Precision Medicine for PTSD

The National Center for PTSD Fiscal Year 2022 Annual Report



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Acronyms Used in the Text

Abbreviation	Definition
BRIDGES	Building Re-Integration from Dreams and Goals to Execution and Success
CAPS-5	Clinician Administered PTSD Scale for DSM-5
СВТ	Cognitive Behavioral Therapy
CDC	Centers for Disease Control and Prevention
CHIIPS	Center for Harmonizing and Improving Interventions to Prevent Suicide
СРТ	Cognitive Processing Therapy
DNA	Deoxyribonucleic Acid
DoD	Department of Defense
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EEG	Electroencephalogram
EHR	Electronic Health Record
EMDR	Eye Movement Desensitization and Reprocessing
FY	Fiscal Year
IPV	Intimate Partner Violence
MD	Medical Doctor
MOUD	Medication for Opioid Use Disorder
MRI	Magnetic Resonance Imaging
MST	Military Sexual Trauma
MVP	Million Veteran Program
NHRVS	National Health and Resilience in Veterans Study
OUD	Opioid Use Disorder
PAI	Personalized Advantage Index
PE	Prolonged Exposure
PET	Positron Emission Tomography
TRACTS	Translational Research Center for Traumatic Brain Injury and Stress Disorders
PTSD-Repository	PTSD Trials Standardized Database
RISE	Recovering from IPV through Strength and Empowerment

Abbreviation	Definition
SP-CRC	Suicide Prevention Clinical Resource Center
STRONG STAR	South Texas Research Organizational Network Guiding Studies on Trauma and Resilience
TIC	Tech into Care
TMS	Transcranial Magnetic Stimulation
VA	Department of Veterans Affairs
VHA	Veterans Health Administration
VISN	Veterans Integrated Service Network
WET	Written Exposure Therapy

From the Executive Director

About 80% of Veterans make dramatic improvements with the treatments available today. But what if we could better that number? That is the goal of Precision Medicine for the treatment of PTSD—finding the right treatment for the right individual at the right time, to improve treatment outcomes for all patients.

While maintaining our work across operational priorities, from biomarkers to implementation, the NCPTSD elevated its interest in Precision Medicine for PTSD. Our current work establishes the building blocks of a research program to advance knowledge about a Precision Medicine framework for treating PTSD. The initiative is no doubt a challenging endeavor, but there is an immense opportunity to improve clinical outcomes for all patients. You can read more about our work on page 6.

In parallel, we continued our focus on equity and inclusivity in research, education, and work culture. We have created Spanish versions of web pages and podcasts, completed research exploring disparities and differences in VA mental health care, and have many other ongoing education, research, and work culture efforts to ensure that NCPTSD's work is equitable and inclusive. This work will surely continue into 2023 and beyond.

I'd also like to take this opportunity to formally thank Dr. Matthew Friedman, founding Executive Director of the National Center for PTSD, for his tireless and generous work. Recognized as a world leader in clinical research and treatment of



Paula P. Schnurr, PhD

PTSD, Matt originally retired from the NCPTSD in 2015, though he continued working with us part time until March of 2022. I can't imagine a National Center without Matt, but he taught us to persevere, and persevere we will. Thank you, Matt, for everything you've done over the years. Your legacy will continue, I'm sure.

In other news, I'm sad to report that we lost a dear member of the NCPTSD family, Dr. Steve Southwick, one of the world's leading experts on psychological traumatization and human resilience. A longtime senior investigator with NCPTSD, Steve passed away in April 2022. His humor, kindness, and selflessness will be greatly missed by all of us at NCPTSD.

As always, we've learned a lot this year. And we've taken that knowledge and put it to work successfully, treating the thousands of Veterans who count on us to provide them relief from the effects of PTSD.

Paula P. Schnurr, PhD Executive Director

Precision Medicine for PTSD: The Big Picture

Since its establishment in 1989, the National Center for PTSD has been at the forefront of research and education on PTSD treatment, and on underlying psychological and biological factors of PTSD. In just over three decades, effective treatments for PTSD have been developed and disseminated within and outside of VA. This progress is remarkable, but there is still room to improve PTSD treatment outcomes. In pursuit of this goal, the National Center is turning toward a new goal: Precision Medicine for PTSD.

John Krystal, MD, Director of NCPTSD's Clinical Neurosciences Division, explains Precision Medicine: "Precision Medicine involves the identification of predictive markers of any kind—molecular, brain imaging, biochemical, clinical, cognitive markers—that can inform the types of treatments that are likely to work most effectively for groups of patients." Simply stated, it's finding the right treatment for the right individual at the right time.

Top 3 Things to Know about Precision Medicine for PTSD

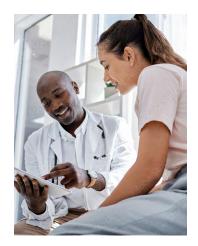
- 1. There are effective treatments for PTSD, but there is room for improvement.
- 2. The goal of Precision Medicine is to get the right treatment, to the right patient, at the right time.
- 3. Precision Medicine for PTSD will be a long-term endeavor, requiring many researchers from across the spectrum of research—from genetics to clinical research to digital specialists.

The National Center for PTSD is taking a particular interest in Precision Medicine for PTSD because some people aren't responding—or aren't responding enough—to available treatments, says Paula Schnurr, PhD, Executive Director of the National Center. "There's a need to improve treatment outcomes for PTSD. We need to make people better, and we need to make them well. Precision Medicine is a strategy that can help us do that." "We know a fair amount about predictors—how likely a patient is to respond to treatment, regardless of the treatment," Schnurr continues, "but we know close to nothing about what treatment is best for any given individual."

To illustrate, let's say a single mother with three children and two jobs gets assigned a PTSD treatment that involves daily homework. That treatment might not be effective for her, because doing homework takes time that the patient

doesn't have. After evaluating her social circumstances and preferences, we might suggest a treatment that does not require homework to be effective. This process is called shared decision making (see sidebar, page 7).

But, in the future, when we know more about how the effective treatments for PTSD



work, we might be able to test for certain physiologic or genetic markers, or understand that certain symptoms improve after specific treatments, or know that women do particularly well in a certain treatment. A clinician could then use this information to decide which PTSD treatment is right for an individual patient.

What Treatments Do We Have Now?

