapeutic effects of ketamine by pretreatment with the immunosuppressant sirolimus, which may prolong the efficacy of a single dose of ketamine for at least 2 weeks.

CNS researchers are also conducting the following treatment based trials: 1) a 7-day trial of PE enhanced with a single infusion of ketamine; 2) a project examining Mindfulness Based Stress Reduction for anger and aggression in Veterans with PTSD; 3) a study examining non-suicidal self-harm in PTSD using ecological momentary assessment (EMA); 4) a trial of buprenorphine and CPT for patients diagnosed with PTSD and opiate use disorder; 5) a study that examines the effect of WET in Veterans diagnosed with PTSD and comorbid substance use disorder; 6) a study examining the potential polysomnographic signature of suicidality in PTSD; and 7) studies of the neural and anti-suicidal effects of serotonin-releasing agent 3,4-methylenedioxy-methamphetamine (MDMA) in individuals with PTSD and obsessive compulsive disorder.

CNS is also leading Cooperative Studies Program study #2016 conducted at 34 VA medical centers. This VA Cooperative Study compares three commonly prescribed pharmacotherapies for insomnia, trazodone, gabapentin and eszopiclone. Insomnia is among the most common (>80%) persisting symptom of PTSD among patients who are actively engaged in other behavioral and pharmacologic treatments. Currently, there are no medications approved for the treatment of the PTSD-related insomnia.

Dissemination and Training Division

The Dissemination and Training Division in Palo Alto, California, conducts research on patient needs and preferences, implementation science, novel and adapted treatments that attend to patient preferences and technology-based delivery of treatment.

TREATMENT EFFICIENCY, EFFECTIVENESS, AND ENGAGEMENT

A key focus of Division researchers is increasing patient engagement into care. An ongoing study is developing a brief measure of patient characteristics associated with effective engagement in care, which will guide identification of the type and amount of service resources needed to engage Veterans. A second study is focusing on racial and ethnic minority patients who have experienced disparities in trauma exposure and mental health care. The project will develop a screening tool that identifies patients at risk for subsequent mental health problems and identify resources tailored to particular patient problems and needs to increase engagement into care.

Several ongoing studies are assessing the ability of telehealth and web- and mobile-based technologies to increase Veteran access to mental health care and to improve outcomes. Telemental health services to the home are expected to increase patient engagement and access, and recently with the COVID-19 pandemic, this service has seen a dramatic increase in use. A study is underway that compares two treatments delivered to women Veterans in their homes via video teleconference: Skills Training in Affective and Interpersonal Regulation (STAIR) and Present-Centered Therapy. The goals of the study are to assess the relative effectiveness of these treatments and to identify barriers and facilitators for using video-to-home delivery of treatment.

Regarding web-based interventions, in collaboration with researchers from the Philadelphia and Minneapolis VAs, the Division has recently launched a study to test a web-based intervention developed by the National Center called Community Reinforcement and Family Training ([VA CRAFT](#)) for PTSD. This program is coupled with telephone coaching to help spouses and intimate partners of Veterans with untreated PTSD encourage their Veteran to seek mental health care. A web-based version of PE, called Web-PE, is being tested in reducing symptoms of PTSD in military personnel and Veterans. Web-PE is delivered with therapist assistance and could have significant potential to increase the reach of PE to those who cannot otherwise access traditional face-to-face care. Web-based interventions with support from VA peer support specialists are also being tested to see if such support increases adherence to online treatment. This includes a trial that is nearing completion that compares patient engagement and outcomes from using [Moving Forward](#), a VA online version of Problem Solving Therapy, with and without peer support. Finally, a noninferiority trial is evaluating the impact of WET when delivered online with peer coach support, comparing written with verbal imaginal exposure among Veterans.

Division investigators are also studying mobile mental health apps. This includes a two-site study testing the efficacy of [PTSD Coach](#) with clinician support compared with existing treatment for reducing PTSD symptoms in Veterans utilizing primary care services. It also includes a recently completed mobile cognitive control training program for the treatment of alcohol use disorder and PTSD to determine the efficacy of a novel neurocognitive intervention for improving recovery outcomes.

Several pilot studies of mobile apps have been launched or are wrapping up, including a study of [Insomnia Coach](#), an app intended for Veterans to self-manage insomnia symptoms; a study of [Couples Coach](#); two studies of [Mindfulness Coach](#) in Veterans with PTSD and as an adjunct for Veterans receiving other types of medical care, a study of a self-guided exposure therapy-based app for PTSD comparing the outcomes of those receiving versus not receiving support from a person providing reminders and reinforcement for use via the app. We are also launching two studies (one with Veteran mothers and one with VA healthcare providers) of [COVID Coach](#), a recently released app designed to help improve self-care and overall mental health during the pandemic.