Individual, manualized trauma-focused psychotherapy is recommended as the first-line treatment for PTSD by the VA/DoD. Trauma-focused psychotherapy means that the details of the traumatic event are a focus of the therapy.

The most effective trauma-focused psychotherapies for PTSD include Prolonged Exposure (PE), Cognitive Processing Therapy (CPT), and Eye Movement Desensitization and Reprocessing (EMDR). There is also evidence to support the use of medications such as paroxetine, sertraline, and venlafaxine for PTSD, as well as select non-trauma-focused psychotherapy.

The way in which a patient is matched with a treatment varies. In some cases, it has to do with what is available—in other words, what treatments a provider or clinic offers. In other cases, the provider may offer the treatment that they think is best for the patient. In the ideal case, shared decision making occurs. Sonya Norman, PhD, Director of the PTSD Consultation Program, explains.

"We'll educate the patient about the different effective treatment options and have an informed discussion about what makes sense to them," she said.

That includes understanding the patient's values, preferences, and goals, as well as what works with the individual's schedule. Shared decision making helps the patient invest in their own



The <u>PTSD Decision Aid</u> is a tool that helps patients understand evidence-based PTSD treatments, and to work with their provider to choose the best option for them.

treatment. The PTSD Decision Aid, developed by the National Center for PTSD, is a tool to help patients understand evidence-based PTSD treatments, as well as their own priorities about treatment.

No matter how we get there, people being treated for PTSD deserve improved outcomes. With our current best treatments, more than half of people improve to the point where they are no longer diagnosed with PTSD, Norman says. "They feel better, their symptoms are less distressing to them, they're doing better in their job, and they're having healthy relationships. Treatment sets them on a path to a better quality of life."

Where We Are Now

To date, there have been many studies done that aim to understand what treatments work best for whom—but they're relatively small and not necessarily connected. But that's changing, thanks to the National Center and its diverse group of investigators.

Rather than create more and more interventions, the focus needs to be on how to improve upon and tailor what already exists to make those interventions more effective. Schnurr says the National Center's main research priority is to design trials aimed at assessing differential treatment response. Its secondary priority is to reanalyze existing data. "Creating a large dataset will allow more sophisticated analyses," she said. Right now, there isn't sufficient data to guide individualized treatment selection, which is one of the factors that makes Precision Medicine such an important topic in terms of PTSD.

Brian Marx, PhD, Deputy Director of the Behavioral Science Division, says the National Center is focused on exploring which studies have been done in Precision Medicine for PTSD specifically, then identifying gaps in the findings and a plan to address those gaps.

"We are actively figuring out what the agenda is, where we need to go from here, what studies need to be done, how we pool our resources, and how we create datasets that help us move the field forward in a revolutionary kind of way," he said.

Despite these promising building blocks, developing Precision Medicine for PTSD does come with challenges.

Precision Medicine Has Its Challenges

Precision Medicine for psychiatric care is still in its infancy

PTSD (and other mental health disorders) is not like cancer; there's no biopsy to confirm its presence. "A lot of these symptoms are variations of a normal response to experiences," said Paul Holtzheimer, MD, Deputy Director for Research. "It's normal to have certain biological and psychological reactions. It's normal to feel grief when somebody dies. What's abnormal is when it doesn't go away."

Going forward, an accurate assessment of PTSD will be key to understanding which treatments are effective for which patients. PTSD is currently best diagnosed through structured clinical interviews such as the <u>Clinician</u> <u>Administered PTSD Scale for DSM-5 (CAPS-5)</u>, which relies on clinician judgment. The CAPS-5 is an effective diagnostic tool, but the field is seeking out more biologic signatures of PTSD.



A training tool developed by NCPTSD uses a "virtual" patient to train clinicians and researchers to administer the CAPS-5.

"The assessment, and how we actually assay these various components, whether they're chemicals, brain waves, whatever, has to improve tremendously to get a more meaningful signal," leading to more accurate diagnosis, said Holtzheimer.

These challenges mean that Precision Medicine for PTSD is a complicated endeavor. However, the potential eventual gains are great. Having a better understanding of which

treatments are likely to work best for an individual patient means that more patients will receive effective PTSD treatment and relief from their symptoms.

The field of Precision Medicine and PTSD is so new that researchers would admit that they don't know a lot about it. But that's changing.

Big data

Precision Medicine almost necessarily depends on "big data"—having large datasets that allow investigators to understand and compare how differences in clinical, biological, and social characteristics are related to treatment. One area of focus is genetics. The National Center's Clinical Neurosciences Division has created a unique resource for the field of PTSD, where there is largescale gene discovery from genetics research. This research, led by Joel Gelernter, MD, involves geneticists based at the National Center and affiliated faculty within the Division.

"This gene identification process is really important, as there are genes related to the vulnerability for developing PTSD or related to symptom profiles once it develops," Krystal said. In fact, different kinds of genetic markers have emerged from this research.

NCPTSD investigators are involved with several largescale collaborations designed to understand the genetic markers of PTSD and other illnesses. The Million Veteran Program (MVP), a national research program to learn how genes, lifestyle, and military exposures affect health and illness, is expressly focused on Precision Medicine. The MVP aims to collect DNA samples from a million Veterans, and is banking those samples and combining them with data gathered from questionnaires and medical records of participants in the MVP with the hope that this data will lead to important discoveries, like how to best treat various kinds of cancer among Veterans. For example, not everyone with breast cancer requires the same treatment or level of treatment. The hope is that the collection of all these DNA samples will lead to discoveries that might lead to better medications and interventions. National Center investigators Gelernter, Robert Pietrzak, PhD, and Mark Logue, PhD, have all contributed to research helping to understand what genetic markers contribute to PTSD risk.

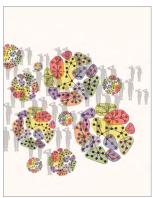
Genetics research is on the cutting edge of Precision Medicine for other disorders and is informing ongoing PTSD work at the Clinical Neurosciences Division.

"We'll take the genes we identify in the postmortem brain tissue of PTSD patients and from the genetics we identified into genetically engineered animals so we can try to understand how these gene changes affect brain circuit function and behavior," Krystal said. These research paradigms can then be used to test novel therapeutics in the animals and identify potential new treatments. "We can grow neurons derived from people with PTSD and grow these neurons from stem cells, which we can collect in the blood from people with PTSD," he said. This is just one of the dozens of studies that are currently taking place at the National Center.