In addition, to these research studies, investigators have launched a handful of evaluations of the Division's publicly available mobile apps to better understand their reach, reception, use and impact to inform their continued improvement. Finally, the Division is helping to advance the mobile and technology research of VA investigators around the nation through its Center for Mobile Applications Research Resources and Services (CMARRS).

CARE DELIVERY, MODELS OF CARE AND SYSTEM FACTORS

Division researchers rapidly produced a series of papers to inform adaptation of mental health care delivery during the COVID-19 pandemic. These different papers review the mental health effects of pandemics, detail lessons learned from VA's expansion of telemental health services in response to COVID-19, describe how a psychotherapy training program was modified during the pandemic, suggest approaches for treating pandemic-related moral distress and outline best practices for deciding when to use or not use trauma-focused psychotherapies for PTSD with people affected by the pandemic.

Efforts are continuing on improving patient access to care by using participatory systems dynamics modeling, a collaborative quality improvement approach in which stakeholders identify specific system problems, use computer modeling to compare the likely outcomes of different potential solutions and then select an optimal solution to implement. These models were recently updated to address factors related to COVID-19. Preliminary pilot data indicate this method substantially improved access to evidence-based psychotherapy at two facilities. Technical Assistance Specialists in the VA Office of Mental Health and Suicide Prevention (OMHSP) have been trained in this approach and are partnering with the National Center in two randomized controlled trials testing the effects of participatory systems dynamics modeling on increasing provision of evidence-based treatments.

IMPLEMENTATION

A study evaluating how to simplify assessment of the quality of delivery of cognitive-behavioral therapy (CBT) for PTSD, depression and anxiety disorders is underway. A second ongoing study is evaluating competing strategies intended to enhance and sustain the delivery of CPT; one strategy emphasizes fidelity to the protocol through expert consultation and online resources, and the other focuses on using continuous quality-improvement strategies to improve fit and to address barriers to treatment delivery.

Investigators involved in the evaluation of the national rollout for PE therapy for PTSD are studying the effectiveness of different virtual training models on therapist delivery of PE. Another study compares methods of assessing treatment quality and fidelity, two important implementation outcomes for CBTs, including CPT. National Center staff are also supporting VA's efforts to implement measurement-based care (MBC).

In collaboration with the Minneapolis VA, investigators at two National Center Divisions completed a study which found that external facilitation guided by an implementation toolkit has increased use of evidence-based psychotherapy (EBP) in two VA PTSD clinics relative to six control sites. A larger trial involving toolkit-guided facilitation is underway in clinics in eight military bases. The study will assess whether a tailored approach combining an implementation toolkit, a guide for matching solutions to local problems and support from an external facilitator increases the use of PE more than does standard provider training alone.

PTSD AND SUICIDE

Recent research has identified insomnia as a risk factor for suicide. Division investigators have developed innovative ways to accurately monitor sleep without requiring Veterans to come to a clinic-based sleep lab. A new study leverages this technology to conduct in-home sleep monitoring to detect suicide risk in Veterans who have other risk factors for suicide.

Division staff have developed participatory system dynamics modeling tools that clinic teams can use to optimize and allocate staff resources to different clinical activities. These tools have been expanded and employed to suicide management to help teams ensure effective management of Veteran patients at high risk for suicide, without compromising overall access to or quality of care.

Evaluation Division

The Evaluation Division in West Haven, Connecticut, supports the National Center's mission through a programmatic link with VA's [Northeast Program Evaluation Center \(NEPEC\)](#). NEPEC has broad responsibilities within the VA OMHSP to evaluate their treatment programs, including those for specialized treatment of PTSD. Although researchers are primarily engaged in evaluation research, they also work on independent research projects related to the treatment of PTSD.

TREATMENT EFFICIENCY, EFFECTIVENESS, AND ENGAGEMENT

NEPEC has continued to monitor and assess PTSD treatment at VA. The monitoring includes both residential and outpatient specialty treatment programs, as well as PTSD treatment by trained providers not working within one of the specialty programs. The Evaluation Division also monitors efforts to improve psychotropic medication prescribing practices at the VHA. Two of the measures in this initiative are the use of antipsychotics to treat PTSD and the use of benzodiazepines without an appropriate diagnosis or medical indication.

In FY 2020, the PTSD evaluation launched a transition from paper and pencil form collection to the utilization of new templates in the electronic medical records system. By the end of FY 2021, NEPEC expects to collect all the evaluation and monitoring data directly from the Corporate Data Warehouse (CDW). The new templates collect data from both the outpatient PTSD Clinical Teams (PCTs) and the PTSD Domiciliaries. This transition to collecting data via electronic and administrative means reduces burden on both Veterans and providers.

Additionally, the PTSD specialty programs (both outpatient and residential) participate in Measurement Based Care (MBC) and led the adoption of this new initiative. A significant number of programs are now utilizing the PTSD Checklist (PCL-5) to assess and track Veteran-level symptoms. This shared approach of consistent measure utilization across sites and programs enables enhanced evaluation; specifically, the PTSD Evaluation Team at NEPEC is in the process of creating a newly designed long-term evaluation of PTSD treatment and recovery that follows Veterans across multiple years.

The Clay Hunt Suicide Prevention Act of 2016 required that VA employ an outside independent evaluator to determine the effectiveness, cost effectiveness and satisfaction with VA mental health programs. Evaluation Division staff served as the primary liaison to the Clay Hunt team, providing data, methodological consultation and contextual interpretation for findings of the evaluation studies. The third annual report of these findings concluded that both outpatient specialized PTSD care and residential PTSD services are effective at reducing symptoms and improving functioning in the first 90 days of treatment, that they are cost effective and that Veterans are largely satisfied with services. The evaluation studies will continue annually, with a more in-depth look at the role of concurrent mental health treatment and comorbidity as a focus of evaluation in the coming year.

Several Division investigators are using administrative data to explore treatment patterns and outcomes of PTSD care. Studies of medication use for the treatment of PTSD, as well as on correlates of self-reported symptom severity scores over time, have been published. Research continues on PTSD health services, pain management and the role of pain in the treatment of PTSD, as well as on sex differences in the health of returning Veterans. In the upcoming year the Division will further examine the role of pain in specialized PTSD treatment and in the treatment of comorbid PTSD and pain, and will continue publishing results from the Survey of Returning Veterans (SERV) interviews.

During the past year, NEPEC staff, in collaboration with others, published a manuscript on courses of suicidal ideation among Veterans receiving PTSD residential treatment. This paper examined various courses of suicidal ideation (onset, remitted, chronic and none) including the prevalence and correlates of these courses. As reducing suicide among Veterans is a top priority in the VA, this paper sought to better understand suicidal ideation and find ways to mitigate risk. This paper found the PTSD symptom improvement and PTSD symptoms at baseline were the most consistent predictors of courses of suicidal ideation.

NEPEC staff, along with other collaborators, also published a paper looking at the role of military sexual trauma (MST) history on symptom outcomes for Veterans receiving residential PTSD treatment. This investigation found that MST survivors exhibited greater treatment gains from admission to discharge, but also greater symptom exacerbation from discharge to follow-up. This indicates that considerations for MST survivors need to be made for relapse prevention and follow-up care.

Additionally during the past year, there has been quarterly publication of a new discharge report for the residential rehabilitation treatment programs (RRTPs), which enables a better understanding of the PTSD RRTP outcomes related to housing, employment, irregular discharges (e.g., rule violations, against medical advice, etc.) and program completion. This information is now collected across all RRTPs through the discharge template. The discharge template is currently undergoing a complete overhaul during which we will begin collecting information on whether Veterans received treatment for PTSD and details about this treatment. These templates will replace the scorecard that is now completed with pen and paper and will be collected for all RRTPs, not just PTSD specific bed sections.

CARE DELIVERY, MODELS OF CARE AND SYSTEM FACTORS.

The MBC in Mental Health Initiative, was formally launched by the OMHSP in June 2016. As part of Phase II of the initiative, every intensive substance abuse outpatient program and every residential treatment program was required to implement MBC. Two members of the Evaluation Division are supporting this initiative together with members of the Executive Division and the Dissemination and Training Division are involved in the senior leadership of the initiative. Additional investigators from within the National Center are closely involved in the evaluation study itself, as well as in the Communications, Education and Training and Coaching work groups.

The national Psychotropic Drug Safety Initiative continues to play a major role in the monitoring of PTSD pharmacotherapy. This study has been tracking data on changes in practice in prescribing for PTSD and has noted a continuing drop in the use of benzodiazepines among Veterans with PTSD. The Division continues its work with technical advisors at the PTSD Mentoring Program and at the OMHSP to provide technical assistance to this initiative. The Division also continues to respond to requests from specialized programs and staff in the field on policy, operations, handbook implementation and the provision of evidence-based practices.