Big data is not limited to genetic studies. Schnurr recently completed a study of over 900 Veterans with PTSD, with the goal of better understanding which individuals might be best served by <u>Cognitive Processing Therapy (CPT)</u> and which would be better served by <u>Prolonged Exposure</u>. (PE). Those analyses, which utilize a novel analytic technique called the Personalized Advantage Index (PAI), are underway. Built on prior work done by Schnurr and Shannon Wiltsey Stirman, PhD, the PAI is a prognostic index that can shed light on which patients are likely to do better in one treatment versus another.

Often, very large sample sizes are needed in order to have something significant to say. Even the largest psychotherapy trials to date (such as Schnurr's CPT vs. PE trial) are small, relative to what is needed to perform the kind of analyses needed for Precision Medicine.

Researchers believe big data will help them learn how to choose and tailor treatments for people with PTSD. "We know that people who are more symptomatic may



impact the outcome of treatment, but we don't know anything about how to match people to the various treatments that are available," Marx said.

National PTSD Brain Bank

The PTSD Brain Bank collects postmortem brain tissue from PTSD patients, and facilitates research that helps understand the genetic and molecular underpinnings of PTSD. One approach to understanding how treatments work for PTSD and finding new treatment targets involves understanding how genes (and the

proteins they code for) are different in people with PTSD. Under the leadership of Dr. Holtzheimer, the National Center collaborates with academic partners to operate the National PTSD Brain Bank, which is doing this type of research. Last year, the National Center published a groundbreaking transcriptomic analysis of PTSD (i.e., a study of which genes are expressed in people with PTSD), led by Matthew Girgenti, PhD. This analysis was extremely important in guiding work within the Center, as there were signs that the genes implicated in the risk for PTSD were playing out in changes in gene expression found in the postmortem brain tissue of people who had been diagnosed with PTSD. In addition, work by Girgenti's group showed differences in the genetics of men and women with PTSD and depression, providing a possible avenue for future Precision Medicine efforts.

The analysis also showed, says Krystal, that there's only limited overlap between the gene expression pattern in postmortem brain tissue of people with major depression and people with PTSD. There were distinct molecular changes in the brain associated with major depression and with PTSD, also with only limited overlap. So, although PTSD and depression commonly occur together and share many symptoms, they appear to be biologically distinct disorders.

The power of digital

Precision Medicine for PTSD isn't limited to largescale genetic studies like MVP or to psychotherapy trials. Thanks to more than a dozen mobile apps developed by the National <u>Center</u>, we have digital mental health interventions that can be responsive to where the patient is.

"Thanks to smartphones and wearables, as well as the internet, we could gather moment-tomoment data that can be used to discover patient characteristics," said Eric



PTSD Coach, and other mobile apps developed by NCPTSD, can be used to track symptoms and handle stress symptoms in the moment.

Kuhn, PhD, investigator at NCPTSD's Dissemination and Training Division. "We can develop dynamic, personalized interventions in the real world, where people are in need. We can actually be out there in the hands of our patients with powerful interventions that are truly personalized to what that person is experiencing in that moment and what they need." For example, the PTSD Coach app has tools for users to screen for PTSD symptoms, learn to handle stress symptoms in the moment, and connect them with more support as needed. These apps provide a low-resource way to provide care to patients who may benefit from a lighter touch. Digital mental health has the potential to vastly expand the potential reach of evidence-based care for PTSD.

"We do not have the resources to deal with everybody in the same way—nor should we," Marx said. "Some people need more assistance, more services, and more intensive care than others. It makes sense to get the services to the people that need those services—the care they need in order to address their specific concerns. It's what confronts mental health in general."

Looking to the Future

Precision Medicine clearly has a lot of promise, but the field of Precision Medicine for PTSD is still at an early stage. "A lot will be determined by what we learn in the present," Marx said. And while the National Center doesn't yet have the data itself, "we are doing a really good job in terms of figuring out how to pool datasets together, create a huge data repository, and produce a set of common data elements that all the investigators in the Center can use in order to provide the opportunity to collect the necessary data," he said.

Designing new studies

Investigators are working on new studies that help predict up front which patients can benefit from which

treatments. Dr. Holtzheimer, for instance, is currently working on two complementary studies that use imaging to try to identify brain activity patterns that predict who will respond to transcranial magnetic stimulation (TMS) for patients with depression, many of whom also have PTSD.

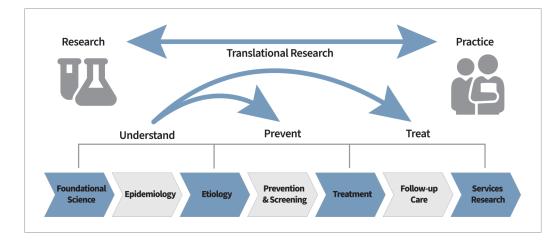
The National Center is leveraging a VA-wide program that helps set up TMS clinics that make it possible to collect multiple sessions of EEG and MRI, at baseline, then after several treatments, and at the end point. This allows investigators to look at early changes in brain activity that may predict eventual response.

"This is related to Precision Medicine because the goal is to identify actual biological predictors for who will respond to relatively novel, niche treatment that's different than medication and different than psychotherapy," Holtzheimer said.

Positioned for success

A focused mission, a multidisciplinary research program, organization around translation from science to clinical practice, strong partnerships within and beyond the VA, and unique resources including the National PTSD Brain Bank all uniquely position the National Center to contribute to the investigation of Precision Medicine approaches for the treatment of PTSD.

The National Center has investigators focused on treatment of PTSD as well as on the development of new or better treatments, whether they be biological, psychological, or other approaches. "We have an infrastructure in place that will let us look for potential markers—biological, clinical, and sociological," Holtzheimer said.



Research at NCPTSD spans from basic bench science to applied clinical and implementation science, and everything in between.



Effective PTSD treatment can look different for different patients at different times.

"We're the world leader in PTSD and the science of PTSD," Kuhn said. "We have an incredibly talented, world-class workforce, sustained resources, multidisciplinary research programs—all divisions are working on this. We're in the game of trying to translate science into practice. We have really strong academic partners. We're uniquely positioned to advance this field. I think we've demonstrated as a Center that we can rise to the challenges."