PTSD AND SUICIDE

Suicide prevention has been a focus of the VA, with a particular emphasis on Veterans with elevated risk, such as those with PTSD. Members of the NEPEC team have published papers examining stigma as a barrier to community-based suicide prevention programs

for rural Veterans. As mentioned in the section on treatment efficacy, evaluation data has also been used to examine suicide-related outcomes among Veterans in PTSD residential programs.

The Division has enhanced its evaluation and program monitoring products to better illuminate suicide-related considerations. Working with the wait list of Veterans seeking to enter a RRTP, the system indicates if a Veteran currently has a high risk flag or has a lifetime REACH VET (Recovery Engagement and Coordination for Health—Veteran Enhanced Treatment) status, two pieces of information that are critical to determining priority admission status. The report also links directly to a dashboard that includes important information related to suicide prevention, such as recent safety plan, access to lethal means and other factors.

The RRTP workload report now also includes the prevalence of high risk flags in the six months preceding admission and the six months following discharge. We are also working to secure data from the Suicide Behavior and Overdose Report template in order to better understand these items in the context of RRTP. We are also currently developing and testing revised Screening and Status update templates that will pull in risk information so that clinicians can easily view different aspects of risk, such as recent suicide attempt, current inpatient hospitalization, overdoses, etc. In the PTSD outpatient treatment, a new dashboard to track all admissions to the PTSD clinical team was developed, and it was linked to the MBC patient health questionnaire (PHQ-9) measure to track any suicidal death or ideation in this population. Each PCT director who utilizes the PTSD Status Form template, which tracks MBC data at admission, has the capacity to pull its site data in real-time and define the observed period they are interested to best capture their site data. This dashboard allows for real time and customizable data reports.

OTHER IMPORTANT RESEARCH

Recruitment is complete for the SERV study, which is a repeated panel study of gender differences in psychiatric status and functioning among Veterans of Iraq and Afghanistan. The study recruited 850 participants, with women making up more than 40% of the sample. Participants were interviewed at three-month intervals for at least a year with follow-up rates of 80%-85%, and a sizeable subset continued interviewing for up to three years. Analyses in a number of areas have been undertaken, and 19 manuscripts have been published, are in press or are under review.

The Division is looking for investigators interested in analyzing the SERV data, or in leveraging the SERV sample in 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 endorsing sex addiction items. Other paper and presentation topics include insomnia and PTSD symptoms, suicidal ideation and behaviors and behavioral addictions. SERV data and an add-on study have been used to develop a pornography addiction scale that has been testing for psychometric properties.

VETERANS OUTCOME ASSESSMENT

The PTSD Evaluation is currently analyzing Veterans Outcome Assessment (VOA) data to best model Veterans' experience when receiving PTSD Specialty care. One aim of this project as it relates to PTSD is to determine which factors are associated with better long-term outcomes. Another aim is to identify those Veterans who do not get better during the course of treatment or who experience worsening of PTSD symptoms while undergoing care at the VA. Other projects are related to Veterans seeking residential treatment in the VA system. Current evaluation has been limited to evaluating the effectiveness of PTSD treatment within PTSD specific programs. However, many sites have different administrative bed sections and treat Veterans with PTSD. As such, this new project will better understand PTSD-related outcomes across the RRTP continuum and will enable comparisons between different bed types.

Executive Division

The Executive Division in White River Junction, Vermont, provides leadership, directs program planning and promotes collaboration to facilitate optimal functioning of the other Divisions both individually and collectively. The Executive Division specializes in the development and evaluation of innovative and authoritative educational resources, in programs that disseminate and implement best management and clinical practices and in the use of technologies to reach a broad range of users. The Executive Division also oversees the administration of VA's National PTSD Brain Bank.

BIOMARKERS

Dr. Matthew Friedman, Senior Advisor to the National Center, continues to coordinate the operations of VA's first [National PTSD Brain Bank](#). The PTSD 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 advancing assessment and treatment techniques.

The PTSD Brain Bank has seven parts, with facilities at five VA medical centers (Durham, North Carolina; Boston, Massachusetts; Waco, Texas; West Haven, Connecticut; and White River Junction, Vermont), the University of Miami and the Uniformed Services University of the Health Sciences. The Clinical Neurosciences Division in West Haven is the primary data analysis site; ongoing research endeavors utilizing PTSD Brain Bank tissue are described in the Clinical Neurosciences Division narrative.