The National Center is committed to learning how to best use Precision Medicine for PTSD. "The desire to be able to predict up front who needs what, and which patient is more likely to benefit from a certain combination of individual treatments," said Holtzheimer, "that's our ultimate goal."

Getting help

If you are experiencing symptoms of PTSD, here is a list of resources that may be helpful:

https://www.ptsd.va.gov/

https://www.ptsd.va.gov/understand_tx/tx_basics.asp

https://www.veteranscrisisline.net/

Where to find us

Keep in touch with the National Center for PTSD on our <u>website</u> and social media:

https://twitter.com/VA_PTSD_Info

https://www.facebook.com/VAPTSD/

https://www.instagram.com/stepupforptsd/

Major Research Initiatives in 2022

National Center researchers work across the scientific spectrum, from examining the genetic and molecular underpinnings of PTSD to system-level implementation work. Fiscal year (FY) 2022 brought new advances across this spectrum and in each of NCPTSD's <u>operational priorities</u>. In addition, much of the work detailed below represents the base of the pyramid that will inform Precision Medicine for PTSD—understanding which treatments work best for which patients.

During FY 2022, researchers at the National Center led 158 funded studies, including research undertaken in collaboration with partner organizations in the government, academic institutions, and international agencies. Investigators published 590 peer-reviewed journal articles, book chapters, and books (see appendices C–G for a full list of grants, publications, and scientific presentations in FY 2022).

The National Center's research and educational activities are driven by five operational priorities: Biomarkers, Treatment, Care Delivery, Implementation, and PTSD and Suicide. The following narrative highlights some of the FY 2022 research initiatives undertaken to address these five operational priorities. (Appendix C contains a more comprehensive listing of research projects conducted by investigators at each of the National Center's six divisions.)

Biomarkers

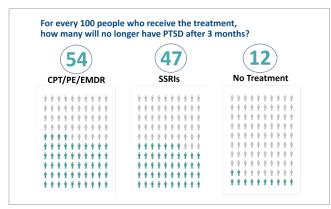
Work taking place under the Biomarkers Operational Priority aims to establish reliable and valid biomarkers to aid in predicting who develops PTSD, diagnosing PTSD, predicting treatment outcome, and measuring treatment response. Neurogenomics and neuroimaging guide biomarker development, including molecular, biochemical, structural, and functional approaches to better understand the sequence of pathological events associated with posttraumatic stress and PTSD treatment.

The <u>VA National PTSD Brain Bank</u> primarily studies gene expression in postmortem brain tissue of PTSD and major depressive disorder donors; this work aims to identify biomarkers and potential novel pharmacologic targets. This year, researchers evaluated the role of orexigenic neuropeptides in modulating negative affective states, specifically in the context of trauma exposure. One study employed a gene co-expression analysis strategy to uncover PTSD-specific networks containing appetitive neuropeptides. Three PTSD-associated modules containing appetitive peptides *NPY*, *GHRL*, and *NPY2R* were uncovered, and differences in biological sex and body mass index were discovered.



The VA PTSD Brain Bank facilitates research that helps understand how the brains of people with PTSD are different.

Neuroimaging is another pillar of NCPTSD's biomarkers work—using functional and structural magnetic resonance imaging, spectroscopy, and PET to understand the neural circuitry and activity involved in PTSD. In collaboration with the <u>Translational Research Center for Traumatic</u> <u>Brain Injury and Stress Disorders (TRACTS)</u>, ongoing studies suggest distinct biotypes of PTSD characterized by neurocognitive and network-based connectivity abnormalities, which may be associated with greater chronicity of PTSD. Center researchers have also used magnetic resonance spectroscopy to examine neurodegeneration and neuroinflammation. Novel work in an animal model of PTSD shows that the glutamatergic system (measured with PET technology) is altered as a function of stress—specifically, animals who developed PTSD symptoms showed changes in the glutamatergic system, whereas resilient animals did not, addressing a knowledge gap in the PTSD literature regarding whether observed brain alterations in patients are a consequence of or predisposition to the disorder.



In addition to research to understand treatment effectiveness, NCPTSD investigators also research how to communicate to patients and clinicians about effective research. Work published in 2022 explored how best to communicate the effectiveness of different PTSD treatments.

NCPTSD researchers also contribute to several largescale genomic research programs. Data from the <u>Million</u>. <u>Veteran Program (MVP)</u> have been paired with data from survey studies that provide longitudinal information to provide rich data on the biomarkers for PTSD. Using data from the <u>National Health and Resilience in Veterans Study</u> (<u>NHRVS</u>), which surveyed a nationally representative sample of 4,000 U.S. Veterans in the MVP, investigators found that polygenic risk scores for PTSD were associated with greater severity of PTSD symptoms. NHRVS data also showed that PTSD was linked to a two-fold greater likelihood of accelerated epigenetic aging.

Biomarkers can also be leveraged to better understand the mechanisms of effective PTSD treatments. A recently launched study is examining whether Prolonged Exposure (PE) is more efficacious during the morning hours when endogenous cortisol levels are at their highest, compared with later in the day when cortisol levels are relatively low. Another ongoing study uses electroencephalogram (EEG) markers to predict response to transcranial magnetic stimulation treatment in depression and PTSD. Also, researchers are using genomic data to establish an analytic biomarker pipeline to predict ketamine treatment response via EEG patterns.

Treatment Engagement, Efficiency, and Effectiveness

Several lines of work at the Center aim to increase the efficiency and effectiveness of existing PTSD treatments, and to develop strategies to enhance engagement in treatment. Several large-scale studies focus on the real-world effectiveness of PTSD treatments. CSP #591, conducted at 17 VA Medical Centers, published results showing that PE and Cognitive Processing Therapy (CPT) were both effective for PTSD in Veterans. Ongoing secondary analyses are examining which patients do best in PE and in CPT. CSP #2016 is being conducted at 34 VA Medical Centers and compares three commonly prescribed pharmacotherapies for insomnia: trazodone, gabapentin, and eszopiclone.

Other recently published work using large-scale medical record data, in conjunction with the Northeast Program Evaluation Center, has provided information about the relative effectiveness of PTSD treatments and treatment response patterns in VA PTSD specialty and residential care. This body of work supports existing evidence that first-line psychotherapies for PTSD are generally effective for Veterans, but also shows that Black Veterans have (on average) worse outcomes in VA specialty care than White Veterans.

Multiple lines of research examine ways to make effective treatment more efficient—e.g., delivered in fewer sessions or over less time. Written Exposure Therapy (WET), developed by NCPTSD investigators, is a five-session exposure-based treatment for PTSD that has been shown to be highly effective with non-Veteran patients. A recent DoD-funded study found that WET was non-inferior to CPT in the treatment of PTSD in service members. An ongoing VA-funded study is directly comparing the treatment efficacies of WET and PE among Veterans. Two recent studies examine the effectiveness of massed or intensive versions of PE and CPT. Additional efforts to improve the effectiveness of CPT include an ongoing, large-scale study designed to test the impact of a case formulation enhanced version of CPT on treatment adherence, functioning, and PTSD symptoms.

Digital technologies, including telehealth, mobile apps, text messaging, and websites, can increase the engagement of effective treatment and supportive care for PTSD and commonly comorbid conditions. One study will compare an asynchronous messaging-based version of CPT for PTSD to messaging-based therapy as usual. Center investigators are also involved in trials to understand the efficacy of mobile mental health apps. Also, a series of naturalistic studies are examining how users engage with some of our most widely used apps: <u>Mindfulness Coach</u>, <u>COVID Coach</u>, <u>PTSD Coach</u>, AIMS for Anger Management, and Beyond MST.

National Center research also targets the effectiveness of existing treatments by augmenting treatment with medication or psychotherapy. For example, studies are investigating ketamine plus PE, Cognitive Behavioral Therapy (CBT) for Insomnia, and CPT for Veterans with comorbid PTSD and insomnia, and buprenorphine plus CPT for patients diagnosed with PTSD and opiate use disorder.

Care Delivery, Models of Care, and System Factors

The Center continues to engage in research to ensure that Veterans with PTSD nationwide receive access to VA mental health care. An ongoing VA-funded study is using a mixed methods approach to understand which Veterans who screen positive for PTSD in VA primary care clinics do not access follow-up VA mental health care. Results of this project, which leverages the Veterans Health Administration (VHA) Electronic Health Record, can inform the development and implementation of targeted access interventions nationally.

Survey data indicate that Veterans with PTSD are interested in family involvement in their care, but investigators have found that the number of Veterans with PTSD who receive a family-inclusive visit during VA care is relatively small. Investigators recently published outcomes from a systems-focused project examining factors that contribute to or inhibit family-inclusive care. Many providers described incorporating families into Veterans' care to provide psychoeducation, enhance the Veteran's sense of social support and connection, and facilitate safety planning.

Additional activities include improving access to gold-standard medication for opioid use disorder (MOUD) and to counseling among VHA patients with opioid (OUD) and other co-occurring psychiatric disorders (e.g., PTSD). Ongoing analyses of VHA EHR and Commercial and Medicaid claims data highlight key gender and racial disparities



Apps like Beyond MST are being evaluated by NCPTSD researchers to understand how they are used, and how they can be effective for Veterans and others.

regarding treatment utilization and health outcomes (e.g., opioid overdose), but also positive effects of receiving MOUD via telehealth and expansion of MOUD coverage among some existing patients, and other successes following VHA's swift response during the COVID-19 pandemic.

One area of work that bridges systems of care and implementation science is Modeling to Learn. This initiative trains frontline staff in 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 potential solutions, and select an optimal solution to implement). The third major release, Modeling to Learn 3.0, was distributed nationally in 2022. Two randomized trials are underway, testing whether Modeling to Learn is superior to other quality improvement approaches in increasing the number of VA patients who receive evidence-based psychotherapy and pharmacotherapy for mental and addictive disorders.

Implementation

Facilitating implementation of best practices in PTSD care and studying barriers and facilitators of best practices is another Operational Priority. One study is underway evaluating how to simplify assessment of the quality of delivery of CBT for PTSD, depression, and anxiety disorders. A second study is comparing two different 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



The Modeling to Learn dashboard is a quality improvement approach that provides feedback to clinics on potential solutions to VA clinic system problems.

other uses continuous quality improvement strategies to improve fit and to address barriers to treatment delivery. Another trial on eight U.S. military bases tested whether a tailored approach that includes 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.

Following the WET treatment development efforts detailed above, an implementation study

is examining real world treatment outcomes among Veterans treated by VA mental health providers who are trained to deliver WET. Center investigators are also involved in studies comparing WET with medication and collaborative care to treat PTSD in both VA and non-VA primary care clinics, and are studying the effectiveness of different virtual training models and implementation support approaches for therapist delivery of treatment in WET and PE. Another study compares methods of assessing treatment quality and fidelity, two important implementation outcomes for CBTs, including CPT, and is finding that more scalable models of fidelity assessment have good agreement with the more labor-intensive observer method of assessing fidelity. The Center also facilitates implementation efforts associated with Intimate Partner Violence (IPV) screening and intervention. 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. Findings from this trial demonstrated that a blended implementation facilitation strategy (an operations-funded external facilitator working for six months with a facility-funded internal facilitator) nearly tripled the reach of IPV screening programs in primary care compared with implementation as usual in VA care, resulting in a two-fold increase in IPV detection rates among patients. Researchers also published findings from a randomized clinical trial demonstrating the effectiveness of a brief counseling intervention, Recovering from IPV through Strength and Empowerment (RISE), for women who are experiencing violence in their intimate relationships. A collaboration with the national VHA IPV Assistance Program resulted in a rollout of RISE with IPV Assistance Program Coordinators across the country for implementation among Veterans of all gender identities. Published findings from an initial program evaluation support the effectiveness of RISE in routine VA care.

PTSD and Suicide

Research under the PTSD and Suicide Operational Priority aims to investigate the relationship between PTSD and suicide and develop strategies to predict and prevent suicide among individuals with PTSD. To support our efforts, BSD investigators received funding for a new suicide prevention clinical resource center (SP-CRC). This SP-CRC will serve suicide prevention investigators by providing highly critical research resources to facilitate programmatic and scientific needs. The mission of the new SP-CRC, called the Center for Harmonizing and Improving Interventions to Prevent Suicide (CHIIPS), will be to advance a Precision Medicine approach to suicide prevention research.