The VA National PTSD Brain Bank currently has 150 living donors and approximately 280 frozen hemispheres (roughly one-third each from donors with PTSD, donors with major depression and healthy controls). The PTSD Brain Bank is collaborating with PinkConcussions to encourage donations from women with traumatic brain injury; this collaboration began in 2018 and has yielded thirty living donors. The PTSD Brain Bank is also working with the Vietnam Era Twin Registry; 8 referrals have enrolled. Staff are currently forming a relationship with the Armed Forces Retirement Home to further increase enrollment.

In collaboration with the Lieber Institute for Brain Development, National Center for PTSD (NCPTSD) investigators are using Brain Bank tissue to conduct groundbreaking research into the genetic basis of PTSD. Furthermore, control tissue is being collected via an agreement with the National Disease Research Interchange. The Brain Bank's intramural research program has made significant progress, with a number of peer reviewed (published or in press) articles on transcriptomic, synaptic and neuroinflammatory alterations in key brain regions associated with PTSD.

The Biomarkers portfolio also includes examinations of biomarkers of treatment response and neuroimaging research. Transcranial magnetic stimulation (TMS) is a device-based, Food and Drug Administration-cleared intervention for depression that is being tested as a treatment for PTSD. Executive Division investigators are currently examining electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) biomarkers of response to TMS among Veterans with treatment-resistant depression.

Investigators are also evaluating the utility of other neuromodulatory therapies in pre-clinical models of PTSD and shockwave-induced traumatic brain injury. Vagus nerve stimulation (VNS) is an FDA-approved treatment for epilepsy, depression and migraine, with ongoing research for inflammatory conditions. Executive Division investigators are evaluating the utility of VNS for inflammatory-mediated neuropsychiatric consequences of PTSD and brain injury in rodent models, to inform future studies in Veterans.

TREATMENT EFFICIENCY, EFFECTIVENESS AND ENGAGEMENT

The Executive Division has a long history of participation in VA's Cooperative Studies Program (CSP). During FY 2019, CSP #591, a groundbreaking study comparing PE and CPT at 17 VA facilities across the country, was completed. The investigators enrolled 916 participants, more than the 900 that were anticipated. The primary results will be submitted for publication early in FY 2021, and many secondary manuscripts are in preparation. 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 National Center previously developed [AboutFace](#), a public awareness campaign to help Veterans recognize PTSD and motivate them to seek treatment. Recruitment for a project in which investigators are examining the impact of AboutFace on engagement in and completion of evidence-based treatment among Veterans with PTSD is ongoing. They will also examine the impact of AboutFace on stigma and attitudes toward mental health services.

Investigators continue to focus on treatments for conditions that frequently co-occur with PTSD and to examine novel treatments for PTSD. Multiple manuscripts focused on secondary outcomes from a trial comparing two psychotherapies for comorbid alcohol use disorder and PTSD (PE and Seeking Safety), such as trauma-related guilt and insomnia, were published in FY 2020. Recruitment continues for a trial that is evaluating the combination of topiramate and PE for co-occurring PTSD and alcohol use disorder. An ongoing study is testing Cognitive Behavioral Therapy (CBT) for Insomnia versus Sleep Hygiene integrated with PE as a strategy for improving sleep problems in PTSD. Investigators also completed a pilot study showing the feasibility of obstructive sleep apnea screening and treatment in a residential treatment program for Veterans with PTSD and substance use disorders.

With respect to novel treatments, the first study of cannabidiol-enhanced PE in Veterans launched in FY 2019, with the first participant enrolled in May 2019. A trial to evaluate a brief protocol to reduce guilt and shame related to a traumatic event among Veterans of Iraq and Afghanistan finished recruitment. This project was extended such that the intervention will be tested among OEF/OIF/OND Veterans who served in Iraq and Afghanistan with guilt related to the COVID-19 pandemic.

During FY 2019 the National Center partnered with the Agency for Healthcare Research and Quality to create the [PTSD Trials Standardized Database Repository \(PTSD-Repository\)](#), a large publicly available database of PTSD clinical trials. The data were abstracted from 318 published randomized controlled trials of PTSD interventions. Data are freely available to researchers, clinicians and other stakeholders. This online repository will inform future study design and conduct and will aid researchers and policymakers in identifying

important gaps in the research. In FY 2020, National Center staff created featured stories and visualizations that provide an overview of the studies included in the PTSD-Repository and information about how investigators can use the data for their own research. More detailed stories are in development. In addition, the developers published a manuscript in which they described how they created the PTSD-Repository and discuss how it can be used to advance research and education initiatives.