Several lines of ongoing work examine risk factors for suicide. Center researchers have identified functional connectivity markers of suicide attempt history, compared categorical and dimensional approaches to understanding the association between PTSD and future suicide attempts, and identified distinct trajectories of suicidal ideation following psychiatric hospitalization discharge that were differentially related to future suicide attempts. Recent research has identified insomnia as a risk factor for suicide, using newly developed innovative methods to accurately monitor sleep without requiring Veterans to come to a clinic-based sleep lab. A secondary analysis of data from <u>The Veterans Metrics Initiative Study</u>, a longitudinal study of recently discharged male and female Veterans, identified post-separation life circumstances (e.g., vocation, finances, and social relationships) as predictors of change in suicidal ideation during the first three years after leaving military service.

Other research explores interventions to reduce the risk of suicide. In collaboration with the STRONG STAR Consortium, Center investigators have completed a study in which they tested a modified version of WET with a sample of Army soldiers and Veterans with PTSD symptoms who were hospitalized for suicide risk. A related study was recently funded to evaluate the efficacy of WET for Suicide Prevention (WET-SP) in reducing the incidence and severity of self-injurious thoughts and behaviors. Another project will be testing the feasibility and acceptability of Brief Cognitive Behavioral Therapy for suicide prevention in a sample of Veterans hospitalized for suicide risk. Center researchers are also investigating the use of medications 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.

Other research examines the prevalence of suicidal thoughts and behavior. Several studies using data from the 2019–2020 NHRVS wave examined suicidality and



National Center researchers work to understand how best to implement effective treatments into real work settings.

posttraumatic growth in Veterans. Investigators found that younger age, PTSD, depression, and adverse childhood experiences were the strongest correlates of suicidal thoughts and behaviors. NHRVS researchers also found that greater posttraumatic growth was associated with a 40% reduced likelihood of contemplating suicide, which suggests that interventions to help bolster posttraumatic growth may have utility in suicide prevention and treatment efforts.

Promoting PTSD Education: Training, Dissemination, and Communication

The National Center for PTSD's educational mission is to improve PTSD outcomes by developing and disseminating authoritative, culturally competent, equity-informed programs and information on PTSD and related conditions. Our stakeholders, including Veterans and other trauma survivors, the professionals who care for them, and the family and friends in their personal orbit, rely on NCPTSD to create products and programs that are rooted in science. From web-based resources to apps and training, our offerings innovate as they inform.

PTSD Awareness and Public Education

This year's PTSD Awareness Month campaign was our most ambitious effort yet. As in years past, we offered the public, providers, and medical centers an array of resources that could help them spread the word that PTSD treatment is available and that it works. This year, however, we also promoted June 27 as PTSD Screening Day. Thanks to an <u>interactive version of the Primary Care</u> PTSD Screen that we hosted on our website, Veterans and others who had experienced trauma could quickly learn whether symptoms that they have been experiencing following a trauma could be PTSD. Once they completed the screen, users received information about whether

their screen

was positive for

had a couple of

symptoms, and

next steps they

could take. There

30.000 visits to the

were more than

screening page

on the website,

PTSD or they just



PTSD Screening Day is part of June's PTSD Awareness Month.

and more than 380,000 people viewed PTSD Screening Day promotions from agencies and organizations that partnered with NCPTSD. Thousands more participated in our Step Up for PTSD Awareness Virtual Walk, signed a pledge to help raise PTSD awareness, or attended one of 20 PTSD Awareness Month presentations. In the month of June, 3.1 million people watched or listened to media interviews by National Center for PTSD experts that aired nationwide.

Another cornerstone of our awareness efforts is the <u>AboutFace website</u>. This video gallery features hundreds of interviews with Veterans, family members, and clinicians delivering the message that PTSD treatment

can turn lives around. This year we continued an extensive redesign of the site that will allow visitors to access the content through a guided experience. With the continued ability to explore videos with robust search and filtering functions, plus a new, clearer path through the site, visitors will have more options for learning about PTSD treatment and experiencing compelling stories. We also continued to expand our featured topic pages on the site, developing



New content on the AboutFace website highlights the connection between race and culture and PTSD.

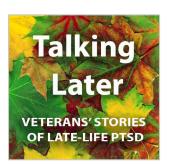
the page "Race, Culture, and PTSD," which focuses on how Veterans' experiences of identity, bias, and discrimination intersect with trauma and PTSD. The revised site launches in FY 2023.



The *PTSD Bytes* podcast features innovative ways that technology is being used to support people with PTSD.

For those who prefer their information on PTSD in bite-sized portions, the Dissemination and Training Division's Tech into Care initiative (see Support for Providers in the Field, below) has developed a podcast called <u>PTSD Bytes</u>. Clocking in at under 15 minutes, each episode of *PTSD Bytes* features

an expert or innovator discussing how technology can support people with PTSD or related mental health concerns. Topics have included PTSD and emotions, specific treatments, military sexual trauma (MST),



Hear about older Veterans' experiences with recovery, resilience, and PTSD in the *Talking Later* podcast.

and relationships. New episodes are released twice a month. Another podcast, *Talking Later: Veterans' Stories of Late-Life PTSD*, focuses on recovery, resilience, and meaning-making in older Veterans who are grappling with PTSD in late life. Each episode starts with a Veteran's life story, told in their own words, followed by discussion of what the

story can teach listeners about late-life PTSD and related experiences. This podcast was developed by researchers at the Behavioral Science Division and the New England Geriatric Research Education and Clinical Center.

The National Center for PTSD website continues to be perhaps our most important vehicle for information dissemination, with 6.5 million visits to the site in FY 2022. For the most part, new and extensively revised articles posted on the site for the public focused on evidencebased treatments—including an article on <u>recognizing</u>. <u>good PTSD care</u>—and helping family members whose loved ones need or are in PTSD treatment. We also created new articles on coping with current events, including the <u>war in Ukraine</u> and <u>school shootings</u>. Staff at the Executive Division began laying the groundwork for a revision of our popular resource, the PTSD Treatment Decision Aid. Originally created in 2015 and updated two years later to reflect the 2017 VA/DoD Clinical Practice Guideline (CPG), the <u>PTSD Treatment</u> <u>Decision Aid</u> is an online resource that educates users on their PTSD treatment options and guides them through the process of making informed PTSD treatment decisions. Both Veterans

and civilians can use the Decision Aid on their own, with loved ones, or with their providers as part of a shared decisionmaking process. The next revision of the website will be mobilefriendly and will incorporate new features that reflect



The PTSD Decision Aid, with new content scheduled for FY 2024, can help educate Veterans and civilians about their PTSD treatment options.

updated treatment recommendations based on the 2023 CPG and changes in online technology. Redesign work will begin in earnest at the tail end of FY 2023.