CARE DELIVERY, MODELS OF CARE AND SYSTEM FACTORS

The Executive Division is working on several initiatives aimed at assessing models of care and improving evidence-based practice. Investigators continue to analyze data from a national survey that assessed whether the format of the way treatment information is presented impacts individuals' treatment preferences. The acceptability of specific treatments improved in a side-by-side comparison chart as compared to sequential text. These findings, and previous findings from the same survey, informed the development of the [PTSD Treatment Decision Aid](#). This is the first publicly available online treatment decision aid for PTSD, and it has received more than 250,000 views since its release in 2017. Ongoing work using novel informatics and operational methods includes funded work to compare the effectiveness of evidence-based antidepressants, including fluoxetine, sertraline, paroxetine and venlafaxine, in routine practice.

Executive Division investigators continue to examine the impact of facilitation and academic detailing, in which a pharmacist and psychologist reach out directly to VA clinicians in rural clinics to improve PTSD treatment practices. An ongoing initiative is focused on sharing guideline-recommended practices for PTSD with rural facilities outside New England.

Work that aims to improve access to evidence-based treatments for Veterans with PTSD at rural facilities utilizing facilitation, academic detailing and collaboration with the National Center's Mentoring Program continues. Expansion of this project includes measuring the sustainability of the implementation work done in FY 2020 and development of a learning collaborative with the Mentoring Program that focuses on facilitation skills. A second initiative was delayed because of the COVID-19 pandemic, but hopes to build a collaboration with the team's local Office of Community Care to identify providers in the area who are planning to treat Veterans through the Maintaining Systems and Strengthening Integrated Outside Networks (MISSION) Act, which allows Veterans to access care in the community. The project will also create a streamlined network with local community providers to enhance their knowledge of the 2017 VA/DoD (Department of Defense) PTSD Clinical Practice Guideline (CPG) treatment recommendations and share current best practices regarding suicide risk assessment.

IMPLEMENTATION

The Executive Division continues to support quality improvement projects aimed at increasing access to effective treatments for PTSD within the VA. A recent series of quality improvement projects established thresholds for high and low evidence-based psychotherapy (EBP) reach (i.e., access to EBPs) and identified characteristics of PTSD Clinical Teams within VA contributing to higher reach. Investigators are currently beginning the second year of a five-year project to translate the findings of this series into practice through collaboration with the PTSD Mentoring Program. This program is sponsored by the Executive Division and serves as a dissemination network targeting best practices in the administration of PTSD Clinical Teams.

The staff within the Executive Division are also studying the implementation of intensive models of PTSD care (defined as PTSD EBP protocol sessions three to five times per week) following a successful pilot within one medical facility. The goal is to implement the model in three to four more sites to examine the feasibility and effectiveness in additional sites of care.

PTSD AND SUICIDE

Executive Division researchers continue to advance the priority area of PTSD and suicide through collaborations with the National Center for Patient Safety (NCPS), OMHSP and the Center of Excellence for Prevention of Suicide (CoE). A study using semantic analysis of clinical note text to evaluate ruptures in therapeutic alliance preceding death by suicide in a VA PTSD treatment was recently published and led to funding to expand this work in the overall VA user population. Work examining a 15-year national longitudinal cohort of VA users continues to answer important questions about compositional and contextual factors accounting for rural-urban differences in death by suicide. Finally, based on previous work showing elevated risk of suicide during high-risk care transitions, investigators are developing and implementing an effective suicide prevention intervention for rural VA facilities to decrease suicide risk in Veterans living in rural settings. A new project is aimed at further developing this intervention by adding mHealth features. Importantly the team has successfully transitioned to a virtual enrollment format during the COVID-19 pandemic.

Appendix B: Research Narratives By Division

Pacific Islands Division

The Pacific Islands Division in Honolulu, Hawaii, was created to advance PTSD work in the Pacific Rim; to focus on improving access to care by increasing understanding of cultural attitudes and the bases of racial and ethnic disparities in treatment; and to evaluate the use of advanced technology, such as telemedicine, to reach out to Veterans who are otherwise unable to access adequate care.

TREATMENT EFFICIENCY, EFFECTIVENESS AND ENGAGEMENT

Three major projects are aimed at evaluating different methods of delivering PTSD treatment. Investigators are in the final phase of a large trial that examines the clinical efficacy of brief Cognitive-Behavioral Conjoint Therapy and compares home-based care to traditional office-based care. An additional trial in collaboration with the Dissemination and Training Division is looking at home-based STAIR treatment for women Veterans who have experienced MST. A third study is also a collaboration, involving a multi-site trial comparing standard PE with PE incorporating a partner.

OTHER IMPORTANT RESEARCH

Several ongoing studies examine the prevalence of PTSD, response to treatment and presence of related mental health comorbidities in ethnic minority populations. These studies identify unique risk and resilience correlates of PTSD among ethnically and racially diverse Veterans, and the effects of those correlates on Veterans' response to evidence-based PTSD treatments.

Researchers are continuing a study initiated in FY 2017 that uses data from the Honolulu Asian-Aging project to look at the effects of military service combat exposure in particular on late-life dementia, as well as on marital and family structures, mental health and physical health among Japanese-American men.

An ongoing project conducted in conjunction with the Military Family Research Institute at Purdue University examines sociocultural and community influences on mental health decision-making among male and female African-American, Asian-American, Latino and non-Latino white Veterans who are starting PTSD care in a VA mental health clinic. This mixed-methods study uses qualitative phone interviews, follow-up surveys and census information. Initial analyses have examined privacy rules and boundary management among women Veterans. More recent analyses have characterized Veterans' mental health social support confidante network structure, quality and function.

The Division is also working on a national qualitative study examining dropout from evidence-based treatments, in collaboration with investigators from the Women's Health Sciences Division and Minneapolis Health Services Research & Development Center of Innovation. Finally, a statistical methodology project is underway to develop an estimation method to delineate individual factor contributions in observational studies, where models include functional data as either an outcome or as one of a large number of covariates.

Women's Health Sciences Division

The Women's Health Sciences Division in Boston, Massachusetts, specializes in the study of women Veterans and non-Veterans, with a particular focus on understanding sex and gender differences in trauma exposure and posttrauma psychopathology.

BIOMARKERS

Research on biomarkers includes studies aimed at explaining the basic biological processes underlying PTSD with particular relevance to women. One study is examining the role of neurobiological and psychosocial factors that affect negative pregnancy outcomes among women with PTSD. A second study, currently in the data analysis phase, examines sex hormones and derivatives associated with decreased retention of extinction learning across the menstrual cycle in women with PTSD. Recently published results reveal that allopregnanolone, an anxiolytic metabolite of progesterone, contributes to deficits in recall of extinction learning exhibited by women with PTSD. In an effort to improve the effectiveness of PTSD treatments, a new study is investigating the impact of intravenous allopregnanolone on extinction retention and fear memory reconsolidation.

Studies examining the role of biomarkers in intervention efforts also include a study investigating whether a specific electrophysiological response pattern to a series of loud tones is predictive of clinical responses to selective serotonin reuptake inhibitors (SSRIs). Investigators are also working on a series of studies looking into the role of progressive exercise training in reducing symptoms of comorbid chronic pain and PTSD, perhaps by improving participants' capacity to release pain- and stress-reducing neurohormones such as allopregnanolone and neuropeptide Y (NPY) through achieving exercise maintenance.

Division researchers have also recently concluded a pioneering study in the area of head injury in women suffering from PTSD secondary to intimate partner violence (IPV). The aim is to understand the interactive biological and psychological mechanisms that underlie comorbid PTSD and TBI. Investigators are analyzing data to identify sex differences across domains of measurement (psychiatric, psychosocial, neuropsychological, blood-based biomarkers and imaging) by comparing this sample with comparable male samples.

PTSD AND SUICIDE

Division investigators are examining associations between trauma history, PTSD and suicidal behavior among Veterans in a secondary analysis of data from The Veterans Metrics Initiative Study, a longitudinal study of recently separated male and female Veterans. The aims of this newly funded investigation include identifying factors in place at the time of military separation as well as post-separation life circumstances (e.g., health, vocation, finances and social relationships) as predictors of change in suicidal ideation during the first three years after leaving military service.

TREATMENT EFFICIENCY, EFFECTIVENESS AND ENGAGEMENT

With support from the [South Texas Research Organizational Network Guiding Studies on Trauma and Resilience \(STRONG STAR\)](#) Consortium, investigators are testing the efficacy of CPT delivered in an intensive outpatient format with active-duty Service members. Investigators recently completed a pilot study of this intensive outpatient format of CPT, delivered in one week, for female survivors of intimate partner violence with PTSD and traumatic brain injuries. Additional efforts to improve the effectiveness of CPT include a large-scale study designed to test the impact of a case-formulation enhanced version of CPT on treatment adherence, functioning and PTSD symptoms. Other intervention studies on traumatized populations include an open trial to test the effectiveness of a therapist-assisted self-management intervention intended to increase self-efficacy and facilitate greater community engagement following a successful course of PTSD treatment and a comparative effectiveness study of trauma-focused versus non-trauma-focused therapy for the treatment of Veterans with PTSD and substance use disorders.