Support for Providers in the Field

For more than 10 years, the <u>PTSD Consultation Program</u>, a program of NCPTSD's Executive Division, has supported providers who treat Veterans with PTSD. Whether they



The PTSD Consultation Program provides expert consultation to any provider treating a Veteran with PTSD.

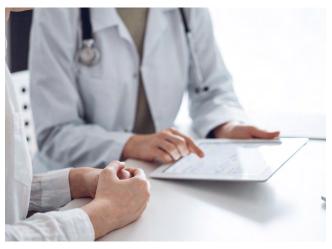
are experienced clinicians wellversed in evidencebased treatment, new providers who are just beginning to serve Veterans, or somewhere in between, any medical or mental

health professional can contact the PTSD Consultation Program for consultation on issues relating to care for Veterans with PTSD. This year, consultants responded to more than 2,100 requests on subjects as varied as disaster response, program development, diagnosis, and medication. In addition to the tailored consultation it provides on demand, the PTSD Consultation Program also distributes a <u>monthly newsletter</u> that features articles and links for providers. The program also continued its popular monthly lecture series. These online webinars attracted an average of more than 600 learners each month; the archived sessions continue to draw learners accessing the lectures on their own schedules.

In addition, the PTSD Consultation Program has continued its partnership with the <u>Center for Deployment Psychology</u> and <u>VA's Suicide Risk Management Consultation Program</u>, hosting trainings for rural community providers. This year, a total of 233 clinicians attended one of three live virtual sessions on military culture, suicide prevention, and PTSD assessment. The virtual format has allowed the trainings to reach more providers, drawing students from throughout the country who want to further their skills assessing and treating Veterans with PTSD.

With its focus on improving the reach of evidence-based PTSD treatment, supporting time-limited care, and making measurement-based care a standard practice throughout VA PTSD specialty care, the PTSD Mentoring Program had an active year. Staff worked closely with specialty care programs to identify areas of improvement and monitor progress on goals. In addition to providing standard levels of consultation ("Mentoring as Usual"), the program was able to offer more intensive levels of help across the nation. This included a continued effort to work with PTSD Clinical Teams (PCTs) to implement outpatient massed treatment programs. VISN mentors attended panels and flash talks that showcased PTSD Clinical Teams' implementation work and best practices for clinical care and program management.

The Tech into Care (TIC) initiative, which operates out of the Dissemination and Training Division, facilitates the implementation of technology into clinical care for PTSD and other mental health issues in VA and beyond. The initiative unites practitioners, administrators, and researchers to improve the uptake of innovative best practices and evidence-based interventions for Veterans. TIC has created tools including videos, handouts, and online courses in support of these efforts. To capitalize on interest in the project from new sites within VA, the team is piloting Tech into Care+ (TIC+), an online, self-guided



The Tech into Care program facilitates the implementation of technology into PTSD clinical care.

implementation tool to help VA health care systems integrate apps for PTSD and other mental health concerns into care with minimal support from implementation facilitators. There are now 54 mobile health champions at 31 VA sites across the United States, with more than 1,200 VA staff trained on using NCPTSD apps and other technology in their work with Veterans. TIC continues to offer an <u>online lecture series</u> that is open to anyone interested in the intersection of technology and mental health care. The series offers free continuing education credits to learners. TIC also holds a monthly community of practice call for VA staff, addressing opportunities and barriers in implementation of mobile health.

Every year, thousands of providers turn to the NCPTSD website for access to assessment instruments for PTSD, trauma exposure, and other mental health concerns. In order to better serve that audience, this year we completed a full overhaul of the assessment section of the site. As has always been the case, the focus is on providing key NCPTSD measures, including the gold standard Clinician-Administered PTSD Scale for DSM-5, but the site also guides users in how to obtain other traumaand PTSD-related instruments. The changes to the site, including the creation of a category that groups together measures that assess functioning and other outcomes, have streamlined the user experience.

Working Toward an Inclusive Website for All Groups

Since the inception of the NCPTSD website, staff have worked hard to make sure that articles are free of biased language. This year we have deepened that commitment by embarking on an effort to make sure our site is not only bias-free but also uses inclusive language. In practice, this means reviewing our content—starting with articles for the public—and revising it as necessary so that it adheres to <u>principles suggested by the Centers for</u>



Disease Control and Prevention (CDC) and other authorities. We want to ensure that our content uses preferred terms for population groups and communities; employs person-first language; avoids words with violent connotations, such as "tackle," "target," or "combat" when talking about people; and does not use language that dehumanizes or blames individuals and communities. We have also made a commitment to develop new content for and about people who are disproportionately affected by trauma, such as transgender individuals, or have been previously left out of our resources, such as disabled people. We envision that this valuable work will be a multiyear effort.

Self-Help and Treatment Companion Resources

Staff at the Behavioral Science Division are hard at work on their longstanding effort to have a providerfacilitated version of VetChange hosted on the VA network. VetChange is an intervention that addresses Veterans' problematic drinking through a mix of online modules and provider assistance. By transitioning VetChange to a VA server, providers will be better able to integrate the program into care for Veterans who want to cut down on their drinking or stop drinking altogether.

The National Center for PTSD released PTSD Coach—VA's first-ever app-in 2011. PTSD Coach made its debut in an era when owning a smartphone was hardly the norm. Fast-forward to today. NCPTSD continues to innovate, with the Dissemination and Training Division creating free, secure apps for an array of mental health and behavioral issues. Our current portfolio contains 16 apps that earn high user ratings in the app marketplaces and are featured in articles in the national press on a steady basis. Continuous improvement through ongoing user testing and programmatic enhancements keeps NCPTSD apps as cutting-edge today as the pioneering PTSD Coach was more than 10 years ago. Two completely new apps-Well Within (focused on women's mental health) and Safety Plan-were in development in FY 2022, even as updates to existing apps were ongoing.

The Women Veterans Network (WoVeN) is now active in more than 200 cities with upwards of 4,000 women Veterans enrolled in the program to date. Staff at the Women's Health Sciences Division established WoVeN to foster social support among women Veterans. Because of its peer-led structure, WoVeN thrives on the commitment of its members across the country. Members connect in person and online, creating a vibrant community for women Veterans of all eras and branches of service. An adaptation of WoVeN, called WoVeN in VA, is currently being piloted inside the VA health care system in collaboration with Women's Mental Health and Peer Support Services. In addition to the work with Veterans, in FY 2022 WoVeN successfully completed a pilot of BRIDGES (Building Re-Integration from Dreams and Goals to Execution and Success), which pairs women about to transition out of military service with Veteran peers called "Guides." These Guides provide ongoing support to women service members during the period of reintegration into civilian life.

Educational Resources for Professionals

This year saw the completion of the final course in the <u>Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)</u> <u>Training Curriculum</u>. Staff at the Executive Division and the Behavioral Science Division have been collaborating for four years, developing virtual patient courses that complement a traditional didactic course. In FY 2022, a third and final virtual patient made his debut. Robert Sheridan, like the prior virtual patients, Anthony Price and Kathy McKenna, is a Veteran who experienced trauma during military service. Working with Robert gives learners an immersive experience in administering and scoring the gold standard PTSD assessment measure. This year we also redesigned the evaluations that learners receive at the end of each virtual patient course and made some adjustments to the program interface. As with our other education courses, free continuing education credits are available to providers in VA and the community who complete each training.

Our ongoing commitment to providing continuing education opportunities on a variety of important topics related to PTSD treatment is evident in the addition of 12 new one-hour lectures to our website. Covering topics as disparate as PTSD and eating disorders, cultural considerations in the treatment and assessment of insomnia, and supported employment for Veterans with PTSD, these lectures were each originally presented in the Consultation Program Lecture Series. NCPTSD courses offer free continuing education credits for both the live and on-demand versions of lectures, which is not always the case when Veterans Health Administration (VHA) program offices make live lectures available as enduring content. We know from our contact with VA providers that having the ability to earn continuing education credits on their own schedules is an investment that is worth making.

PTSD-Repository

The National Center for PTSD continues to expand the PTSD Trials Standardized Database Repository (PTSD-Repository), a web-based platform that hosts data from 389 randomized controlled trials (RCTs) of PTSD treatment. In 2022, the site began including standardized effect sizes and added a data story on medications. Efforts are underway to refine the categorization of treatment types so that users can work with the data in a more precise manner. Publicly available and free to use, the PTSD-Repository helps researchers, clinicians, Veterans, and family members better understand the treatment literature. The PTSD-Repository is included in <u>VA's Open</u> <u>Data Portal</u>, which provides public access to VA data.

PTSDpubs

In FY 2022, the Resource Center staff continued to develop its new content management system and to expand its indexing thesaurus, which will be updated in PTSDpubs in the first quarter of FY 2023. PTSDpubs currently holds nearly 67,000 records and remains the largest database of PTSD and traumatic stress literature in the world. Staff educated new PTSDpubs users through a national online training offered by the VA Library Network and will continue to make presentations to internal customers. During FY 2023, staff will focus on an overhaul of records templates and the implementation of auto-indexing capabilities.

FY 2022 Communication Resources at a Glance

Website: 6,737,122 visits

Facebook: 162,536 followers and 184,582 likes

Twitter: 38,671 followers with 358,289 impressions

PTSD Research Quarterly: 68,571 subscribers

Clinician's Trauma Update Online: 58,844 subscribers

PTSD Monthly Update Newsletter: 460,015 subscribers Assessment Instruments: 693,739 assessments downloaded Mobile Apps: 16 mobile apps; downloaded 604,727 times in FY 2022.

<u>Professional Articles</u>: 508,006 unique views of professional articles on the NCPTSD website

<u>PTSDpubs articles</u>: 67,907 PTSD- and trauma-research articles available on PTSDpubs

Educational items distributed free of charge: 994,440 items printed

About the National Center for PTSD

History

The National Center for PTSD was created in 1989 within VA in response to a Congressional mandate (PL 98-528) to address the needs of Veterans and other trauma survivors with PTSD. The National Center was developed with the ultimate purpose of improving the well-being, status, and understanding of Veterans in American society.

The mandate called for a Center of Excellence (CoE) that would set the agenda for research and education on PTSD without direct responsibility for patient care. Convinced that no single VA site could adequately serve this unique mission, VA initially established the National Center as a consortium of five Divisions.

Organization

The National Center now consists of six VA academic CoEs across the United States, with headquarters in White River Junction, Vermont. Two Divisions are in Boston, Massachusetts; two in West Haven, Connecticut; and one in Palo Alto, California. Each contributes to the overall



NCPTSD mission through specific areas of focus. In fiscal year 2022, the National Center closed its Pacific Islands Division (PID) in Honolulu, HI, integrating PID's cross-cultural mission and focus on racial and ethnic disparities in PTSD care, telehealth and virtual care, and cultural factors in PTSD treatment, into each of the remaining six Divisions.

The National Center for PTSD is an integral and valued component of VA's OMHSP, which is part of VHA. OMHSP and NCPTSD receive budget support from VA, although NCPTSD also leverages this support through successful competition for extramural research funding.

Quick Facts



The National Center for PTSD was formed in 1989.



It has six Divisions across the United States, each with a distinct area of focus.



The National Center for PTSD manages the largest PTSD brain bank in the world.

Leadership in 2022



Paula P. Schnurr, PhD

Executive Director, <u>Executive</u> <u>Division</u>, White River Junction, VT Professor of Psychiatry, Geisel School of Medicine at Dartmouth



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Paul E. Holtzheimer, MD

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Terence M. Keane, PhD

Division Director, <u>Behavioral Science</u> <u>Division</u>, Boston, MA

Professor of Psychiatry and Assistant Dean for Research, Boston University School of Medicine



John H. Krystal, MD

Division Director, <u>Clinical Neurosciences</u> <u>Division</u>, West Haven, CT

Robert L. McNeil, Jr. Professor of Translational Research and Chairman of the Department of Psychiatry, Yale University School of Medicine



Craig S. Rosen, PhD

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Professor of Psychiatry and Behavioral Sciences, Stanford University School of Medicine



Rani A. Hoff, PhD, MPH Division Director, Evaluation Division,

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