The Division is also focused on intervention research among those who have not necessarily been diagnosed with PTSD. Researchers continue to test the effectiveness of a national network of peer-facilitated support groups for women Veterans, titled [WoVeN: The Women Veterans Network](#), which is intended to increase social connections and support and to improve well-being. Recent efforts have focused on a comparison of groups offered in person to groups offered via a videoconferencing platform, and the expansion of peer-support services to women transitioning out of active duty military service through the complementary [BRIDGES \(Building Re-Integration from Dreams and Goals to Execution and Success\)](#) program that is designed to partner women Veterans with women Service members during reintegration to civilian life.

CARE DELIVERY, MODELS OF CARE, AND SYSTEM FACTORS

Relevant research within the Women's Health Sciences Division has focused on understanding Veterans' experiences at the time they separate from service and their implications for Veterans' service use. The [Veterans Metric Initiative](#) Study is a large-scale investigation of newly separated Service members' reintegration experiences and use of transition programs, services and supports in the first three years after separation. Comparisons between female and male Veterans suggest that female Veterans experience unique areas of risk, including greater likelihood of experiencing depression and anxiety, and greater declines in well-being. Investigators also continue to analyze data from a study of the effects of deployment stressors and resulting mental health conditions on Veterans' quality of life and health care needs. Recent findings suggest that healthy work functioning in recently returned women Veterans may be important to prevent a cascade of negative effects on mental health as well as psychosocial functioning in other domains, highlighting the potential value in mental health treatment efforts that target resilience in the work setting.

The Division's focus on care delivery also emphasizes care for conditions with particular relevance to women Veterans. Two studies are investigating VHA health care use related to eating disorders, in a nationally representative sample of male and female Veterans and a large cohort of post-9/11 male and female Veterans. These investigations are also examining barriers to mental health care use, both in general and specifically related to eating disorders. A newly initiated follow-up study is focused on the impact of the COVID-19 pandemic on respondents' mental health symptoms with a specific focus on eating disorders.

Other key work has focused on research with important subpopulations within the Veteran community, including a focus on Veterans of color and sexual/gender minority Veterans. An ongoing longitudinal study (Longitudinal Investigation of Gender, Health and Trauma, or LIGHT) in which investigators over-sampled for women, individuals in high crime communities and racial and ethnic minority Veterans seeks to assess the impact of community and gun violence on trajectories of mental health and in health care utilization. This study includes a host of potential risk (including perceived discrimination and race-based stress) and resilience factors (e.g. social support) that may influence these associations. In terms of potential interventions to support Veterans of color, Division investigators

are evaluating the impact of a group intervention that aims to reduce the impact of race-based stressors on health through the provision of evidence-based content to enhance coping skills and social support. Division investigators also continued work refining a model focused on trauma recovery among sexual and gender minority people that considers their unique minority context and ongoing exposures. Ongoing work in this area is focused on conceptualizing the sequelae of discrimination, minority stress and microaggressions among transgender trauma survivors. The health of older women Veterans is another area of focus, including a study examining the impact of military and other lifetime stress exposures and mental health, with a focus on PTSD, later-life health and related quality of life in Vietnam-era women Veterans. Current analyses are focused on cardiovascular disease risk among this population.

IMPLEMENTATION

The Division is also focused on implementation efforts associated with IPV screening and intervention. For example, investigators are evaluating a national rollout of IPV screening programs within women's health primary care clinics to determine implementation outcomes and the clinical effectiveness of IPV screening programs. In the area of IPV interventions, researchers continued a multi-site effectiveness-implementation clinical trial of a brief counseling intervention, Recovering from IPV through Strength and Empowerment (RISE), for women who are experiencing violence in their intimate relationships. This study incorporates a hybrid methodology to inform both the effectiveness of the intervention and expansion of the intervention throughout VA. A complimentary pilot implementation feasibility project conducted with the national VHA IPV Assistance Program demonstrated the scalability of RISE in routine care and extended its use to male and non-binary Veterans.

Division investigators are conducting a range of implementation studies focusing on evidence-based practices for specific patient populations and settings, including an examination of Written Exposure Therapy, a brief PTSD treatment, for pregnant women with comorbid PTSD and substance use disorder who are engaged in prenatal care within a high-risk obstetrical and addiction recovery program; the project is using a hybrid effectiveness implementation design. Another effort involves a qualitative study investigating mental health clinicians' experiences with delivering VHA's evidence-based psychotherapies in metro and non-metro community-based outpatient clinics (CBOC). This investigation will inform the scale-out of evidence-based psychotherapies in these unique settings.